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ABSTRACT SUPPLEMENT

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JAPAN COLLEGE OF RHEUMATOLOGY ABSTRACT SUPPLEMENT

CONTENTS

ABSTRACTS

Presidential Lecture

PL-1

Rheumatology: with sincerety, go above and beyond

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Conflict of interest: Yes

It is my great honor to be appointed as the President of the 67th Annual Scientific Meeting of the Japanese College of Rheumatology held in Fukuoka on April 24 to 26, 2023. The theme of the meeting is “With sincerity, go above and beyond” I hope that the meeting will serve as a starting point for challenging and proposing advanced treatment strategies. The number of venues has increased from previous years due to the submission of >1,500 abstracts from both domestic and overseas and such great supports are highly appreciated. The year 2023 is a milestone, as it has passed 20, 10 and 5 years since the first biologic for rheumatoid arthritis, the first JAK inhibitor and the first biologic for systemic lupus erythematosus were launched, respectively. Although a major revolution in the treatment of rheumatic diseases has been brought about, many unmet needs and challenges remain, including safety, economics, refractory diseases, organ damage, treatments under the Corona pandemic, precision medicine, etc. Many joint programs with the ACR, APLAR and EULAR are scheduled to approach to these issues. During the meeting, 24 symposium, 26 educational lectures, 39 international concurrent workshops, 29 Meet the Expert by all board members, 120 workshops and poster session for more than 1,500 abstracts and 60 by “future rheumatologist”, 3 late breaking sessions are scheduled. We appreciate supports beyond industry-academia collaboration in the invitation of overseas leaders and in the approximately 80 sponsored seminars We have received tremendous cooperation from many members of the Board of Directors, the Scientific Meetings Committee, the Informatics Committee, the International Committee and many. We would like to express our sincere gratitude. I hope that the Annual Scientific Meeting will serve as a new starting point for “going above and beyond” to the future. We look forward to your participation, continued support and cooperation.

Special Lecture

SL-1

Usefulness of Useless Knowledge

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Conflict of interest: None

While Japan experienced continuous economic growth after World War II, its GDP has not been growing in real terms over the past thirty years. As one result of the internet’s global popularization, which began in the 1990s, the focus of the economy is currently transitioning from manufacturing to digital technology. Japan is also lagging behind in the field of academics. Among factors that led to this decline, the low number of researchers and low investment in academic fields are often mentioned. However, looking at the number of researchers, despite the fact Germany has fewer researchers than Japan, Germany has only fallen one position to fourth place. This suggests a low number of researchers is an unlikely factor for decline. If we examine investments in academic fields, the amount invested per researcher in Japan is comparable to the amounts invested in countries like Germany and France. One factor behind might be that Japan’s vertically-structured society is reflected in the culture at domestic universities. Nurturing the seeds of new research in such a rigid environment is difficult. Japan lagging behind in the academic field is not a problem for the Government to address; rather, it is a problem for universities and research communities. Based on these perspectives, I would like more people to go abroad, especially young people. Gaining exposure to and interacting with different cultures helps you understand the strengths, weaknesses, and unique characteristics of both Japan and yourself. In particular, I want to communicate the “Usefulness of Useless Knowledge” to young researchers in Japan. What the researcher just wants to know, rather than whether that research will be useful or not. This is what is meant by the “Usefulness of Useless Knowledge”.

Symposium

S1-1

Molecular targeted therapies for rheumatoid arthritis

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Conflict of interest: None

Owing to molecular targeted therapy, therapeutic strategy for rheumatoid arthritis (RA) makes great progress. Anti-TNF-alpha, anti-IL-6, anti-T cell costimulatory molecules, and JAK inhibitors are currently available for RA therapy. The results of clinical trials revealed that almost similar efficacy is expected in these bDMARDs and tsDMARDs. On the other hand, approximately 20% of RA patients are still in a state of moderate-or-higher disease activity, and there are still many problems to be resolved in this field. The 2021 edition of the ACR guideline for the treatment of RA indicated future research issues. Especially, more evidences regarding the comparison of efficacy and safety among molecular-targeted therapies will be required for better clinical practice and personalized medicine. Genetic, immunophenotyping, and biomarker research have been conducted for this purpose, and recent advances of comprehensive transcriptome analysis promotes our understanding of RA pathogenesis. In particular, the R4RA study, which compared the efficacy of molecular-targeted therapies based on synovial biopsy, suggested the good evidence of the selection of molecular-targeted therapies according to the individual immunological pathogenesis. We can expect that the selection strategy of molecular targeted therapies based on understanding of the individual pathogenesis of RA patients will lead to better clinical outcomes. Nevertheless, some patients are refractory against several molecular-targeted therapies. Nobel therapeutic targets, such as synovial fibroblasts-related pathway, would be expected in future. In this lecture, I will outline the current understanding, and future prospects of molecular targeted therapy for RA.

S1-2

Newly developed molecular-targeted drugs for systemic lupus erythematosus

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease with varied clinical manifestations and a complex pathogenesis. Glucocorticoids (GC) has been the cornerstone in the treatment of SLE, irrespective of immunosuppressive agents. Nevertheless, prolonged use of GC may cause irreversible organ damage, leading to impaired quality of life and even increased mortality. To reduce systemic damage caused by GC use and disease activity, patients should be properly monitored, and therapy should be adjusted according to clinical status. Because prevention of damage accrual should be a major therapeutic goal in SLE, new therapeutic strategies without using GC or with using low dose of GC have been expected. New insights in the pathogenesis of SLE and advances in biotechnology provided new potential therapeutic targets. However, a number of clinical trials failed to show the efficacy in subjects of SLE because of its heterogenous pathology and lacking proper measurement for assessing disease activity. As newly developed biologic agents, belimumab and anifrolumab have been approved for SLE in Japan by using systemic lupus erythematosus responder index-4 (SRI-4) and British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA). These measurements are now internationally accepted, and many clinical trials have been under development. In this symposium, we are going to discuss the newly developed molecular-targeted drugs by classifying its mechanism, the cellular and the cytokines approaches. Furthermore, agents selectively inhibit intracellular biochemical pathways are also introduced.

S1-3

Polymyositis/Dermatomyositis

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Conflict of interest: Yes

Polymyositis/dermatomyositis (PM/DM) is one of the idiopathic inflammatory myopathies (IIMs), commonly involved in extramuscular manifestations such as interstitial lung disease (ILD). The measurement of myositis-specific autoantibodies (MSAs) is useful to predict clinical course, treatment response, and prognosis. The cornerstone of the treatment for PM/DM is corticosteroids. In addition, steroid-sparing agents such as methotrexate and azathioprine are administered simultaneously. Those standard medications have a multi-target mode of action on the immune system to ameliorate the disease activity of IIMs. On the other hand, molecular targeted therapies have been revolutionized in rheumatic diseases in the past two decades. Biologics can specifically inhibit cytokine signals such as TNF-α, IL-6, and IFN-α as well as acquired immune systems such as CD20 on B cells and CTLA4 on T cells. Thus, we can implement therapeutics based on the pathophysiology of individual autoimmune diseases. The subclassification of IIMs has encouraged us to consider the treatment applicable to each form of IIMs. A recent study has demonstrated that neonatal Fc receptor inhibitors ameliorate muscle inflammation in mice with anti-HMGCR-positive necrotizing myopathy. In addition, a clinical trial is conducted to investigate the efficacy of anti-monoclonal antibodies against IFN-β which is strongly involved in the pathophysiology of DM. A therapeutic algorithm for PM/DM-ILD has been provided by the Japanese Respiratory Society and Japan College of Rheumatology, leading physicians to conduct personalized medicine based on the result of MSA and other prognostic factors. The establishment of targeted therapeutic strategies for refractory rapid progressive ILD and chronic fibrosing ILD is currently demanded. In this session, we would like to introduce previous studies regarding molecular targeted therapy for PM/DM and share perspectives for ideal therapy based on the stratification by subforms of IIMs.

S1-4

Systemic sclerosis

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Conflict of interest: Yes

Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, immune dysregulation, and fibrosis. Interstitial lung disease (ILD), pulmonary arterial hypertension, and cardiomyopathy are currently major factors in determining the prognosis and outcome of SSc. Recently, a ray of light is glowing in the management of SSc, as it were “the long darkness”, with the tyrosine kinase inhibitor nintedanib licensed for SSc-ILD in 2019 and the anti-CD20 monoclonal antibody rituximab for SSc in 2021. Moreover, clinical studies have suggested the efficacy of the anti-IL17 receptor A monoclonal antibody brodalumab, that of the anti-IL-6 receptor monoclonal antibody tocilizumab, and that of the JAK inhibitor tofacitinib for skin sclerosis, ILD, and skin sclerosis of SSc, respectively. Lysophosphatidic acid receptor 1 and soluble guanylate cyclase are other potential therapeutic targets in SSc with clinical trials currently ongoing. In this symposium, we introduce novel treatment strategies in SSc and our recent work on the potential molecular target therapy for SSc-associated cardiomyopathy, one of the unmet medical needs in modern rheumatology (Kato M, et al. Rheumatology (Oxford). in press).

S1-5

The Role of Molecularly Targeted Therapies in the Treatment of Vasculitis: 2023 Update

Ryu Watanabe
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Conflict of interest: None

Vasculitis is classified into large-, medium-, and small-vessel vasculitis according to the size of the affected artery, and causes severe organ damage due to bleeding, infarction, arterial dissection, aneurysm forma-

tion, and others. In the past, the treatment relied on high-dose glucocorticoids and cyclophosphamide, and adverse events were almost inevitable. In recent years, however, various molecularly targeted therapeutic agents have appeared and made it possible to induce and maintain remission in most cases. In parallel, reducing the dose of glucocorticoids to minimize adverse events has become feasible therapeutic goal in the treatment of vasculitis. For instance, anti-IL-6 receptor antibody tocilizumab in giant cell arteritis and Takayasu arteritis (GiACTA and TAKT studies), anti-IL-5 antibody mepolizumab in eosinophilic granulomatosis with polyangiitis (MIRRA study), and anti-CD20 antibody rituximab (RAVE, RITUXVAS, MAINRITSAN, etc.), and complement C5a receptor antagonist avacopan (ADVOCATE study) in ANCA-associated vasculitis (microscopic polyangiitis and granulomatosis with polyangiitis) have been shown to induce remission, maintain remission, and reduce glucocorticoid dose. In addition, several attempts to treat vasculitis without high-dose glucocorticoids (LoVAS and PEXIVAS trials) have also been reported. However, there are still many cases in which remission cannot be achieved, multiple relapses occur, or glucocorticoids are difficult to reduce, indicative of clinical unmet needs in vasculitis. In this symposium, I would like to review the history of molecularly targeted therapies in vasculitides and reconfirm the evidence that has been accumulated to date. I will also summarize the unmet needs in current therapies and explore new therapeutic strategies. Through these processes, I would like to discuss with you the past, present, and future of molecularly targeted therapies in vasculitis.

S1-6

Precision medicine using molecular targeted therapy in spondylarthritis

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Conflict of interest: Yes

Recently, attempts have been made to establish precision medicine to improve patient outcomes in highly heterogeneous systemic autoimmune diseases. Patient stratification and selective use of molecular-targeted drugs are essential in establishing precision medicine. Spondyloarthritis (SpA) is a representative disease group with high heterogeneity, and it is assumed that not only clinical features but also immunological backgrounds differ among each disease included. We performed comprehensive peripheral blood immune phenotyping in 30 healthy controls, 33 psoriatic arthritis (PsA) cases, and 22 cases of pustulotic arthro-osteitis (PAO). Although an increase of activated Th17 cells was common in PsA and PAO, PAO was more dependent on activated Th17 cells. Even in the same disease group, the therapeutic target might be different, which may lead to a difference in the treatment response. In addition, PsA can be classified into four subgroups based on helper T cell phenotypes, and strategic treatment using molecular-targeted drugs based on these classifications has better disease control. Furthermore, by using serum IL-22 as a biomarker, it was possible to use TNF/IL-17 inhibitors selectively, and it was shown that the PsA patient could be stratified into TNF-dependent type and IL-17-dependent type. Patient stratification and selective use of molecular-targeted drugs not only bring about higher clinical efficacy but also accumulate novel knowledge for elucidating the pathogenesis of SpA.

S2-1

Overview of D2TRA

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Conflict of interest: Yes

The current treatment of rheumatoid arthritis (RA), using highly effective molecular targeted therapies such as biologics and JAK inhibitors, and guideline-oriented treatment strategies based on the T2T concept of targeted intensified therapy, has made it possible to control disease activity, prevent progression of joint destruction, and improve prognosis in the early stages of the disease. However, some patients with RA remain symptomatic, with low disease activity and no remission, even with use of several DMARDs. EULAR refers to these patients as difficult-to-treat RA (D2TRA) patients who are refractory to csDMARDs and have failed two or more b/tsDMARDs with different mode of action. It is also defined as the presence of one or more signs suggestive of active disease, the management of which is perceived as difficult by the rheumatologist and the patient. Beside a moderate or higher disease activity index, the definition also includes rapid progression of radiological joint destruction with a der Heijde-modified Sharp score of 5 points or more at 1 year, residual symptoms that reduce quality of life even when these indices are under control, or difficulty in reducing the dose of prednisolone to 7.5 mg/day or less. These D2TRA patients are reported to be present in about 10% of patients in Japan. The factors responsible for D2TRA include not only the biological aspects of the disease, but also psychological and socioeconomic aspects, in addition to fibromyalgia-like pain and comorbidities. The presence of comorbidities can influence treatment choices, drug adherence, and patient assessment of disease activity. The management of D2TRA requires not only pharmacotherapy, but also non-pharmacologic therapies such as surgical treatment, orthotics, rehabilitation, lifestyle guidance, and patient education, along with the care for complications. This lecture provides an overview of the D2TRA concept and its problems.

S2-2

Possible novel therapeutics against intractable RA by specifically targeting inflammatory 'bad' osteoclasts

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Conflict of interest: None

Intravital imaging of various live tissues and organs has launched a new trend in the field of biology. By using this advanced imaging technique, we first succeeded in visualizing the various dynamic phenomena within bones and joints, where various kinds of immune cells are produced and functioning although poorly analyzed by conventional methodology such as histological analyses with decalcified sections. We have so far identified the real modes of migration, differentiation and function of bone-destroying osteoclasts, special kind of macrophages responsible for bone and joint erosions. Moreover, based on the observation of pathological bone destruction, we could identify a novel subset of osteoclast specifically involved in inflammatory bone erosion. In this lecture I will show the recent updates in the field of basic rheumatology - which surely leads to development of new lines of therapeutics against rheumatic diseases and revolution of the future daily practice in clinic.

S2-3

Imaging defines D2TRA and Imaging prevents D2TRA

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Conflict of interest: Yes

Difficult-to-treat rheumatoid arthritis (D2TRA) was defined by EULAR to collectively represent RA patients who do not achieve good clinical outcomes for various reasons despite following the EULAR recommendations for the management of RA. Imaging is a part of the definition of D2TRA. In the definition, "2. Signs suggestive of active/progressive disease" includes "b. Signs (including acute phase reactants and imaging) and/or symptoms suggestive of active disease (joint related or other).", where imaging means ultrasound and MRI. Also included is "Rapid radiographic progression (with or without signs of active disease).", indicating that inflammation and bone/cartilage damage detected only by imaging can be considered as a type of D2TRA. In addition, in the EULAR points to consider for the management of D2TRA, one of the 2 overarching principles reads "The presence or absence of inflammation should be established to guide pharmacological and non-pharmacological interventions.". Furthermore, the use of ultrasound is recommended when there is doubt of the presence or absence. However, the most important thing in daily practice is to prevent D2TRA in the first place. This can be achieved by early diagnosis, early intervention, and tight control, and ultrasound and MRI can be a tool to support these strategies. In addition, ultrasound also supports less invasive biopsy of synovium in early cases, which has been stud-

ied in recent years for better disease classification and treatment optimization to avoid D2TRA.

S2-4

Surgical treatment for difficult-to-treat rheumatoid arthritis (D2T RA)

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Conflict of interest: Yes

Drug therapy for RA has advanced dramatically with the advent of methotrexate (MTX) and molecular targeted therapies. Along with advances in drug therapy, surgical treatment has changed. Synovectomy, once a routine procedure, has been drastically reduced as it has been replaced by drug therapy. Nowadays, synovectomy is performed only in a few joints with residual synovitis and when intra-articular steroid injections are ineffective under adequate medical treatment. When performing arthroplasty, I feel that bone quality has definitely improved compared to the past, and that the number of cases with synovial proliferation has decreased. Many cases are now indistinguishable from osteoarthritis of the knee at the time of surgery, including osteophyte formation, although they should have been RA in the beginning. Perhaps the most significant change has been in forefoot arthroplasty. The theory is that if there is no arthritis, it is reasonable to use a joint-sparing procedure rather than a metatarsal head resection, as was previously the case. Surgery for hand deformities is also increasingly indicated for cosmetic reasons. In recent years, the patient reported outcomes, or patient satisfaction, has been emphasized in addition to objective measures when discussing treatment outcome, and it has already been stated that the goal of treatment in treat to target RA is to maximize the patient's quality of life. The concept of D2T-RA has also emerged, and patients are considered to have D2T-RA if they continue to have RA symptoms that impair their quality of life despite adequate medical therapy, or if they are identified as having symptom management problems. This would include problems due to destroyed or deformed joints. The limitation of pharmacotherapy is its inability to approach the destroyed joints. In this lecture, we will consider the place of surgical therapy in the current treatment of RA.

S2-5

Treating D2TRA with molecular targeted therapy

Kunihiro Yamaoka
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Conflict of interest: Yes

The first essential condition to be met for Difficult to treat rheumatoid arthritis (D2TRA) is an inadequate response to at least two molecular targeted therapies with different mechanisms of action (biologic or Janus kinase (JAK) inhibitors) in patients refractory to synthetic anti-rheumatic drugs (csDMARDs) (unless contraindicated). Currently, molecular-targeted therapies for RA can be divided into TNF inhibitors, IL-6 inhibitors, T-cell selective co-stimulation modulators, and Janus kinase (JAK) inhibitors. Since at least two of these drugs with different mechanisms of action have failed to provide a satisfactory therapeutic response, according to the European College of Rheumatology RA Treatment Recommendation 2022, patients should be treated with the two remaining molecular-targeted therapy with different mechanisms of action or a second drug with the same mechanism of action as the preceding drug. The drug selection process is not uniform, as it depends on a variety of factors, including patient background, particularly disease activity, organ damage, and comorbidities. Several observational studies have identified the time from RA diagnosis to initiation of therapy, high disease activity, serologic positivity, and coexisting lung disease as key factors involved in the progression to D2TRA. In other words, it is important to review whether treat-to-target has been practiced and whether coexisting lung diseases have been taken into account. Before considering the selection of a new molecular-targeted therapy, it is important to start by reviewing whether or not the prior molecular-targeted therapy and concomitant csDMARDs have been administered in sufficient doses. If not, improvement of D2TRA may be challenging or become more complicated, with molecular-targeted therapy with the third mechanism of action. At present, there is no established therapeutic evidence for D2TRA, and observational studies are limited. In this talk, I will report on the current notion of molecular-targeted therapies for D2TRA and discuss how to respond to these therapies in real-world clinical practice.

S2-6

Medical care and economic issues of patients with difficult-to-treat rheumatoid arthritis from the IORRA cohort

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Conflict of interest: Yes

The sufficient use of methotrexate and the introduction of biological DMARDs (bDMARDs) and/or tsDMARDs (JAK inhibitors) have resulted in significant advances in treatment strategies for rheumatoid arthritis (RA). In the IORRA cohort, the proportion of the patients who achieved DAS28 remission increased from 8.4% in 2000 to 63.1% in 2021, and approximately 80% of the patients with RA were well-controlled. However, despite these advances in RA treatment, some patients still experience moderate or high disease activity. Therefore, appropriate treatment should be considered an unmet need of these patients. The EULAR definition of difficult-to-treat (D2T) RA was proposed in 2020. The IORRA study revealed that RA patients with persistent moderate to high disease activity were older, had longer disease duration, and had higher proportions of comorbidities and corticosteroid users. I would like to explain various issues that may contribute to D2T RA, including (1) treatment for RA when methotrexate cannot be prescribed, (2) treatment for multidrug-resistant RA, especially for inadequate response to bDMARDs, (3) treatment for RA with various types of complications, and (4) treatment for elderly patients with RA, using data from the IORRA cohort. In addition, rising RA care costs along with the progress of RA treatment have caused concern, placing a heavy burden on society as well as patients with RA. The IORRA study has shown that direct and indirect costs were associated with the progression of functional impairment or decline in quality of life (QOL). Therefore, RA care costs are also expected to be higher for D2T RA from a societal perspective. I also would like to explain D2T RA from a health economic perspective.

S3-1

Overview of management from childhood to AYA generation in pediatric rheumatology

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Conflict of interest: Yes

Pediatric rheumatic diseases are in the category of intractable diseases. Thanks to remarkable advances in inflammatory and rheumatologic studies, diagnostic techniques, therapeutic drugs, and methods of treatment have advanced remarkably, but the pathology has not yet been elucidated, and children with the disease continue to grow older. In general, as a transition management system, 1) basic stance of transition, 2) timing and program of transition, 3) importance of communication during the transition period, 4) transition support system, 5) transition support policy, 6) education of support staff, 7) socio-economic support, 8) access to information, and so on. Over a three-year period from 2017 to 2019, the Ministry of Health, Labor and Welfare Science Research about the transition of the pediatric rheumatology investigated was done. We conducted research with the aim of building a nationwide clinical network in which pediatric rheumatologists and adult rheumatologists cooperated by analyzing prognostic factors and examining the details of diagnosis and treatment actually performed in clinical settings. At the same time, various enlightening activities related to transitional care and transitional support by this society and Pediatric Rheumatology Association in Japan (PRAJ) have led to further progress in transitional care and support in the field of rheumatoid arthritis and connective tissue disease. However, in order to implement transitional support from childhood to the AYA generation, the pediatric side and the adult clinical departments must exchange opinions

and have a system in which each patient is examined seamlessly based on a common understanding. In order to come up with concrete measures for adult rheumatologists to be able to engage in the medical care of children and AYA patients without hesitation, it is necessary to solve various issues. In this symposium, I will overview management from childhood to the AYA generation.

S3-2

Epidemiology conduction of pediatric rheumatic diseases based on the registry database of the Pediatric Rheumatology Association of Japan (PRICUREv2)

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Conflict of interest: None

Pediatric rheumatic diseases are rare, and it is difficult to encounter many cases in a single institution. Although epidemiological surveys of Pediatric rheumatic diseases in Japan have been conducted they were single surveys with no continuity. Therefore, a nationwide case registration system was desired, based on the collection of basic information for more detailed investigations and updating of survey contents by conducting continuous, nationwide epidemiological surveys. Therefore, PRICURE (Pediatrics Rheumatology International Collaboration Unit Registry) was established by the former Disease Registry System Committee of the Japanese Society of Pediatric Rheumatology and started in April 2016 PRICURE was launched in April 2016. In March 2019, It has been updated to PRICUREv2 include measures for pediatric chronic diseases and designated intractable diseases. Initially, the number of participating facilities was small due to the barrier of individual ethical review by each participating facility, but gradually more facilities were added, and by March 2021, more than 400 cases had been accumulated at 29 facilities over a five-year period. The target disease groups included juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), juvenile dermatomyositis, Sjögren's syndrome, mixed connective tissue disease, scleroderma, Behcet's disease, vasculitis syndrome, and autoinflammatory syndrome. The present analysis included 402 cases of JIA (66.4%), SLE (10.0%), JDM (9.0%), SS (7.2%), MCTD (2.0%), SSc (1.5%), BD (1.7%) and VS. (2.2%). The JIA and JDM had significantly lower age of onset compared to SLE and SS. Furthermore, a comparison in JIA subgroups showed that systemic and oligoarticular JIA developed at a younger age than polyarticular JIA. Furthermore, the JIA and SLE required less time for diagnosis than other diseases. In this study, we analyze statistically sexual differences, age of onset, time required for diagnosis, and seasonality of each disease, and reported the results in Modern Rheumatology. At this symposium, we will present the results of the analysis, present some of the latest data, and outline the future prospects of the study.

S3-3

Guidance/guideline for juvenile idiopathic arthritis and Transition management

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Conflict of interest: None

Juvenile Idiopathic Arthritis (JIA) is defined as chronic arthritis of unknown origin that develops before the age of 16 and is also referred to patients older than the age of 16. A practice guide on JIA has been prepared by JCR ("JIA Primary Care Practice Guide 2015", "JIA Practice Handbook 2017", "JIA Guide to the Use of Biological Products 2020"). JIA-associated uveitis is also described in the 2020 edition of the Guide to Primary Care for Pediatric Noninfectious Uveitis. JIA is the most common pediatric rheumatic disease, with a prevalence of about 1 in 10,000 children. The 2-thirds of patients do not go into remission off-medication and reach adulthood. In the practice of adult JIA patients, it is important to understand that the pathophysiology is different and the indicators of disease activity and approved drugs are different from adult diseases. For transitional management of pediatric rheumatic diseases, the Guide for Adult Physicians has been published. The understanding and support of medical staff and guardians is essential for transitional care support. The Health-Welfare-Labor Research Group has developed a transitional support guide for medical staff including nurses, pharmacists, dietitians, and physical/occupational therapists involved in transitional care support (to be published in 2023). A Q & A series was also prepared as a support guide for patients and guardians. If the transition does not go smoothly, patients may be at increased risk of relapse or inappropriate drug use due to poor adherence and poor disease and health management. I will introduce the practice guides and support tools currently being developed, and hope that they will help to deepen the understanding of better transitional management.

S3-4

Childhood-onset systemic lupus erythematosus and transition of the adolescent patients

Masaki Shimizu
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Conflict of interest: Yes

About 15-20% of the patients with systemic lupus erythematosus (SLE) develop their disease in childhood. Childhood onset SLE is more severe compared to adult onset SLE. Furthermore, prevalence and severity of lupus nephritis is also higher in childhood onset SLE. Patients with childhood onset SLE need many supports not only for severe organ damage but also for phycological problems, growth and development, side effects of glucocorticoid including bone metabolism and cosmetic problems, pregnancy and delivery. In this presentation, I will overview clinical characteristics of childhood onset SLE and show important points to keep in mind for the transition of the adolescent patients with childhood onset SLE.

S3-5

Overview of the progress of the management of patients with rheumatic disease in reproductive age

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Conflict of interest: None

With recent advances in the treatment of rheumatic diseases, an increasing number of pediatric patients with rheumatic diseases are continuing treatment while pursuing higher education, finding employment, getting married, and having children. In addition, due to the recent increase in the age of first pregnancies in Japan, many women wish to become pregnant after suffering from rheumatic diseases. In response to this growing demand, research and clinical practice in this field are advancing daily. The development of the pregnancy guidelines published by ACR and EULAR based on evidence from cohort studies is one of the progress. As the identification of risk factors for pregnancy complications has progressed, it has been suggested that proper drug therapy during pregnancy may contribute not only to controlling maternal disease activity but also to improving pregnancy outcomes, and this has been reflected in the guidelines. In the respect to the safety of drug use during pregnancy and lactation, the experts have tried to meet the consensus using expert panels, as it is difficult to establish the evidence in this field. The transcriptome analysis of peripheral blood cells has also been conducted to clarify the molecular pathogenesis of the obstetric complication with SLE patients during pregnancy. Since 2018, the Japan College of Rheumatology has conducted a prospective cohort study (PLEASURE-J study) on the current status and long-term and short-term prognosis including pregnancy outcomes of young patients with SLE in Japan. We also try to elucidate the effects of SLE on pregnancy outcome and relapse during pregnancy and postpartum based on gene expression and immune cell changes in each case. In this symposium, we will review the recent trends in epidemiological and basic research on pregnancy with rheumatic diseases in Japan and abroad, and discuss the strategies that we should proceed with in the future.

S3-6

Pregnancy in rheumatoid arthritis and collagen disease from the standpoint of obstetrics and gynecology

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Conflict of interest: None

The number of births in Japan in 2022 will be 790,000, a decrease of about 20% during only seven years from 1 million in 2015. In addition, About 10% of couples are infertile, while 4-6% are loss of pregnancy, but the risk of infertility varies greatly with the age of the woman, especially from the late 30's. There is also concern that medical illnesses increase with age and that complicated pregnancies are on the rise. Pregnancy in rheumatoid arthritis (RA) is important to consider disease control and medications used prior to pregnancy. MTX use without being aware of the pregnancy nearly doubles the miscarriage rate and doubles the risk of fetal birth defects. Frequent use of NSAIDs and use of prednisolone 7.5 mg/day or higher has also been reported as a possible cause of implantation failure (infertility). In addition, Smeele et al. in 2021 reported that in the preconception care intervention group, the median DAS28CRP decreased to 2.5, and approximately 90% of recent RA complicated pregnancies are in remission or have low disease activity. It was reported that maintaining RA in remission or low disease activity before pregnancy maintains disease control throughout the pregnancy and postpartum period. On the other hand, Tsuda et al. reported in 2019 in Japan that the disease activity of RA before pregnancy was 84.6% for remission and 15.4% for active disease, which is not much different from the reports in Smeele et al. However, maternal and neonatal outcomes were substantially different, with 27.5% of pregnancies in RA resulting in preterm delivery (<37 weeks gestation) and 51.6% resulting in low birth weight (<2500 g). This symposium discusses life support for childbearing among women with rheumatoid arthritis in Japan. When considering life support for women throughout their lives and for their children to grow up without disabilities, physicians and obstetricians must learn from each other's specialties and cooperate with each other.

S3-7

The management of pregnant women with autoimmune disease

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Conflict of interest: None

Autoimmune diseases such as lupus are more prevalent in young women than older women. Women with autoimmune disease are at higher risk for maternal complications. Therefore, the treatment and care for pregnant women with autoimmune disease are important to achieve better outcome of child birth. The guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases was published by American college of Rheumatology in 2020. Japanese Society of Nephrology also published the guideline for management of pregnant women with renal diseases, in which lupus nephritis was listed. Although these guidelines give us the suggestion for management of pregnant women with autoimmune diseases, each patient shows different disease activity, medication etc. Therefore, the pregnant women with autoimmune diseases should be managed according to their background. I would like to discuss these points in this session.

S4-1

Recent understanding of Pre-RA and Early 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 full-blown persistent RA. Anti-citrullinated protein antibodies (ACPAs) in RA patients display a unique feature defined by the abundant presence of N-linked glycans within the variable domains domains (v-domains). These N-glycosylation sites are introduced by somatic hypermutation V-domain glycans are already present up to 15 years before disease onset in presymptomatic individuals and there abundance increased closely to symptom onset. HLA-SE alleles are associated with the presence of V-domain glycans on ACPA. Next we showed that the V-domain glycans affects autoantigen binding and act as a treshold for human autoreactive B-cells activation. Taking together both epidemiologic evidence and functional evidence is present that V-domain glycosylation of ACPA is an essential part in RA development.

S4-2

Safety profile of bDMARDs and tsDMARDs for inflammatory arthritis

Kevin Winthrop
Oregon Health & Science University, USA

S4-3

Management of psoriatic arthritis with pharmacological therapies

Daniel Aletaha
Medical University of Vienna, Austria

S4-4

Molecular understanding of phamacological treatment of osteoporosis

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Conflict of interest: Yes

Osteoporosis is a serious health concern in the global community. In aged societies such as Japan, an increasing number of people are suffering from osteoporosis and osteoporotic fractures such as vertebral fractures and hip fractures. Approximately 13 million osteoporosis patients are estimated to live in Japan, and the burden of osteoporosis with its associated morbidity and mortality issues due to fractures has become a critical socio-economic problem. Skeletal integrity is maintained through a balance of bone resorption and bone formation. The bone turnover process, called bone remodeling, continues throughout life. Bone remodeling is a sequential process and starts with the "activation" phase, defined as the conversion of bone surface from quiescence to active, which is followed by the differentiation of osteoclast precursors into mature osteoclasts in the "resorption" phase. In the "reversal" phase, osteoclasts complete the resorption process and produce signals that directly or indirectly initiate bone formation, and in the final "formation" phase, mesenchymal cells differentiate into functional osteoblasts to make the bone matrix. The length of the resorption phase is very short (2 - 4 weeks) compared with that of the formation phase (4 - 6 months), and the life span of osteoclasts is much shorter than that of osteoblasts. Therefore, increased bone remodeling necessarily leads to increased bone resorption and negative bone mass balance. Recently, many anti-osteoporosis drugs with excellent anti-fracture effects have been developed. They are mainly classified into two groups according to their effects on bone remodeling: anti-catabolic agents and anabolic agents. Anti-catabolic agents suppress bone resorption, and therefore reduce bone remodeling, while anabolic agents enhance bone remodeling by increasing bone formation more than bone resorption. In this talk, I would like to summarize the molecular mechanisms of action of anti-osteoporosis drugs.

S4-5

Real world evidence of locomotive syndrome and frailty: The ROAD study

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Conflict of interest: None

According to the recent National Livelihood Survey by the Ministry of Health, Labour, and Welfare, Japan, frailty is the third leading cause of disability requiring support or long-term care, followed by dementia and cardiovascular disease. Moreover, osteoporotic fractures and falls were ranked the fourth, while osteoarthritis was ranked the fifth cause of disability requiring support or long-term care. Musculoskeletal diseases including osteoporosis and osteoarthritis can affect mobile function, activities of daily living, and consequently, the quality of life. In this context, the Japanese Orthopaedic Association proposed the term 'locomotive syndrome' to designate a condition requiring nursing care or the risk of developing such a condition, following a decline in mobility resulting from one or more disorders of the locomotive organs, which include the bones, joints, muscles, and nerves. To prevent disability, it is important to examine epidemiological indices, however, little information is available regarding locomotive syndrome and frailty because only a few population-based studies have yet been conducted in this context. The Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study started in 2005-2007 and is a prospective cohort study that aims to elucidate the environmental and genetic background of musculoskeletal diseases. It was designed to examine the extent to which risk factors of these diseases are related to clinical features, laboratory and radiographic findings, bone mass and geometry, lifestyle, nutritional factors, anthropometric and neuromuscular measurements, as well as fall propensity. We will report in this symposium the epidemiology, co-existence, and prognosis of locomotive syndrome and frailty, based on the data of individuals in whom all measurements relevant to the diagnosis of such disorders were collected in the ROAD study.

S5-1

Antiphospholipid Syndrome: 40 Years of History and Our Contributions

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Conflict of interest: None

Listed below are some of our contributions to APS research over the past 40 years. 1) The corresponding antigen of the anticardiolipin antibody found in APS patients isβ2Glycoprotien I (β2GPI). 2) In 1998, the 8th International Symposium on Antiphospholipid Antibodies in Sapporo established classification criteria for APS (Sapporo Criteria). 3) Phosphatidylserine-dependent antiprothrombin antibodies are the primary antibodies of LA in APS patients. 4) Signaling pathway via p38 mitogen-activated protein kinase (MAPK) is involved in the induction of TF in APS patients. 5) We found that patients with APS have hypocomplementemia, that there is a strong correlation between low complement and antiphospholipid antibodies, especially LA, and that blood TNF levels are predominantly higher in the low complement group. The concept of APS is undergoing a major transformation from mere coagulopathy.

S5-2

The History of Rheumatoid Arthritis Treatment in Japan and Future Proposals

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Conflict of interest: None

There is no conflict of interest to be declared in this session. In this lecture, I will sequentially discuss present treatment of rheumatoid arthritis (RA) and future proposals in Japan. RA is a chronic inflammatory disease affecting joint synovium resulting in permanent joint destruction. The lungs and many vital organs are often involved in this disease. Disturbed quality of life (QOL) in RA patients is therefore frequently encountered in the disease. Elderly-onset RA increased in recent years are prone to joint destruction if not treated properly. As a result, life expectancy is approximately 10 years shorter when compared to normal individuals of the same age. However, with the advent of early diagnosis of the disease and development of efficacious treating drugs, this situation has no more expected in recent years. Reduction or cessation of drugs especially known as drug holidays may be possible in some cases. However, many rheumatic diseases need to be differentiated from RA, and correct diagnosis and proper interventions are essential to prevent joint destruction. Present goal of the disease is clinical remission of RA, and proper and early treatment makes possible for image remission and even functional remission. Drug holidays or reducing drugs are sometimes possible in some cases. Although the drug discovery took many years and was sometimes difficult, RA classification criteria was invented by both the American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR), applied to clinical science for early diagnosis. Furthermore, development of efficacious drugs of RA treatment have dramatically improved both joint and life prognosis. I will introduce RA clinical trials in Japan for methotrexate, leflunomide, tacrolimus, various biological agents and target-specific JAK inhibitors in this lecture. Moreover, future proposals will be delivered.

S5-3

Rheumatology Research: transforming environments and future directions

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Conflict of interest: None

The most important item in research activity has been suggested as research question. In clinical situation, the proper course of research is believed as the construction of a research question from clinical questions followed by the development of a hypothesis that can be tested and the consideration of ways to test the hypothesis. This is known as hypothesis-testing research. Our attitude and approach to research are in fact greatly influenced by the environment surrounding science and technology. Research queries themselves are often based on the research results of that era. There have been tremendous advances in science and technology surrounding rheumatology in recent decades. They are: monoclonal antibodies, cell sorters, gene transfer into cells, transgenic mice, knockout mice, PCR methods, deciphering the human genome, genome-wide association studies, next-generation sequencers, artificial intelligence, and others. It is possible that research has progressed along with these progresses. Recently the importance of hypothesis-generating research has been noticed as a new way of science. This is also called data science or data driven life science. It could be a science that leads to new discoveries by appropriately analyzing a large amount of data, such as multi-omics data. On the other hand, it appears to be hard wall for clinicians to participate in research activities in such areas. However, data science may track back to hospital medicine, which in the past blossomed in Leiden, Edinburgh, i.e., medical research to understand patients based on detailed descriptions of their clinical symptoms. Even today, one of the major problems in medical research is how to extract the appropriate patient information from electronic medical records. This is precisely where clinicians participate in. As long as there are intractable or incurable diseases, we should keep the mindset of research.

S6-1

Cellular metabolism in systemic lupus erythematosus

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is an autoimmune disease that involves the kidney, the central nervous system, and the skin. Since many patients with SLE are resistant or unresponsive to conventional therapy, new therapeutic drugs are desired. Many studies have revealed that T cell metabolism is central to proliferation, survival, differentiation, and function. As each T cell subset uses a preferred metabolic pathway, T cell metabolism is considered a therapeutic target. We previously showed that glutaminase 1 (Gls1), the first enzyme of the glutaminolysis, is increased in Th17 cells, and Gls1 inhibitors reduced Th17 cell differentiation and

disease activity of lupus-prone mice, MRL/*lpr* mice. Another group reported that 2-deoxy-d-glucose (glycolysis inhibitor) and metformin (mitochondrial electron transport chain complex I inhibitor) leads to the normalization of T cell metabolism and reversal of disease activity of lupus-prone mice. Moreover, we reported that an inhibitor of nuclear factor kappa B kinase subunit epsilon (IKBKE) is increased in microglia of MRL/*lpr*. IKBKE inhibition reduced glycolysis, which dampened microglial activation and phagocytosis, and ameliorated the cognitive function of MRL/*lpr*. In this symposium, I would like to review the role of cellular metabolism, especially lupus T cells.

S6-2

Pathogenesis and therapeutic strategy for Sjögren's syndrome from the point of view of dysregulated acquired immunity~Pathogenic roles and therapeutic potential of autoantibodies and autoantigens specific T cells~

Hiroto Tsuboi, Saori Abe, Hirofumi Toko, Fumika Honda, Ayako Kitada, Hiromitsu Asashima, Haruka Miki, Yuya Kondo, Isao Matsumoto
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Conflict of interest: Yes

Sjögren's syndrome (SS) is an autoimmune disease which affects salivary and lacrimal glands, accompanied with various autoantibodies and extra-glandular manifestations. In this symposium, we will discuss the pathogenic roles of 1) autoantibodies, and 2) autoantigens specific T cells, as well as 3) the development of novel therapeutic strategy targeted on the dysregulated acquired immunity in SS, including autoimmune response against M3 muscarinic acetylcholine receptor (M3R). 1) Anti-SS-A (Ro52/60) antibody (Ab) is adopted in diagnostic and classification criteria for SS, having diagnostic values and association with the pathogenesis and clinical features. We revealed that the effect of anti-M3R Abs on salivary secretion via M3R might be altered according to their epitopes in SS. 2) Salivary glands infiltrating T cells including Th1, Th2, Th17, and Tfh cells could induce activation and proliferation of B cells, and differentiation into plasmacytes, as well as contribute to apoptosis of glands cells via FasL and perforin. We recently revealed that peripheral Tfh cells were significantly increased, while $CD8^+$Treg cells were significantly decreased in SS patients compared with healthy controls. We also showed that M3R reactive Th1 and Th17 were detected in peripheral blood, and M3R reactive Th17 associated with disease activity and anti-M3R Abs in SS. Moreover, we confirmed that M3R reactive T cells could develop autoimmune sialadenitis in mice. 3) Many drugs targeted on acquired immunity including antigen presentation/co-stimulation (abatacept, prezalumab, iscalimab), B cell activation factors (rituximab, belimumab, ianalumab, lanraplenib, tirabrutinib), and germinal center formation (baminercept) have been examined for SS in RCTs. Among them, iscalimab (anti-CD40), ianalumab (anti-BAFF-R), and combination of rituximab and belimumab could improve ESSDAI compared with placebo. Moreover, nipocalimab (anti-FcRn) which inhibits recycling of IgG is now investigated in RCT.

S6-3

The role of B cells in Autoimmune Diseases and recent topics

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Conflict of interest: None

B cells play a central role in the pathogenesis of autoimmune diseases. Belimumab, an anti-BAFF antibody, was approved for patients with disease-active SLE in Japan in 2017, and has recently been widely used for lupus nephritis as remission induction therapy. Rituximab (RTX), an anti-CD20 antibody, is a major B-cell-targeted therapy, and was approved in 2013 for ANCA-associated vasculitis and in 2021 for systemic sclerosis in the field of rheumatic diseases. Obinutuzumab, a fully humanized anti-CD20 antibody, has shown efficacy for the patients with lupus nephritis in a phase II study and is currently on-going in a phase III trial. Recently, anti-CD19 CAR-T therapy has also been shown to be useful for SLE. However, the role of B cells in autoimmune diseases remains unclear. The most characteristic roles of B cells in RA are anti-CCP antibody (ACPA) and RF production. Recently, ACPA-producing B cells was characterized as proliferative memory B cells that express activation markers such as CD80/86. ACPA-producing B cells also have high cytokine production capacity, and produce amphiregulin (AREG). AREG promotes synovial fibroblast proliferation and osteoclast differentiation. We found that mTOR-phosphorylated CXCR3+ memory B cells are increased in RA patients and are involved in disease activity via IL-6 production and RANKL expression. Recently, it has been reported that CD11c+T-bet+ B cells are increased in SLE patients compared to healthy controls and are related to the pathogenesis, such as autoantibody production and lupus nephritis. Dysfunction of regulatory B cells have also been reported in SLE. We have shown that abnormalities of immunometabolism in B cells of SLE patients are related to disease activity and exacerbation of disease in SLE. In this session, we will discuss the role of B cells in autoimmune diseases, especially RA and SLE, novel therapeutic strategies, and future developments.

S6-4

Landscape of immunological responses to anti-rheumatic drugs in synovial fibroblasts

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Conflict of interest: Yes

In rheumatoid arthritis (RA) pathogenesis, synovial fibroblasts (SFs) are major local effectors in the destructive joint inflammation. Current treatment strategies that target cytokines (e.g., tumor necrosis factor [TNF]-α, IL-6), cell surface proteins (e.g., CD20, CD80/86) or signaling molecules (e.g., Janus kinase [JAK]) have brought a paradigm shift in RA treatment. Contrary to their potential clinical benefits, the immunological properties underlying these efficacies have largely remained elusive. Here, we featured immunological action of JAKis and a TNF-α inhibitor on activated SFs by integrative methods to analyze chromatin accessibility and genome-wide gene expression. First, by constructing gene co-expression networks, we clarified the distinctive action points of JAKis and a TNF-α inhibitor. Moreover, it was suggested that there are inflammatory cascades that are not fully compensated by existing therapeutic agents (e.g., complement pathway, IL-6 signaling). Second, by constructing enhancer-gene map using activity-by-contact (ABC) model, JAKis and a TNF-α inhibitor were revealed to directly regulate the expression of some disease susceptibility genes in SFs. For example, putative enhancer regions of *CD40* and *TRAF1*, consistent with disease susceptibility variants, were closed in chromatin structure and gene expression suppressed by JAKis and a TNF-α inhibitor, respectively. We also identified causative variants (rs6074022-*CD40*, rs7021049-*TRAF1*) in these region by using luciferase assay and CRISPR-Cas9 system. That is, each class of drug was thought to have different points of action on CD40-TRAF1 signaling related to cell survival and inflammatory cytokine production. A comprehensive understanding of the immunological properties of therapeutic agents could offer the potential for future repositioning of drugs and form the basis for accelerating precision medicine.

S6-5

Targeting muscle fiber necroptosis for treatments of inflammatory myopathies

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Conflict of interest: Yes

Inflammatory myopathy (IIM) is a group of diseases including polymyositis (PM) and dermatomyositis (DM). Current treatments for IIM depend on glucocorticoids and immunosuppressive agents. However, these therapies sometimes fail to settle muscle inflammation leading to prolonged muscle weakness, and some patients suffer from infectious diseases during the treatments. Therefore, the development of safe and effective treatments is awaited. Muscle fiber death is a key histological feature of all IIM subgroups. We assumed that injured muscle fibers release inflammatory mediators, which would promote muscle injury, and the inhibition of muscle fiber death could be a novel treatment for IIM. The integrative analysis including histological examination on muscles from PM/

DM patients and functional studies with in vitro model which recapitulates the muscle injury in PM, showed that muscle fibers undergo necroptosis. Necroptosis is a regulated form of lytic cell death, which accompanies the release of inflammatory mediators such as HMGB1. The inhibition of necroptosis suppressed not only the myotube cell death but also the release of HMGB1 from the injured myotubes in vitro. Treatment with a necroptosis inhibitor or anti-HMGB1 antibodies for C protein-induced myositis (CIM), a murine PM model, ameliorated muscle weakness and inflammation. Furthermore, we have focused on GLP-1R agonists as a candidate for novel treatments targeting muscle fiber necroptosis, given their pleiotropic actions such as suppression of muscle wasting and inhibition of cell death. GLP-1R was upregulated on the inflamed muscle fibers of PM/DM patients. PF1801, a GLP-1R agonist, inhibited the myotube necroptosis in vitro through suppressing PGAM5 and reactive oxygen species, which are crucial in myotube necroptosis. The treatment with PF1801 for CIM suppressed muscle weakness, atrophy, and inflammation. Thus, the treatments targeting necroptosis in muscle fibers could be a promising strategy for IIM.

S7-1

Creating a new field of osteoimmunology

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Conflict of interest: None

It has been an important question in the field of rheumatic diseases how the immune system breaks the bone, since they include numerous autoimmune diseases that lead to the bone and joint symptoms. However, the interaction of the bone and the immune system had not been studied much, until osteoimmunology was created to understand the immune induction of RANKL-expressing synovial fibroblasts. It has long been appreciated that bone marrow is a primary lymphoid organ that harbors hematopoietic stem cells. It has been shown that CXCR12-expressing osteoprogenitor cells represent the hematopoietic niche, proving the bidirectional relationship between the bone and the immune system. Here I reflect on the development of osteoimmunology and discuss how osteoimmunology influenced rheumatology.

S7-2

Discovery of regulatory T cells

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Conflict of interest: None

Regulatory T (Treg) cells were discovered in the 1980's as a T-cell subpopulation whose removal evoked autoimmune disease and whose reconstitution suppressed disease development. Tregs are constitutively expressing the transcription factor Foxp3 in the nucleus, CD25 and CTLA-4 on the cell surface, and actively engaged in the maintenance of immunological self-tolerance and homeostasis. Depletion or functional impairment of Treg cells is able to enhance cancer and microbial immunity, while their numerical expansion or functional augmentation is instrumental in treating autoimmune disease and establishing graft tolerance. How to achieve these aims by targeting Treg cells with biologicals (such as monoclonal antibodies) or chemicals has been an issue of intense investigation. We have recently made attempts to pharmacologically control Treg-specific transcriptional and epigenetic changes and thereby control Treg cell development and function. We found that certain tyrosine kinase inhibitors that blocked T-cell receptor-proximal signaling in T cells were able to specifically deplete mature Treg cells, thereby enhancing tumor immunity in humans. On the other hand, inhibitors of a serine threonine kinase involved in a T-cell signaling pathway evoked Foxp3 expression in conventional T cells including effector/memory T cells and converted them to functionally competent Treg-like cells, which effectively suppressed autoimmune disease and allergy in animal models. It will be discussed how the development and function of Treg cells can be controlled by transcriptional and epigenetic interventions and how Treg cells be targeted to control a variety of physiological and pathological immune responses.

S7-3

Interleukin 6: From Arthritis to CAR-T cell therapy and COVID-19

Tadamitsu Kishimoto
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Conflict of interest: None

Interleukin-6 (IL-6) possesses the diverse biological activity that contributes to the maintenance of homeostasis. Emergent cases of infection or tissue injury induce rapidly production of IL-6 and activates host defense through the augmentation of acute phase proteins and immune responses. However, excessive IL-6 production and uncontrolled IL-6 receptor signaling have critical roles in disease pathogenesis. Over the years, therapeutic agents targeting IL-6 signaling, such as tocilizumab, a humanized anti-IL-6 receptor antibody, have shown remarkable efficacy for rheumatoid arthritis, Castleman's disease, and juvenile idiopathic arthritis, and applicable diseases are continuously being reported. Emerging evidence has demonstrated the beneficial efficacy of tocilizumab for several types of acute inflammatory diseases including chimeric antigen receptor T-cell therapy-induced cytokine storms and coronavirus diseases 2019 (COVID-19). Here, we refocus attention on the biology of IL-6 and summarize the distinct pathological roles of IL-6 signaling in several acute and chronic inflammatory diseases.

S7-4

Molecular Mechanism of Tissue-Specific Inflammation Development by the Gateway Reflex

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Conflict of interest: None

Autoreactive CD4+ T cells increase with age. Those with specific MHC class II gene alleles are associated with many inflammatory diseases, indicating that autoreactive CD4+ T cells that recognize specific autoantigens are associated with tissue-specific inflammatory diseases. Accordingly, we have been studying autoreactive CD4+ T cell-dependent disease models. In the process, we discovered the gateway reflex, a novel neuro-immune crosstalk, in 2012. The first gateway reflex discovered is based on gravity stimulation activating the soleus muscle to trigger a specific sensory-sympathetic coupling. This coupling induces chemokines such as CCL20 from the dorsal vessels of the fifth lumbar spinal cord via excessive NFkB activation by noradrenaline secretion, resulting in a gateway for immune cells including myelin-specific autoreactive CD4+ T cells to cause tissue-specific inflammation. We have since discovered 6 gateway reflexes that depend on different environmental stimuli: gravity, electrical, pain, stress, light, and intra-articular inflammation. Each of these stimuli activates specific neural circuits and induces inflammatory disease by increasing the permeability of specific vessel sites. In the gateway reflex dependent on stress and intra-articular inflammation, ATP produced from the inflammatory site acts as a neurotransmitter to stimulate novel neuronal circuits and induce inflammatory diseases in remote organs. In this presentation, we will discuss the discovery of the gateway reflex, its types, and future developments.

S8-1

Surgical Tips and Pitfalls Associated With the Rheumatoid Hand

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Conflict of interest: None

Rheumatoid arthritis (RA) is an autoimmune disease characterized by synovitis-induced joint destruction. Following the widespread use of methotrexate and biologics, as well as the availability of novel therapeutic agents including Janus kinase inhibitors, synovitis and bone destruction can be significantly controlled. The rheumatoid hand specifically refers to

RA involving the hand and wrist joint; reportedly, approximately 70% and 90% of patients develop a rheumatoid hand within 2 and 10 years of RA onset, respectively. Progressive RA negatively affects patients' activities of daily living (ADLs); therefore, timely and appropriate treatment is important. Complications associated with the rheumatoid hand include the risk of progressive deformity despite controlled disease and progressive bone destruction and reduced quality of life even in patients with low disease activity. Pain relief following treatment may lead to excessive use of the hand, which however predisposes patients to the risk of secondary hand injury. The overall rate of surgeries for RA-induced joint disorders has declined, although rates of operations on small joints of the hand have continued to increase. Although pharmacotherapy is an important therapeutic aid, appropriately timed interventions such as bracing and surgery are important to maintain ADLs and quality of life in patients who develop hand deformities. RA causes significant soft tissue injury, particularly to the flexor and extensor tendons and the collateral ligaments/palmar plates. Extensive soft tissue destruction and joint inflammation disrupt the soft tissue balance; therefore, treatment of the rheumatoid hand is particularly challenging. Therapy for these deformities should focus on accurate knowledge of the anatomy of this area and restoration of the distorted soft tissue balance. In this presentation, I will discuss tips and pitfalls of surgical treatment for hand and wrist joint disorders associated with RA.

S8-2

Recent advancements in the surgical treatment of elbow disorders associated with rheumatic diseases

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Conflict of interest: None

Total elbow arthroplasty (TEA) for joint destruction of RA achieves excellent pain relief and shows satisfactory improvements in range of motion, stability, and function. TEAs are generally classified into linked or unlinked devices. Based on the good long-term results of the linked TEAs, Discovery, Nexel and Latitude have been developed and used in clinical practice, and their short- and mid-term results have recently been reported. In our study of 44 RA elbows with 48 elbows (3 males and 41 females, mean age at surgery 65 years) with PROSNAP TEA, MEPS improved significantly from a mean preoperative score of 49.5 to 96 points at a mean of 4.8 (0.9~12) years postoperatively. Complications included 2 cases requiring revision due to liner fracture and infection, one case of postoperative fracture and 3 cases of postoperative elbow contracture requiring revision surgeries. However, no cases of aseptic loosening were observed. 12-year survival rate was 93.6% with revision surgery with implant removal as the endpoint and 83.9% with any revision surgery. Among the Unlinked types, the mid- to long-term results of Kudo Type-5, JACE and modular NSK has recently been reported from Japan. In a study of 21 RA patients younger than 50 years (mean age 46 years) with 26 elbows who underwent Unlinked type TEA at our institution, MEPS improved significantly from 47 to 95 at a mean postoperative period of 13.6 (6-27) years. Complications were noted in 6 patients and 6 elbows (23%), of which 4 cases of ulnar neuropathy and one elbow with postoperative traumatic fracture required additional surgery. There was no revision surgery with implant removal and no radiographic loosening around the components. The 25-year survival rate with any revision surgery as an endpoint was 78.1%. In this symposium, the latest clinical results of the implants currently available in Japan will be presented, and the implant selection and measures to prevent complications will be discussed.

S8-3

Shoulder joint disorders associated with rheumatic diseases and the forefront of surgical treatments

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Conflict of interest: Yes

The main shoulder joint disorders associated with rheumatic diseases are limited range of motion of the shoulder joint and shoulder joint pain.

Conservative therapy, including rheumatoid arthritis (RA) control, is the principle, but surgery is also considered in cases of ineffectiveness.

Surgery may be performed speculatively if the injury is limited to soft tissues such as the rotator cuff or long head tendon of the biceps, or by joint replacement with an artificial device if there is also bone and cartilage damage.

The choice of prosthetic treatment for RA shoulder depends on the condition of the rotator cuff, the bone quality of the scapula, and the patient's age and activity. Regardless of the treatment option, the outcome of the artificial head, a-TSA, or RSA is largely determined by the preoperative condition of the rotator cuff, and surgery should be performed before the rotator cuff is completely torn or while it is reparable.

When performing total shoulder arthroplasty (TSA) for RA shoulders, it is important to be aware of soft tissue and bone fragility, decreased or modified immunocompetence, and long-term joint contracture, and to use intraoperative patency, dissection of the entire scapular neck, shortened operative time, and appropriate postoperative care.

The outcomes of TSA for RA have been reported to be worse than those for osteoarthritis (OA), with more postoperative complications; RA is an inflammatory disease that is prone to postoperative reattachment and requires appropriate rehabilitation in the early postoperative period.

S8-4

Pitfall and pearl of foot/ankle surgery against intractable foot cases of rheumatic diseases

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Conflict of interest: None

Key words for intractable foot cases of rheumatic diseases are 1. bone fragility, 2. instability, 3. susceptibility to infection, and 4. complex deformity. 1. Regarding bone fragility, postoperative fractures may occur after starting weight bearing and walking after normal artificial joint surgery. Preparing an internal fixation material is also important, as intraoperative fractures are often experienced. In addition, in artificial ankle joint replacement, it is also important to devise methods such as filling dense artificial bone to enhance bone strength before placing implants. Needless to say, it is important to take measures against osteoporosis before surgery. 2. Regarding instability, we often see cases in which the joint can be preserved with the dramatic progress of drug therapy in recent years. For example, when correction and partial fixation are performed at the surrounding subtalar and talonavicular joints to preserve the talocrural joint, all the braking force of varus/valgus is entrusted to the preserved talocrural joint. Therefore, shin-fibula stabilization and talus-lateral malleolus stabilization are essential, and it is necessary to stick to treatments such as further correction, osteotomy, and ligament reconstruction. Also, in artificial ankle joint replacement, if the anterior talofibular ligament (ATFL) insufficiency exceeds the limit, excessive stress on the medial malleolus will occur, and the implant will move in the varus direction after the medial malleolus fracture/pseudoarthrosis. dislocation may occur. Of course, when performing surgery to preserve joint function, instability must also be taken into consideration. 3. Regarding susceptibility to infection, I have the impression that steroid-treated cases are more difficult than biologics/JAK inhibitor-treated cases. In some cases, postoperative osteomyelitis has occurred, but it is important to make full use of treatment options for osteomyelitis and not to give up. 4. Complexity of deformity, for example, deformity of the forefoot, deformity of the knee joint and deformity of the hindfoot and midfoot are often involved or hidden. As long as it is a disease that destroys and deforms joints, it is important to have a wide field of view and pay attention to deformation of multiple sites. I would like to explain the above contents along with failure cases.

S8-5

Surgical options for rheumatoid knees

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Conflict of interest: Yes

Total knee arthroplasty (TKA) is the most effective surgical treatment for painful knees with deformities due to rheumatoid arthritis. In most cases, the surgical procedures and the implantation settings are performed with the same concept as those for osteoarthritis knees. However, complex rheumatoid knees are sometimes encountered, those include flexion contractures or fixed valgus deformities without osteophyte formations, significant bone defects, ligament instabilities and relatively young age. Surgeons sometimes need to consider extensive ligament releases to correct the fixed deformities and use of implants with constrained surface and/or augmentations. Joint preservation surgeries including the high tibial osteotomy (HTO) and uni-compartmental arthroplasty (UKA) are considered to be contra-indications for rheumatoid knees because histories of failures of these procedures had been recognized. However, recent development of pharmacological treatments for rheumatoid arthritis suggests insights for joint preservation surgeries. In fact, joint preservation surgeries for rheumatoid hand and foot have achieved successful outcomes. Similarly, HTO or UKA may be applied for isolated medial compartmental diseases in patients with clinical remissions. So far, only several case reports have been published. We also have performed HTO and UKA for several cases under those strict inclusion criteria. We experienced some good short-term outcomes, however, long-term results are needed to evaluate the validity.

S8-6

Surgical Treatment for Hip Joint in Rheumatoid Diseases

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Conflict of interest: None

The number of hip surgeries, such as total hip arthroplasty (THA), for rheumatoid arthritis has decreased over the years due to the widespread use of bDMARDs and JAK inhibitors in addition to csDMARDs. The number of typical hip arthritis patients with central dislocation has decreased, but there are still cases of bone destruction and bone defects. The usual primary THA for patients with articular cartilage damage and minimal bone loss is performed in the same way as for other hip diseases such as osteoarthritis. The following points should be noted; 1) the range of motion of the hip is better in many cases than in osteoarthritis, and the impingement point is easily reached after surgery, making dislocation more likely; 2) the soft tissues around the hip are fragile and have a high degree of laxity, resulting in concerns about instability. In recent years, from the viewpoint of preventing dislocation after THA, THA with CT-based navigation and various simple navigation systems as computer-assisted surgical technology for ideal implant placement is becoming popular. In addition, surgical approach focusing on soft tissue reconstruction around the hip joint are also being used, with an increase in anterior and anterolateral approach compared to the previously predominant posterolateral approach. Some have suggested that postoperative motion limitation precautions are less frequent or unnecessary. In initial THA for patients with severe arthritis, synovial proliferation, and bone destruction, or in revision THA for post-THA loosening, the main issue is bone loss and thinning on the acetabular side. Reconstruction of the acetabular components, bone grafts, augmentation, and various support rings. In cases of pelvic discontinuity where pelvic continuity is compromised, a metal plate or cup-cage technique can be used to ensure continuity of the pelvis before acetabular component placement.

S9-1

Patient education and its barriers based on EULAR recommendations

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Conflict of interest: None

For implementing T2T at any life stage in the treatment of rheumatoid arthritis (RA), it is important for patients to actively participate in their treatment, which requires them to improve their health literacy - their ability to obtain, understand, and use basic knowledge and information about their disease and treatment. Interactive communication with healthcare professionals is also important for patients to make decisions. In achieving these goals, educational support from healthcare professionals to patients is required. The EULAR recommendations on patient education have been proposed and contained two overarching principles and eight recommendations. An international survey of medical professionals from 23 countries - 3 Asian countries (Japan, Hong Kong and India) and 20 European countries - was conducted to assess acceptability and identify barriers to implementation of these recommendations[1]. For all recommendations, the level of agreement was high but applicability was lower. Factors that were identified as the barriers to practice included lack of time and staff to provide education, lack of training on how to provide patient education, and lack of assessment tools and resources to provide patient education. Tailoring patient education to individual patients, using group education, linking patient education with diagnosis and treatment, and inviting patients to provide feedback on patient education delivery were the most commonly used facilitators. Another survey indicated that the majority of these recommendations were strongly supported by patients[2]. The benefits of using patient education to facilitate collaborative care and shared decision making, as well as the value of flexible and tailored patient education, were cited as reasons for agreement with these recommendations. I would like to consider the practice and challenges of providing educational support to patients with RA based on EULAR recommendations.

S9-2

Community Collaboration and Tasks in Supporting RA Patients in General Hospitals

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Conflict of interest: None

With the development and marketing of disease-modifying antirheumatic drugs (DMARDs) and immunosuppressive drugs such as biological DMARDs developed based on the latest findings in immunology, pharmacists have an increasing role to play in understanding drug characteristics as well as in managing adverse drug reactions. The role of pharmacists is increasing. Many pharmacists in charge of outpatient dispensing do not have sufficient opportunities to learn how rheumatologists deal with patients and make prescribing decisions on a daily basis. Many pharmacists in charge of outpatient dispensing do not have sufficient opportunities to learn how rheumatologists deal with patients and make prescription decisions. Osaka Saiseikai Nakatsu Hospital accepts insurance pharmacy pharmacists as trainees for six months to allow them to experience ward work and team medicine and learn how to interact with outpatients. Insurance pharmacists who have established a face-to-face relationship with hospital staff can easily share information related to drug treatment with the hospital, facilitate follow-up during the period of medication, and have high expectations for collaboration in drug treatment not only for outpatients but also for those admitted and discharged from the hospital. In this symposium, we will introduce a case study of collaboration with an insurance pharmacy pharmacist, present an appearance of a case study of follow-up of a patient with rheumatic disease during the period of taking medication, and discuss the collaboration performed by a hospital-employed pharmacist and an insurance pharmacy pharmacist.

S9-3

Current status and issues of the nursing support for patients with JIA in a general hospital

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Conflict of interest: None

Juvenile idiopathic arthritis (JIA) is defined as chronic arthritis of unknown cause that begins in patients younger than 16 years of age and

persists for at least 6 weeks. Since adult rheumatology nurses have little experience in caring for JIA patients from the onset, it is considered important to draw lessons from individual case studies. At the age of 15, the patient developed right knee joint pain in October, followed by right wrist joint pain in December and was referred to our department due to a positive result for ACPA. At the first visit, the number of swollen joints was 5, the number of tender joints was 3, and ACPA was 906 U/ml. She had been involved in rhythmic gymnastics since elementary school, and she belonged to a club team in addition to club activities at school. After consulting with her parents, she started methotrexate in combination with a biologic DMARD in order for her to participate in the club competition held in a several months. Since she had a strong fear and stress about self-injection, we took time consulting with her and her mother and checked their acceptance status. Ultimately, she managed to shift to self-injection by changing aids and devices. Two months after the start of treatment, Strengthening and Stretching for the Rheumatoid Arthritis of the Hands (SARAH) program was instructed by occupational therapists. She successfully underwent drug treatment and rehabilitation with the aim of participating in a club activity and competitions. Conferences among physicians, nurses and occupational therapists were held regularly to support the patient as a team. Although we had little experience in supporting JIA patients from onset, the team worked together to support her by listening to concerns and anxieties and sharing information. We would like to continue to listen to patients' complaints and provide support tailored to their life stages.

S9-4

Current Situation and Issues in Supporting RA Patients in Rheumatology Hospitals

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Conflict of interest: None

With advances in pharmacotherapy in rheumatoid arthritis treatment, patients with RA have been able to achieve and maintain low disease activity or remission, and lead a life similar to that of healthy people. Even now that disease activity can be controlled, the White Paper on Rheumatism 2020 calls for more therapists who understand rheumatology. The Rheumatoid Arthritis Guideline 2020 also published algorithms for non-pharmacological and surgical treatment, and the importance of rehabilitation medicine has been reaffirmed. Although there are many therapists in our hospital, 86% of them joined after 2000, when the paradigm shift in drug therapy took place, and the majority of them, 86%, are young therapists. Therapists who lack experience in RA practice have less opportunity to observe changes in joint failure over time, and may not have the ability to anticipate signs of deformity, prevent it, and take action to address it. They may not be able to anticipate the signs of deformity or take action to prevent and manage it. Supplementing the knowledge of experienced therapists will enable them to consider various aspects of patient care. In particular, the overarching principles of Treat to Target (T2T) state "maximize the patient's long-term quality of life". Patients with RA need to be understood better, and their complaints need to be listened to in order to re-establish the life they want, to improve their quality of life, and to maintain it over the long term. Deformity in RA patients may lead to a decline in QOL, and prevention of deformity is important to improve QOL in the long term. In our clinic, young and experienced staff members work together to make splints and share their knowledge in clinical situations to improve their experience in RA treatment. An important issue for the future is how to train therapists who can prevent deformity (prevention of misuse and overuse) in the period of remission.

S9-5

Current Situation and Challenges in Supporting RA Patients in Clinics (from a Physician's Perspective)

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Conflict of interest: None

The proportion of elderly RA patients in the clinic is high. The clinic also sees pregnant and postpartum RA patients of childbearing potential, as well as lactating RA patients. We report on the current status and challenges of RA care for elderly RA patients and women of childbearing age RA patients in a clinic. Elderly RA patients are prone to loss of muscle mass and physical function, and are often characterized by complications of organ disorders such as respiratory disease, chronic kidney disease, and chronic infections. In deciding on a treatment plan, we aim to control disease activity at an early stage in order to prevent deterioration of physical functions, and we propose drugs and doses that take into account various organ complications. In addition, if the patient's physical function as well as cognitive function and motivation deteriorate over time, the treatment needs to be reviewed. In the case of elderly RA patients with this background, team medical care including not only RA specialists but also nurses, pharmacists, dietitians, rehabilitation staff, and care managers is essential to control disease activity and manage physical functions and complications. In addition to this, collaboration with local medical institutions is often necessary. The RA Foundation Care Nurse is the central axis of team medicine and collaboration with other medical institutions. We will report through actual cases. The clinic hosted a meeting called "MIRAI TALK" with five unpregnant RA patients and female medical staff to practice preconception care. Knowledge was shared about the impact of RA itself on pregnancy, childbirth, and childcare, while their impact on RA, contraception while taking MTX or leflunomide, when to start fertility treatment after discontinuation of these drugs, and drug selection for those who wish to become pregnant, expectant mothers, and lactating mothers. The possibility and challenges of preconception care in clinics through the activities of "MIRAI TALK" will be reported.

S9-6

How do we foster independence and the ability to live with illness in children with JIA. Responsibilities of medical professionals during the transition period to adulthood

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Conflict of interest: None

Many families of JIA patients feel that the invisible symptoms associated with JIA, such as pain and lethargy, are not fully understood or adequately treated by healthcare professionals. In reality, neither parents nor medical professionals recognize the children's insufficient ability to explain their invisible symptoms. When the JIA patient says 'I'm OK', he/she means 'l will be OK if I take medicine'. When he/she complains pain, it is intolerable pain for him/her. Thus, they are unable to clearly convey their pain to those around them. Moreover, these invisible symptoms such as pain and fatigue deplete children's normal daily lives and interfere with their physical and mental growth and development. If the disease occurs in adulthood, it should be allowed to maintain its existing function. However, in the case of JIA, which develops in childhood and some carries the disease into adulthood, who should be responsible for the child's physical and mental development? It would not only be their parents, but also the medical professionals who treat them during their physical and mental growing period. Who and how to foster their independence and ability to live with JIA? This is the important issue for the future, and I would like to discuss it with the participants of this session.

S10-1

Targeting B Cells in Systemic Lupus Erythematosus

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Northwell Health

Conflict of interest: Yes

Although evidence for B cell hyperactivity in systemic lupus erythematosus (SLE) was recognized long ago, it wasn't until twenty years ago that the lupus community ventured into clinical trials to determine whether therapeutics targeting B cells could reduce disease activity. The initial approaches were eclectic, focusing on B cell depletion with rituximab and on key B cell survival and growth factors with belimumab. While studies with rituximab in both SLE and lupus nephritis (LN) failed to achieve their endpoints, there were some promising signals. These observations coupled

with the off-label use of rituximab kept the B cell depletion strategy alive. Buoyed by data suggesting that greater B cell depletion yielded enhanced clinical responses, obinutuzumab rose to the challenge. Obinutuzumab, a type II anti-CD20 and more potent B cell depleting monoclonal antibody, yielded favorable results in a 122-patient LN study. The Regency study is putting obinutuzumab to the test in a phase III LN study. Other promising strategies to directly affect B cells or plasma cells are being pursued with proteasome inhibitors, anti-CD19 chimeric antigen receptor T cells (CAR-T), and monoclonal antibodies. Paralleling the development of anti-CD20 monoclonal antibodies was the development of inhibitors of the B Cell Activating Factor (BAFF) / A Proliferation-inducing Ligand (APRIL) pathway. Leading the way was belimumab, which proved itself in two phase III SLE trials. The FDA approval of belimumab in 2011 was an historical event since this was the first drug approval in SLE via the route of a randomized controlled trial. Additional accolades occurred in 2020 when belimumab was approved by the FDA for lupus nephritis; this approval represented the first approval of a drug for lupus nephritis. Targeting the BAFF/APRIL pathway with recombinant receptors (atacicept, telitacicept, ALPN-303) or monoclonal antibodies continues to be investigated.

S10-2

New Frontiers in SLE Therapy: Omics-informed Targeted Therapy to Restore the Aberrant Transcriptional Landscape in Systemic Lupus Erythematosus (SLE)

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Conflict of interest: None

Comprehensive transcriptional analysis of diverse tissues in SLE has shown widespread disturbances that are fueled by failure of multiple regulatory mechanisms within the immune network including extensive functional disturbances of the dendritic cells, T regs, T and B cells. Multi-omics approaches have proposed SLE subtypes as distinct disease entities based on molecular portraits but have failed to translate into new therapies. To this end, high-throughput, data-driven methods have enabled the repurposing of de-risked compounds, with potentially lower overall development costs and shorter development timelines. Omics-based drug repurposing is an alternative to *de novo* drug development and has the potential to bring compounds to patients more efficiently.

S10-3

IFN targeting in SLE

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Conflict of interest: Yes

Type I interferons (IFN) and the pathways involved in IFN expression and function have been identified as potential therapeutic targets in SLE since the first description of circulating IFN more than 20 years ago. Since then, clinical and preclinical studies have confirmed the presence of an IFN gene signature in blood and tissues of SLE patients and the association of this with disease severity, SNPs in IFN pathways as risk alleles for SLE, the ability of IFN to exacerbate murine models of SLE, and the wide range of impacts of IFN on the immune system and target organs of SLE. There remain many unanswered questions in this domain, including exactly which mechanism (s) are operative in human SLE that lead to the activation of IFN expression, the source of IFN that results in the peripheral blood signatures, the relative contribution of local IFN production to tissue pathology, and the biological endotype of IFN-negative SLE. Despite this multiple clinical trials of agents targeting the IFN system have been completed, and the efficacy of such agents confirms the importance of IFN to this disease. Antibodies to the IFN receptor which block signaling by all Type I IFNs have been shown to be efficacious and well tolerated and now approved as a therapy in countries around the world; post marketing studies are needed to understand the overall impact of this on SLE outcomes and long term safety. Encouraged by this success, multiple other agents targeting IFN signaling via JAK and TYK2 kinases, or targeting plasmacytoid dendritic cells that are major producers of IFNalpha, have had positive Phase 2 trials and are entering late stage clinical development, while medicines targeting TLRs that are likely to be key to triggering IFN expression are also entering clinical trials. The coming years will inform on the relative value of such approaches, and carefully designed trials will inform on the relative contribution of these individual elements to the IFN pattern of SLE.

S10-4

Targeting the JAK in the treatment of SLE

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is characterized by immune complexes consisting of antigens, activation of dendritic cells and autoreactive T cells and overproduction of autoantibodies secreted from activated B cells. As glucocorticoids and immunosuppressive drugs are non-specific therapeutic agents that cause many adverse reactions, the development of molecular target therapy is anticipated in the treatment of SLE. The pathogenesis of SLE involves abnormalities in both acquired and innate immune system, which is mediated by numerous cytokines. Janus kinase (JAK) plays important roles in the signaling pathways of those cytokines and is an attractive therapeutic target for SLE. Currently, multiple clinical trials using JAK inhibitors with different selectivities for JAK family proteins such as tofacitinib, baricitinib, filgotinib, upadacitinib, deuravacitinib and brepocitinib are being conducted in SLE. Despite a successful phase II trial of baricitinib, the phase III trial (SLE-BRAVE-II) failed to meet its primary endpoint of SRI-4 response. In contrast, phase II trial with deucravacitinib, a selective inhibitor of TYK2, achieved its primary endpoint of SRI4 at week 32. Interestingly, we found that TYK2 inhibitor suppresses Tfh cell differentiation while preserving Treg cell differentiation, suggesting that TYK2 inhibitor has the potential to efficiently correct the "immune imbalance" in SLE. JAK inhibitors have the potential to modulate various immune networks through a variety of mechanisms, potentially regulating the complex immunopathogenesis in SLE. However, SLE is a clinically and immunologically heterogeneous disease; therefore, precision medicine is required to maximize the efficacy of JAK inhibitors. Further studies are needed to determine their risk-benefit ratio and selection of the most appropriate patients for JAK inhibitors.

S10-5

CAR-T

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S11-1

Notable points of the updated version and Indications/contraindications of MTX

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Conflict of interest: Yes

Methotrexate (MTX) is an anchor drug in the treatment of rheumatoid arthritis (RA). The third edition of the Guide to MTX Use and Management in RA was published in conjunction with the availability of subcutaneous MTX in Japan in 2022. In addition to the description of the dosage and administration of the subcutaneous formulation and points to consider for switching from the oral formulation, the updated edition also attempts to revise the description of contraindications regarding pleural effusions and ascites. In addition, while clarifying the position of MTX as a first-line drug, the use of MTX as a second-line drug and subsequent drug is still allowed. As sufficient doses of MTX are currently available for Japanese patients, the concomitant use of folic acid is further positively described, and the MTX administration algorithm and usage examples have been revised in accordance with the current situation. In addition, the evidence for concomitant use of Janus kinase (JAK) inhibitors and updated information on side effects to promote the proper use of MTX are included, as well as the latest information on lymphoproliferative diseases.

S11-2

Dosage and administration of MTX, including MTX subcutaneous injection formulation

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Conflict of interest: None

The initial starting dose and dosage escalation methods of MTX have been gradually changing, and we have made changes and additions to the content of the previous guideline to reflect actual clinical practice in Japan, referring to studies and new evidence that complement the content of the previous guideline. In 2022, a new MTX subcutaneous injection formulation was approved in Japan, adding a new option for the treatment of RA with MTX. Although it is known that bioavailability differs between single dose and divided dose in the case of oral administration, no study has been conducted in Japan, and in view of actual clinical practice, a single dose up to 8 mg/week was assumed to be the standard. If the therapeutic target is not reached after 4 weeks of treatment, the dose may be increased and administered in 2~3 divided doses at 12-hour intervals. Dose escalation is usually 2 mg/week for oral administration, but can be increased earlier depending on the patient background, and for subcutaneous administration, the dose can be increased by 2.5 mg every 4 weeks. The dose should be increased to the maximum target dose by 8~12 weeks after initiation. In Japan, the dose can be increased up to 16 mg/week. Based on clinical trials in which MTX doses were increased and trials comparing the therapeutic effects of MTX doses, it is recommended that the dose be increased up to 10~12 mg/week in Japan. Based on the risk-benefit balance, dosage should be increased up to 16 mg/week if possible and necessary, and either in combination with other conventional synthetic disease-modifying anti-rheumatic drugs or with molecular targeted therapy. If combination therapy is inadequate, MTX dose escalation (up to 16 mg/week) is an option. When changing from oral to subcutaneous MTX administration, oral 6 mg/week should be subcutaneous 7.5 mg/week, oral 8~10 mg/week should be subcutaneous 7.5 or 10 mg/week, and oral 12~16 mg/week should be subcutaneous 10 or 12.5 mg/week. This presentation will explain the rationale for the main changes and cautions regarding the dosage and administration of oral MTX and the newly approved subcutaneous injection formulation based on previous reports.

S11-3

Side effects and their management under MTX therapy

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Conflict of interest: None

Methotrexate (MTX) is the anchor-drug in the management of rheumatoid arthritis (RA). It is important to know the profile of side effects and to manage them for keeping safety and effectiveness of RA patients under MTX therapy. In the post-marketing surveillance of MTX, bone marrow suppression, interstitial pneumonia, infectious diseases, gastrointestinal disorder, liver dysfunction, and lymphoproliferative disease (LPD) are selectively monitored as notable side effects. Some characteristics of side effects have been reconfirmed by evidence from accumulation of information, but others might have changed with the progression of medicine or change of medical environment. The emergence of COVID-19 has dramatically changed not only the management of infectious diseases of RA patients, but also response to or differential diagnosis of any symptoms under MTX use. On the other hand, although the development of nucleic acid analogue has made possible radical cure for viral hepatitis, fat-depositing liver diseases have emerged as new clinical problems. It has become necessary to remember and understand non-alcoholic fatty liver diseases (NAFLD) or non-alcoholic steatohepatitis (NASH) in RA patients receiving MTX. The JCR sub-committee for arranging MTX treatment guidelines has revised the guidelines as users guide this time and added some new information in the part of side effects. I would introduce the summary of the revision and new information except about LPD and discuss them in this lecture.

S11-4

Epidemiology and Pathogenesis of Rheumatoid arthritis (RA)-related Lymphoproliferative disorders (RA-LPD)

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Conflict of interest: Yes

It has been known that RA patients have an increased risk of developing lymphoma since the 1980's. The link to immunosuppressive drugs raises concern for the development of lymphoma because of the report of reversible lymphoma by withdrawal of MTX. A category of other iatrogenic immunodeficiency-associated LPD (OIIA-LPD) was described in the 4th edition of the WHO classification. Recently, the evidence of OIIA-LPD in RA has been accumulated in Japan, a clinical guide for the diagnosis and management of RA-related LPD by the joint working group of JCR, Japanese Society of Hematology and the Japanese Society of Pathology was published in July, 2022. The standardized incident rate of lymphoma in RA patients was reported between 0.06-1.00/100PY, and it was similar to that from the Western countries (0.06-0.09). Moreover, incidence rate or hazard risk was unchanged by the recent advance in RA drug therapy. The standardized incidence ratio (SIR) of lymphoma varies from 3.43 to 8.21 in the Japanese RA registries. The recent studies demonstrate that LPD occurred in aged (median age was67-68) long-term MTX users with long duration of RA. Pathologically, B-cell lymphoma was common, and EBER-positive cells were found in about 50% of LPD tissues. About 60% of LPDs occurred during MTX treatment regressed spontaneously after MTX withdrawal. Although the pathogenesis of RA-LPD is still unclear, chronic inflammation and immunodysfunction due to RA have been cited previously. However, recent evidence mentioned above suggest that aging or immunosenescence, iatrogenic immunodeficiency and EBV reactivation play more important role in the development of RA-LPD.

S11-5

Management of lymphoproliferative disorders in patients with rheumatoid arthritis

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Conflict of interest: Yes

Development of lymphoproliferative disorders (LPD) should be considered in the management of rheumatoid arthritis (RA). In malignant tumors associated with RA, the incidence is higher than in other solid tumors. First of all, if the onset of LPD is strongly suspected while using immunosuppressive drugs such as methotrexate (MTX), it is important to immediately discontinue the drug. Spontaneous regression (SR) is observed in about half to two-thirds of cases after MTX discontinuation. In MTX users, clinical regression can be confirmed in approximately 90% of cases 2 to 4 weeks after discontinuation. Maximal resolution often takes long time. Consultation with the relevant department should be considered if no resolution is observed by 4 weeks after MTX discontinuation. In patients with SR, the peripheral blood absolute lymphocyte count (ALC) quickly increases after discontinuation of MTX in many cases. Therefore, careful attention should be paid to ALC along with systemic symptoms such as fever. Histologically proven diffuse large B cell lymphoma (DLBCL) may have a low SR rate. The recurrence rate of LPD in RA-LPD is 19-33%, and the recurrence rate within 2 years accounts for two-thirds. Serum sIL-2R>2000 IU/mL and classical Hodgkin's lymphoma of the first onset of LPD have been reported as predictive factors for recurrence. MTX should be avoided and calcineurin inhibitors should be used with caution in the treatment of RA after spontaneous regression or treatment with chemotherapy of LPD. Evidence for biological antirheumatic drugs is limited, whereas high retention rates for tocilizumab have been shown in patients with DLBCL. Although RA-LPD may not be always related to drugs, its association with MTX has been confirmed in multiple cohort studies in Japan. LPD development can affect T2T strategy in RA. RA-LPD is considered to be one of the critical issues that rheumatologists, hematologists, and pathologists should continue to work on in the future.

S12-1

The diagnosis and treatment response of elderly-onset rheumatoid arthritis: A comparison with younger-onset patients

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Conflict of interest: None

***Objectives*:** To compare the characteristics and response to treatment of elderly-onset rheumatoid arthritis (EORA; in patients≧65 years old at the diagnosis) with those of younger-onset RA (YORA; in patients<65 years old). ***Methods*:** From January 2021 to July 2022, 319 patients visited our hospital with "suspected RA". Of them, 146 had a definitive diagnosis of RA, including 83 with EORA (mean age: 74 years old, male/female: 31/52) and 63 with YORA (51 years old, 12/51). The clinical data at the diagnosis (untreated) and after starting treatment were investigated and compared between the two groups. ***Results*:** The mean duration from the onset of the disease to the diagnosis was 28 weeks. At the diagnosis, about 80% of both EORA and YORA patients complained of pain, swelling and/or stiffness in the hands. About half of EORA patients complained of shoulder pain. RF (IU/mL), CRP (mg/dL), and DAS28-ESR (4) at the diagnosis in EORA/YORA patients were 124/75, 3.03/1.10, and 4.87/4.06, respectively ($p<0.05$ for all). ACPA, TJC, SJC, GH (VAS) and HAQ-DI values were similar in the two groups. Notable the EORA group had higher HAQ-DI values than the YORA group for the items of milk carton opening (HAQ7) and housework/chores (HAQ18, 19, 20). In the EORA, SASP (51%) was the most frequently used drug, followed by PSL (43%) and MTX (25%). Almost all clinical data improved at 11 months after starting treatment. The DAS28-ESR (4) improved from 4.87 to 2.51 in EORA patients and from 4.06 to 2.26 in YORA patients, and the HAQ-DI improved from 0.77 to 0.34 in EORA patients and from 0.55 to 0.15 in YORA patients, with deeper functional remission seen in YORA patients ($p<0.05$). ***Conclusion*:** In EORA patients, it is necessary to be aware of the characteristics and make an early diagnosis, start treatment with attention to comorbidities aiming at true remission.

S12-2

Treatment status of elderly-onset patients with RA in the nationwide large-scale RA database "NinJa"

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Conflict of interest: Yes

According to data from our large-scale RA database "NinJa" (National Database of Rheumatic Diseases in Japan), the average age at onset has increased by about 7 years over the past 20 years. More than 25% of patients develop the disease after the age of 65 years, and about 8% after the age of 75 years. At present, no treatment strategies or treatment goals specific to elderly-onset RA (EORA) have been officially proposed. Recently, there are expectations for the development of treatment guidelines that take age and age of onset into consideration, but what is the current status of treatment for EORA? Using data from NinJa, we divided the patients according to the age at onset and the current age into 4 groups; G1a (onset <65 years, current age <65 years) and G1b (onset <65 years, current age ≧65 years) as younger-onset RA (YORA), and G2 (onset 65-74 years) and G3 (onset ≧75 years) as EORA, and the treatment status and disease activity of each group were compared over time. As a result, the G3 group used less MTX and used more corticosteroids than the other groups. The rate of b/tsDMARD use was also lower than in other groups but increased over time. Among bDMARD user, TNF inhibitors were more frequently selected in the younger-onset group and non-TNF inhibitors in the G3 group. The disease activity and remission rate were slightly inferior in the elderly-onset group, but no obvious difference was observed from the younger-onset group. Comparing those who achieved remission in each group, MTX and b/tsDMARD use decreased as G1a → G3, but corticosteroid use increased. These results were similar when comparing only early onset patients with <2 years of disease. From the above, although the disease activity control and remission rate in EORA were almost the same as those in YORA, there was a significant difference in the content of treatment. It is considered necessary to examine the pros and cons of steroid-dependent disease control in EORA patients.

S12-3

Establishment of treatment goals for elderly-onset RA based on existing cohort data

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Conflict of interest: Yes

Prevention of progressive joint destruction and normalization of physical function are important therapeutic goals of rheumatoid arthritis (RA), and these goals can be achieved by maintaining remission. On the other hand, the elderly have an increased prevalence of age-related comorbidities and a higher incidence of adverse events when receiving disease-modifying anti-rheumatic drugs (DMARDs) compared to younger patients. As a result, the elderly are expected to be more prone to higher disease activity or limited use of medications due to comorbidities. In this symposium, we will present data from an existing cohort study: NinJa (The National Database of Rheumatic Diseases in Japan) and IORRA (Institute of Rheumatology, Rheumatoid Arthritis), the representative RA registries in Japan. The use of methotrexate, glucocorticoids, biological DMARDs, as well as disease activity and Health Assessment Questionnaire Disability Index (HAQ-DI) were evaluated separately for ages of onset <65 years, 65-74 years, and 75 years and older. Both cohorts showed that the use of corticosteroids and HAQ-DI in patients in remission increased with the age of onset. The probability of HAQ-DI ≦0.5 was higher in patients in remission than in patients with low disease activity (LDA), regardless of the age of onset. Next, we analyzed factors associated with physical decline in the treat-to-target (T2T) targeting LDA in the CRANE cohort for elderly-onset RA. We have already shown the predictors of joint destruction at year 1. In addition, we reported that patients who were continuously able to adhere to T2T for three years achieved remission in 57.8% at year 3 and normalization of physical function in 70.1%. In this symposium, we will show that disease activity, rather than comorbidities themselves, contributes to lower HAQ-DI and that prolonged corticosteroid use does not improve physical function. Based on these results, this symposium will discuss treatment goals for elderly-onset RA.

S12-4

Assessment of Physical Function in Older-Onset and Elderly Patients with Rheumatoid Arthritis: Treatment Target for the Prevention of Frailty

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Conflict of interest: None

Introduction: Japan is a hyper-aged society, with an aging RA patient population, and more recently, an increase in the number of elderly-onset RA patients has been noted. It is also necessary to keep in mind the goal of

extending healthy life expectancy. Frailty assessment, which includes the evaluation of physical and mental function in the elderly, is important when considering the extension of healthy life expectancy. Treatment to prevent frailty should be important treatment target in these days. Methods: As part of the AMED "Establishment of treatment strategies to extend healthy life expectancy of elderly patients with rheumatoid arthritis", a prospective cohort study (Fairy study) on frailty in RA patients was conducted at Nagoya University, and in addition to walking speed and grip strength, physical function was measured by Timed Up and Go test (TUG), five times standing and sitting Physical function (HAQ-DI) and frailty (Kihon checklist: KCL) were measured by a self-administered questionnaire. The results were compared with those of cohort studies on frailty at Kyoto University, Niigata Rheumatic Center, and Kurashiki Sweet Hospital. Results: In the Fairy study [243 patients: 85.6% women, mean age 64.5 years, disease activity (DAS28) 2.53, HAQ-DI 0.367 (77.1% HAQ remission)], physical frailty (Fried's criteria) was 20.0% and increased with age. Physical function measures cut-off for the RA treatment goal of HAQ-DI≦0.5 were better than those for frailty (walking speed 1.3 m/s, TUG 9.2 s, and five standing sits 10.8 s). The same was true in other cohorts and in patients with HAQ remission. Conclusions: Even in a population with good disease activity control, frailty is present in about 20% of patients, and its assessment is important. HAQ remission seems to be a reasonable first therapeutic goal to aim for in order to prevent frailty in older patients with RA. Further longitudinal analysis should be needed.

S12-5

Medical care and economic issues of elderly patients with rheumatoid arthritis from the IORRA cohort

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Conflict of interest: Yes

Major advances have been made in rheumatoid arthritis (RA) treatment strategies in recent years. In the IORRA cohort, the proportion of the patients who achieved DAS28 remission increased from 8.4% in 2000 to 63.1% in 2021, and approximately 80% of the patients with RA were well-controlled. On the other hand, especially in Japan, not only the aging of patients with RA but also the number of elderly-onset patients with RA is increasing, however, evidence on the management of these patients is considered scarce. More than half of RA patients were aged 65 or older in the IORRA cohort. The choice of therapeutic agents would be difficult due to age-related decline in drug metabolism, immune function, as well as comorbidities in elderly patients with RA. Five-year treatment outcomes and risk of adverse events in elderly-onset patients with early RA (EORA) compared with younger-onset patients with early RA (YORA) were evaluated using the IORRA cohort. The proportion of patients with good clinical and functional outcomes was significantly lower in EORA group. Patients with EORA had a higher risk for unfavorable clinical events than those with YORA. Rising RA care costs have caused concern, placing a heavy burden on society as well as patients with RA. The IORRA study has shown that direct and indirect costs were associated with progression of functional impairment or decline in quality of life (QOL). Similar results were obtained in elderly patients with RA when these analyzes were performed by age. Although the out-of-pocket costs for elderly patients with RA over 75 years old were low, the rest was paid by society. Therefore, RA medical costs for elderly patients with RA are an important issue from a societal perspective.

S12-6

Discuss treatment of elderly patients with rheumatoid arthritis that emerged from the survey

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Conflict of interest: Yes

Rheumatoid arthritis is a systemic, autoimmune disease with arthritis as its main symptom. Without appropriate diagnosis and treatment, the disease causes joint deformity and pain due to inflammation and joint destruction, resulting in physical dysfunction and decreased quality of life. In recent years, with the advent of methotrexate, biologic agents, and JAK inhibitors, the treatment of rheumatoid arthritis has made remarkable progress, enabling patients to achieve remission and normalize their daily lives. On the other hand, it has been pointed out that rheumatoid arthritis patients are ageing and also new cases are occurring at an older age. Elderly patients often have difficulties in applying standard therapies due to decreased physiological functions such as liver and kidney functions, decreased immune functions, increased complications, polypharmacy, atypical symptoms, and increased individual differences, and appropriate management has not yet been established. Currently, rheumatoid arthritis experts have gathered to resolve issues related to elderly rheumatoid arthritis care. Prospective studies, comparisons and integrated analysis of existed large cohorts are underway. Also, expert surveys have been and will be conducted. In a preliminary survey in 2021, 65 specialists with diverse backgrounds responded to the survey on the cutoff age for "elderly" patients in practice, treatment goals for elderly-onset rheumatoid arthritis, and differences in treatment strategies compared with younger-onset patients. The results have indicated that opinions varied even among experts. A larger national survey will be prepared in 2023. In this presentation, I will explain the results of the survey in 2021 and discuss issues in the treatment of elderly patients with rheumatoid arthritis that emerged from the survey.

S13-1

Rheumatoid Arthritis: Key recent developments

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic, progressive, systemic inflammatory autoimmune disease that affects about 0.5% to 1% of the population worldwide. RA can be associated with substantial morbidity and accelerated mortality, and exerts a tremendous economic toll on affected patients, their families, and society. There are an impressive number of established therapies available currently for the treatment of RA, with additional treatments introduced each year. Biologic agents, particularly inhibitors of tumor necrosis factor (TNF), have changed the treatment paradigm for RA. Studies have shown that biologic agents can slow disease progression, control signs and symptoms of disease, improve function, and improve quality of life to an extent not previously achieved, and have thereby changed treatment paradigms, and driven additional research into other mechanisms of action and treatment approaches. Five inhibitors of TNF are widely available: infliximab, etanercept, adalimumab, golimumab, and certolizumab pegol. More recently, biosimilar versions of several TNF inhibitors have become available world-wide; with their lower costs, can have pharmacoeconomic benefits. Additional biologic agents include the B-cell targeting anti-CD20 monoclonal antibody rituximab, the T cell costimulatory molecule inhibitor abatacept, and two monoclonal antibodies targeting the IL-6 receptor, tocilizumab and sarilumab. Jakinibs, inhibitors of the jamus kinase enzymes, are the latest introduction into the RA treatment armamentarium. Crucial topics related to the optimal treatment of Rheumatoid Arthritis include: 1) earlier intervention, 2) treating to target, 3) consideration of non-inflammatory pain, 4) optimizing safety considerations and perhaps the ultimate goal 5) predictors of response to individual agents. With further progress, we are hopefully approaching the era of 'personalized medicine' in the treatment of RA.

S13-2

Spondyloarthritis

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S13-3

EULAR/ACR Convergence 2022 SLE/Early-phase new molecules

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University of Texas Southwestern Medical Center, USA

Conflict of interest: None

At the annual meetings of EULAR and ACR multiple interesting abstracts related to SLE, and new molecules were presented. Of great interest were abstracts on urinary biomarkers in SLE which correlated with histologic changes in lupus nephritis. Abstracts on therapeutic thresholds for HCQ, the impact of GC discontinuation on symptom control in SLE and factors contributing to progression of chronic kidney disease were presented. Post-hoc data on the clinical efficacy of anifrolumab and claims data on the efficacy of belimumab were of interest. An interesting abstract on CAR-T therapy in patients with previous failure to multiple therapies in patients with SLE shows promise as well as multiple new therapies investigated in phase 1-3 clinical trials including studies with jakinibs, molecules that affect B Cell development including a BTK inhibitor and an inhibitor of BlyS and APRIL, an inhibitor of sphingosine-1-phosphate, a regulator of lymphocyte trafficking, an inhibitor of the immunoproteasome which affects multiple inflammatory cytokines, macrophages, B and T cells, an IL2 mutein Fc fusion protein which promotes Treg expansion and a ubiquitin ligase modulator. Several abstracts on molecules of interest for RA were also presented including an agonist of PD-1 which hopefully would restore immune homeostasis, a molecule which selectively upregulated miR-124 which should downregulate inflammatory cytokines, and several CD40L antagonists. Data was presented on another C5a monoclonal antibody for the treatment of AAV which did show efficacy and ability to decrease concomitant GC in this patient population. Several abstracts were presented on improving the metrics used in clinical trials for Sjogren's Syndrome and a positive trial with a BTK inhibitor. Finally, an interesting abstract on clinical trials for OA of the knee was presented as well as a trial which confirms that denosumab is effective in erosive hand OA as shown previously in Japan and my institution.

S13-4

Autoimmune Inflammatory Rheumatic Diseases: Presentations from the American College of Rheumatology Annual Meeting

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Conflict of interest: None

The Annual Meeting of the American College of Rheumatology was held in Philadelphia, Pennsylvania, USA, November 11-14, 2022. The program included numerous presentations on basic science, pathophysiology, clinical features and therapy of numerous autoimmune inflammatory rheumatic disorders. This presentation will cover some of the more significant presentations on the anti- neutrophil cytoplasmic antibody (ANCA) associated vasculitis syndromes, giant cell arteritis, polymyalgia rheumatica, interstitial lung disease, dermatomyositis and Sjogren's disease.

S14-1

Treatment of rheumatoid arthritis considering medical costs

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Conflict of interest: None

The average household income in Japan is 4.37 million yen at the median in, but the drug costs required to treat rheumatoid arthritis (RA) with biologic agents and JAK inhibitors, which are advanced therapies, are expensive, requiring more than 30,000 yen per month for a patient requiring a 30% co-payment for standard weight and standard use. This co-payment is a heavy burden on the patient's family budget. Not only does this make it difficult to introduce treatment, but even if treatment is successful, it may not be sustainable for financial reasons, which can cause RA flares. Although the yen is currently weak, there is a limit in terms of the exchange rate to lowering the price of expensive rheumatoid drugs, which are almost exclusively imported. Also, financially, Japan's total healthcare costs are currently 43.4 trillion yen (10.6 trillion yen for drugs and 1.4 trillion yen for biomedicine in 2008), which accounts for more than 70% of all tax revenues of 58.7 trillion yen. The government's basic policy to control future healthcare costs is to increase the ratio of generic drugs to more than 80% and to recommend the use of biosimilars. For these reasons, RA physicians, who are required to pay high treatment costs, should also make efforts to reduce their own medical costs. Methods to control medical costs include (1) combination therapy with csDMARD, which is inexpensive, (2) selection of the most appropriate drug for each patient, (3) extension of dosing intervals or reduction of doses for patients whose symptoms have stabilized, and (4) application of biosimilars. This presentation report on the therapeutic effect of csDMARD triple therapy, the effect of reducing the bio-dose, the effect of extending the dosing interval, and the effect of biosimilars. Moreover, the presentation report the results of the calculation of the cost of lowering DAS28-CRP based on drug prices and the literatures.

S14-2

Clinical practice of rheumatic diseases at university hospitals -problems and management-

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Conflict of interest: None

Various clinical examinations, imaging examinations, and therapeutic agents are required for the treatment of connective tissue disease and rheumatoid arthritis. Especially in university hospitals, the target diseases are wide-ranging, and patients with first-onset cases of highly specialized rare diseases and patients with severe organ damage are outpatients and some are hospitalized. In general, many outpatient doctors at university hospitals are young doctors, and the doctors in charge often change. Since the knowledge and understanding of insurance medical treatment is not sufficient, education is necessary, but clinical knowledge acquisition is given priority. In addition, patients with rheumatic disease/connective tissue disease, regardless of whether they are inpatients or outpatients, may undergo frequent blood tests, which tends to increase the number of test items. Drugs are often multi-drug prescriptions, including high-price drugs such as molecular target drugs. However, it is not uncommon for the doctors not to reconsider the test items and the prescription drugs due to time constraints. At our department, we are trying to inform our doctors about items assessed inappropriate, but the assessment rate has not improved much. In addition, although medical fee of hospitalized patients is evaluated by using DPC, patients with severe connective tissue disease tend to spend more days in the hospital and have lower scores per day in the comprehensive evaluation part. In addition, there are many examinations necessary for differential/exclusive diagnosis and understanding of the clinical pictures. Especially, expensive PET-CT is taken for purposes such as evaluation of large vasculitis, but it is comprehensive and affects profits. In addition, rheumatic diseases are intractable diseases, and since there are many severe conditions and complications, the burden on ward doctors is not small. In the future, work-style reforms for doctors will become full-fledged, and it is hoped that a system will be created that will allow us to have appropriate health insurance system for patient treatment and receive medical fees that match the burden on the doctors.

S14-3

Practice of Rheumatology at Regional Core Hospitals -Problems and their Responses-

Takeshi Mochizuki
Department of Orthopedic Surgery, Kamagaya General Hospital

Conflict of interest: Yes

Our hospital is a medium-sized general hospital with 331 beds. It is the only hospital in the city that can treat rheumatoid arthritis (RA), and is responsible for diagnosis, treatment, and complications of rheumatism not only in the city as a medical area but also in surrounding areas. The outpatient care is not significantly different from that of the clinic, but the number of patients requiring intensified treatment or with complications tends to be higher. In this respect, the ability to perform a variety of tests immediately is an advantage. To manage complications and diagnose malignant tumors, cooperation with respiratory medicine, gastroenterology, and radiology requires. Since not only RA patients attending the hospital but also emergency RA patients are accepted, especially at night, pharmacists play a role in communicating drug characteristics to emergency physicians. Team care by nurses, pharmacists, and physiotherapists is essential in the

clinic, but one of problems is that there are transfers of staff from one position to another. The nurses who have previously obtained certification are responsible for education for the newly certified nurses. In addition, collaboration with nurses in hospital ward and outpatient care is essential in order to provide care to inpatients. In our hospital, rheumatology care nurses are assigned to both inpatient and outpatient care as much as possible. In surgery, we train operating room nurses in charge of orthopedic surgery to deepen their knowledge of joint surgery. In the surgery for RA patients with worsening HAQ, it is necessary to link the patient to a recovery hospital while considering the progress of rehabilitation. Continuation of team medicine with knowledge of RA is the biggest problem in hospitals, and continuous education is essential. In addition, the hospital needs to be able to maintain the cooperation with clinics and hospitals around our hospital, which is indispensable for rheumatology care.

S14-4

The Actual Condition of Rheumatoid Arthritis Treatment by Practitioners: Problems and Their Countermeasures

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Conflict of interest: None

In this study, we examined the actual treatment status of first-time patients and the results of treatment for elderly patients in their 80s. Actual condition of treatment of first-visit patients at our hospital We examined the background factors of patients who visited our clinic for the first time and remained highly active at the time of diagnosis. Subjects and Methods: 145 rheumatoid arthritis patients (107 women, mean age 61 years, mean disease duration 63 months) who were initially diagnosed between March 12, 2018 and February 17, 2020, followed up for at least 6 months, and had their activity assessed, were included. The clinical background of 34 patients (23%) who were still in HDA at the time of evaluation (mean 10.4 months) was compared with that of 111 other patients, and predictive factors for D2T were investigated. Results: D2T patients tended to have shorter disease duration and higher DAS28CRP than the other groups. Treatment status of elderly patients in the 80s attending our hospital We compared the activity and clinical background of 255 RA patients in their 80s at our hospital at the time of their first visit to two groups: the EORA group (patients who developed RA after age 60 and entered their 80s) and the YORA group (patients who developed RA before age 60 and entered their 80s). Results: The 255 patients were divided into two groups, EORA group (208 patients) and YORA group (47 patients), and their clinical characteristics at the first visit to the hospital were compared. 20% of the patients in EORA group were male, and 4% in YORA group. stage, class, renal function, and liver function were similar between the two groups. ESR, CRP, ACPA, MMP3, and DAS28CRP were all higher in the EORA group. Biologics and JAK inhibitors were used more frequently in the YORA group.

S14-5

The challenges of rheumatology treatment from the perspective of a rheumatologist in insurance medical care

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Conflict of interest: None

As rheumatologists, we have continued to provide rheumatoid arthritis (RA) treatment while struggling with various issues and burdens during the three years since 2020, under of the coronavirus pandemic. (1) Since the frequency of infectious diseases increases just by having RA, our clinic has set up a fever outpatient clinic. (2) Although it is not covered by insurance medical care, proactive coronavirus vaccination has been conducted mainly for the elderly as a national policy, in addition to the daily outpatient visit (which in itself has many inquiries) and combined with vaccination. Both doctors and staff are becoming increasingly fatigued. (3) In 2020, there were more patients who refrained from visiting, and further, there were those who requested self-suspension of visits or reduction of visit frequency (prolongation of intervals between visits). As a result, medical facilities were facing difficulties in medical management. In addition, there were incentives related to coronavirus diagnosis (300 points for internal triage implementation fee and 950 points for emergency medical management fee) and subsidies for securing coronavirus beds in the hospital, so there were facilities that remained in the black. (4) I have been working at the Hiroshima Prefectural Online Medical Center, Sendamachi Night Emergency Center, holiday duty doctors, Year-end and New Year's fixed-point medical care (Itsukaichi Memorial Hospital), and Hatsukaichi City PCR Test Center. (5) Elderly RA patients who are prone to hikikomori have often decreased physical strength, and communication work with patients, patient families, and care facilities has increased. (6) I would like to introduce concrete examples of rheumatology treatment utilizing online medical care and electronic medical information. Above all, I would like to share information on the issues of rheumatology treatment from the perspective of insurance medical care.

S14-6

Questionnaire Report from the Japanese College of Rheumatology Social Insurance Committee

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Conflict of interest: Yes

The Social Insurance Committee works on matters related to the health care services of autoimmune inflammatory rheumatic diseases handled by the Japanese College of Rheumatology (JCR). This committee has been discussing with the Ministry of Health, Labour and Welfare (MHLW) and government officials to ensure that rheumatologists can conduct their daily practices smoothly and with medical safety guaranteed. Depending on the situation, the committee makes requests on behalf of the society to organizations related to the MHLW for medical care and treatment not covered by insurance. This is because all Japanese citizens are covered by insurance, excluding traffic and industrial accidents, and the MHLW has jurisdiction over diseases. Once a year, the committee conducts a survey by questionnaire to the council members of this society, and discusses the items that were not approved for insurance billing in daily practice. The committee will respond to questions and interpretations regarding insurance claims by individual members of the society as much as possible, so that as many members as possible can make insurance claims without any problems and continue their daily medical activities amicably. We received over 20 inquiries for questionable interpretations from all over Japan. The committee discussed each one individually and divided them into questionable interpretations, requests to the authorities, and reminders to our member doctors. We then published in the newsletter, in order of priority, the cases that we believe need to be brought to the attention of our member doctors. We will also report on the JCR Questionnaire at this meeting. The JCR submitted six proposals, and "joint fluid testing" was included in the insurance coverage with the response that "it will be evaluated". We will continue to raise requests to improve the environment for appropriate medical treatment in 2024.

S15-1

Treatment of Systemic Sclerosis from a Dermatological Perspective

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Conflict of interest: None

Systemic sclerosis is a collagen disease characterized by fibrosis of the skin and internal organs and vascular lesions with a background of autoimmune phenomena. The vascular involvement of systemic sclerosis is characterized by Raynaud's phenomenon, nailfold hemorrhage, abnormal capillaries in the nailfold, telangiectasia, pitting scar, digital ulcers and gangrene in the skin, and pulmonary hypertension and scleroderma renal crisis in the visceral lesions. Many of these symptoms are included in the systemic sclerosis classification criteria and are important for diagnosis. Raynaud's phenomenon is often accompanied by pain and numbness, and greatly reduces the patient's quality of life. The first step in the treatment of Raynaud's phenomenon is lifestyle guidance. Patients should be instructed to quit smoking, use gloves and heat pack in winter, and avoid sudden tem-

perature changes. Medications such as vitamin E, prostaglandins, and calcium channel blockers are used for peripheral vasodilatation. Digital ulcers and gangrene are mainly caused by occlusive changes in the arteries and are associated with severe pain. They are often intractable and recurrent, due to decreased elasticity of the skin and complications of infection. The drug therapy for digital ulcers and gangrene includes treatment of Raynaud's phenomenon and oral administration of endothelin receptor antagonists. It is important not to perform amputation for digital ulcers and gangrene. In this lecture, the treatment of Raynaud's phenomenon and digital ulcers will be discussed mainly from the viewpoint of dermatology.

S15-2

Management of cardiac involvement and pulmonary hypertension in systemic sclerosis from the perspective of a cardiologist

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Conflict of interest: Yes

Pulmonary arterial hypertension (PAH) has attracted attention as a serious complication of systemic sclerosis (SSc) along with the dramatic progress in PAH specific agents. However, pulmonary hypertension (PH) associated with SSc includes not only PAH, but also PH associated with left heart disease (PVH) or interstitial lung disease (ILD-PH), and pulmonary veno-occlusive disease. In addition, it is necessary to distinguish whether PAH is caused by SSc or another connective tissue diseases in patients with overlap syndrome. Of course, this differentiation is quite important because different causes lead to different managements. However, it is often seen that this differentiation is insufficient in clinical practice. For example, PVH is diagnosed when pulmonary artery wedge pressure (PAWP) is no less than 16 mmHg, but this is not sufficient for differential diagnosis. It should be checked whether there is an increase in PAWP under saline load, but there are few facilities that carry out this examination. On the other hand, in patients with ILD-PH, administration of PAH specific agents is generally not recommended. However, there are some patients who respond well to acute pulmonary vasoreactivity tests and pulmonary vasodilators may be administered in such cases. In addition, cardiac involvement (CI) is also an important complication. Diastolic dysfunction due to myocardial fibrosis is frequently observed. However, only when it progresses to PVH, it is regarded as CI. The incidence of atrial fibrillation is high in patients with diastolic dysfunction, which often develops to heart failure, so early detection of diastolic dysfunction is considered important. At our institute, cardiologists intervene from an early stage to screen for CI and PH in SSc patients. I would like to discuss how cardiologists should be involved in the management of cardiovascular complications of SSc, while introducing efforts at our institution, such as early detection of CI using cardiac MRI.

S15-3

Characteristics and management of juvenile systemic sclerosis

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Conflict of interest: None

Juvenile systemic sclerosis (jSSc) is rare and is understood to account for 1-9% of all SSc cases. According to a nationwide epidemiological survey of jSSc conducted by the Research Group funded by the Ministry of Health, Labour and Welfare (MHLW) from 2020 to 2014, the number of patients in Japan is 1.8 per 100,000 population under 18 years old, with 0.2 new cases per year. Compared to adult-onset cases, jSSc tends to have fewer or less extensive organ involvement at the onset. Raynaud's phenomenon and positive antinuclear antibodies are the most frequent findings in the early stages of the disease and are present in more than 80% of cases. The Japanese diagnostic guidance for jSSc states that cases that do not meet the diagnostic criteria (2003) by the MHLW Group can be diagnosed as probable cases when characteristic skin pathology is observed. The ACR/EULAR classification criteria for SSc (2013), which have high sensitivity and specificity for SSc, including early stage, are reported to be useful for jSSc. The aforementioned nationwide epidemiological survey of 137 cases of Japanese jSSc showed a high rate of diffuse cutaneous SSc and a tendency for more cases to be positive for anti-Topoisomerase I antibodies compared to those in other countries. The organ complications during 8.1 years of observation were as follows; interstitial lung disease in 40.1%, gastroesophageal reflux in 33.6%, myositis in 12.4%, and pulmonary hypertension in 7.2%. No renal crisis was observed. There is also a possibility that the chronic course of the disease, especially in the diffuse cutaneous sclerosis type, may be significantly influenced by the appearance and progression of interstitial lung disease over the long term. It is essential to recognize the characteristics of jSSc because the time of potential organ involvement coincides with the transition from pediatric to adult care. Therefore, this session will outline the critical points, including management.

S15-4

Management of Dermatomyositis by Dermatologists, focusing on cutaneous manifestation

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Conflict of interest: Yes

Dermatomyositis (DM) is a collagen disease included in idiopathic inflammatory myopathies with specific cutaneous manifestations. In addition, myositis-specific autoantibodies have recently been identified in dermatomyositis cases, and are classified into subgroups based on differences in severity of myositis, interstitial pneumonia, and complication rates of malignant tumors. Skin manifestations also have characteristic signs due to myositis-specific autoantibodies. The typical Gottron papule is often seen in anti-TIF1γ antibody-positive cases, but other well-known examples include mechanic's hands in anti-synthetase antibody syndrome and violaceous palmar papules in anti-MDA5 antibody-positive cases. In anti-MDA5 antibody-positive cases, similar rashes may be seen in the antihelix/helix and sacral/pelvic area, which are favorable sites for bedsores, and unilateral heliotrope rash may be the initial eruption. In anti-SAE antibody-positive cases presented erythroderma avoiding the scapular regions, which we named the angel wing sign. Although many cases of anti-NXP2 antibody-positive cases lack DM-specific eruptions (heliotrope rash and gottron's papules and signs), subcutaneous edema and subcutaneous calcification are frequently observed. The DM-specific eruptions included in the diagnostic criteria are heliotrope rash and gottron's papules and signs, but other itchy erythematous lesions on the head, face, and trunk are also present, and reduce quality of life. It has been reported that there is no difference in ADL decline between amyopathic DM and classic DM with myositis. Not only amyopathic cases, but also some cases, in which myositis and interstitial pneumonia go into remission, but only skin symptoms persist or flare up, required treatments targeting rash. Topical application of steroids and tacrolimus and light-shielding are the basic treatments. However, almost cutaneous manifestations are refractory to the topical treatments. As for systemic therapy targeting skin symptoms, oral hydroxychloroquine, oral steroids, calcineurin inhibitors and mycophenolate mofetil have been suggested. In addition, high-dose intravenous immunoglobulin therapy was shown in a phase III trial to improve not only the overall myositis score but also the skin symptoms (CDASI score). Our group, as well as a group from the United States, reported a clinical trial of oral PDE4 inhibitors for treating DM cutaneous manifestations. I would like to suggest treatment options aimed at improving patient quality of life.

S15-5

Management of Interstitial Lung Disease with Dermatomyositis - from the View Point of Rheumatologists

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Conflict of interest: None

Dermatomyositis (DM) is often accompanied by interstitial lung disease (ILD) which is one of the important prognostic factors. So far, the prognosis of DM-ILD has been estimated by the absence of myositis or the disease progression of ILD, but recent studies have reported promising

new biomarkers for that. Myositis-specific autoantibodies (MSAs) are one of the most useful markers. Among MSAs, anti-aminoacyl-tRNA synthetase (ARS) antibody and anti-melanoma differentiation-associated gene 5 (MDA5) antibody have the strongest association with ILD with myositis. In Japan, anti-ARS can be detected in 40-50% of DM-ILD patients and anti-MDA5 also in 40-50%. ILD with anti-ARS tends to show chronic disease course and respond well to initial glucocorticoid (GC) therapy but often recur. On the other hand, anti-MDA5-positive patients often show rapidly progressive ILD which is resistant to immunosuppressive treatment. Anti-MDA5-positive DM-ILD seems to be more associated with type 1 interferonopathy than anti-ARS-positive DM-ILD. In anti-ARS-positive patients, treat-to-target is to suppress recurrence and progression of the disease with achieving minimal GC dose. With this respect, administration of immunosuppressants, such as calcineurin inhibitors (CNI), in early disease phase is suggested. Moreover, additional antifibrotic agents may give some benefits in patients with progressive fibrosing ILD. In anti-MDA5-positive patients, combined immunosuppressive therapy including high-dose GC, CNI and intravenous cyclophosphamide pulse in early stage of the disease has been widely used in Japan with increasing evidences for its effectiveness. Recently, JAK inhibitor or plasmapheresis has also been expected to be effective. In this symposium, the management of ILD associated with DM will be outlined from the perspective of a rheumatologist.

S15-6

Clinical key points of juvenile dermatomyositis -the differences from adult dermatomyositis-

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Conflict of interest: None

Juvenile dermatomyositis (JDM) is an autoimmune disease which is diagnosed under the age of 18. The common age of onset of illness is 5-10 years (median 7 years), and it is slightly predominant in female. More than 80% of JDM patients have characteristic skin symptoms such as heliotrope rash and Gottron's rash, as well as symmetrical proximal muscle weakness. As children cannot accurately communicate their symptoms, it is necessary to determine muscle weakness from a variety of their chief complaints. The evaluation of muscle strength is recommended internationally using manual muscle testing and the childhood myositis assessment scale (CMAS). The risk of malignancy in JDM is exceedingly low. Contrarily, subcutaneous calcifications, lipodystrophy, and gastrointestinal or skin ulcers are more frequently complicated compared to adult DM. The majority of JDM patients have myositis-specific autoantibodies, although the positivity of each antibody differs from that in adults. In Japan, anti-TIF1, anti-MJ (NXP2), and anti-MDA5 antibodies are common subgroups found in children. In contrast, the frequency of anti-ARS and anti-Mi-2 antibodies positive patients is lower than that of adults. The diagnostic criteria by Ministry of Health, Labour and Welfare research group (2015) and the EULAR/ACR classification criteria (2017) can be applicable to the diagnosis of JDM. Treatment is often initiated with methylprednisolone pulse therapy, and intravenous immunoglobulin and intravenous cyclophosphamide are used in patients with severe disease course. Immunosuppressive agents should be used as early as possible to reduce the cumulative dose of prednisolone, while taking into consideration the growth disturbances. Majority of JDM patients achieve remission, while the incidence of remaining severe functional disability is low. However, respiratory failure because of rapidly progressive interstitial lung disease is one of the most severe complications and requires careful initial treatment.

S16-1

Detection of tissue responses in rheumatic diseases by in vivo imaging

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S16-2

Synovial tissue macrophages in rheumatoid arthritis

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Conflict of interest: Yes

The pathogenesis of rheumatoid arthritis is increasingly recognised to comprise an early adaptive response associated with autoreactivity against modified self proteins. The chronic phase of disease comprises a rather significant stromal myeloid interaction that drives local inflammation and tissue damage. Our recent studies have identified that macrophages exist in functionally significant subsets within the RAE synovium and that their relative proportion can carry prognostic significance. This lecture will review the identity of these subsets and consider how they may drive the chronicity of disease.

S16-3

The mechanism of enhanced production of type I interferon in SLE

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S16-4

Immunophenotypic analysis of systemic lupus erythematosus

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Conflict of interest: Yes

The pathogenesis of systemic lupus erythematosus (SLE) is characterized by immune complexes consisting of antigens, activation of dendritic cells and autoreactive T cells and overproduction of autoantibodies secreted from activated B cells. Increasing evidence points to immunological heterogeneity that is regulated by genetic and epigenetic regulation in SLE. Indeed, molecular targeted therapy for SLE showed considerable variability of efficacy. To elucidate the therapeutic targets for human diseases, we have used an immunophenotyping approach to categorize patients with immune-mediated diseases into distinct subgroups. We have reported the followings: 1) active SLE patients can be divided into three subgroups based on T cell heterogeneity, including T follicular helper (Tfh) cell-dominant and T regulatory (Treg) cell-dominant group. The percentage of patients who were resistant to immunosuppressive treatment was highest in the Tfh cell-dominant group. 2) Tfh1 cells characteristically increased in SLE patients. Our in vitro analysis demonstrated that IL-12-mediated histone modification, resulting in development of Tfh1 cells. 3) By contrast, the proportion of T follicular regulatory (Tfr) cells and the ratio of Tfr/Tfh were decreased. Serum IL-2 levels decreased and exogeneous IL-2 induced conversion of Tfh cells to Tfr cells in SLE. 4) Tyk2 inhibitor suppresses IL-12-mediated Tfh1 cell differentiation while preserving IL-2-mediated Treg cell differentiation, suggesting that Tyk2 inhibitor has the potential to efficiently correct the "immune imbalance" in SLE. Our immunophenotypic analysis demonstrated that 1) subgrouping of heterogeneous diseases could be the basis for precision medicine, which would boost therapeutic strategies for clinically and molecularly heterogeneous diseases such as SLE, and 2) inhibition of Tfh1 cells by blocking Tyk2 or restoring of Tfr cells by promoting IL-2 signal may provide therapeutic approaches for SLE.

S16-5

Immunological pathogenesis of systemic lupus erythematosus revealed by the functional genome analysis

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Conflict of interest: Yes

The treatment of systemic lupus erythematosus (SLE), a prototype of systemic autoimmune disease, remains suboptimal and prognosis is not yet fully improved. Functional genomics, which integrates gene polymorphisms and gene expression, is a promising approach to elucidate the pathogenesis of SLE. We constructed a functional genome database named ImmuNexUT, which consists of 28 distinct immune cell subsets from 337 patients diagnosed with 10 categories of immune-mediated diseases and

79 healthy volunteers. For SLE, eQTL analysis and transcriptome analysis revealed that cellular metabolic pathways, including mitochondrial pathways, were enriched for genetic predisposition and associated with organ damage. When we identified signatures that are increased in clinically stable SLE (disease-state signature) and signatures that are increased in active SLE (disease-activity signature), effective immunosuppressive drug suppressed the disease-activity signature. Notably, the genetic risk of SLE reported by conventional GWAS is associated with the disease-state signature but not with the disease-activity signature, suggesting limitation of conventional GWAS in evaluating disease prognosis. In terms of adaptive immunity, analysis of the B cell repertoire in SLE revealed that a subgroup of IGHV family genes, whose expression is restricted to naive B cells in healthy individuals, are shared by memory B cells in association with type I interferon signalling. When we quantified this sharing as repertoire naïveness score (RNS), RNS exhibited significant association with disease activity of SLE. These results suggested the essential role of B cell repertoire abnormality in the development of SLE. Immunological pathogenesis of SLE is now being clarified through functional genome analysis. Integrated analysis of genetic predisposition and transcriptome reflecting environmental factors will help to elucidate the pathogenesis of autoimmune diseases.

S17-1

What NinJa has verified

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Conflict of interest: None

NinJa established in 2002 is the largest rheumatoid arthritis (RA) registry in Japan. NinJa continues to collect and analyze information on RA patients from cooperating facilities nationwide once a year. There were 12 participating facilities and about 3,000 registered RA patients in 2002, after that the number of facilities and patients has increased to around 50 and 15,000 respectively. In recent years, the number of registered RA patients is estimated to about 2% of RA patients in Japan. NinJa has revealed the following advances in RA treatment. 1) Improvement of disease activity 2) Improvement of physical function (ADL) 3) Improvement of quality of life (QOL) 4) Decrease in the frequency of use of steroids and NSAIDs 5) Decrease in artificial joint replacement surgery 6) Decrease in tuberculosis SIR 7) Improvement of life prognosis The driving force behind these improvements has been the evolution of the RA clinical environment (i.e., development of new anti-rheumatic drugs, revision of classification criteria for early diagnosis and treatment, formulation of T2T for tight control, and treatment of latent tuberculosis infection). On the other hand, NinJa has made it clear that there are still issues to be improved as shown below. We sincerely hope that these problems will be solved. 1) Complication of malignant lymphoma 2) Complication of interstitial pneumonia 3) Infectious diseases such as pneumonia as a cause of death 4) Expensive drug costs NinJa has observed changes in the actual clinical practice of RA in Japan for 20 years and clarified its progress and problems to be solved. These results have been obtained through collaboration facilities and rheumatologists nationwide. We express heartfelt gratitude to all who have contributed to the development of the NinJa. I hope that NinJa will continue to observe and verify the status and changes in RA treatment and play a role in widely reporting the results to RA patients, rheumatologists, and the public.

S17-2

Evolution of IORRA and progress in rheumatoid arthritis research

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Conflict of interest: None

Evidence of various aspects of rheumatoid arthritis (RA) derived from a prospective cohort study providing longitudinal analyses is essential for determining treatment strategy. IORRA study, implemented since October 2000, has built the database with information from the patients and doctors as well as laboratory, imaging and genetic data. Representative results of collaborative genetic studies from the IORRA cohort include identification of the new 34 variants through multi-ethnic genome-wide association study, and association between *RP3-UMAD1* locus and interstitial lung disease in RA. The association between the polygenic score for RA susceptibility and the progression of joint destruction was also reported. As for imaging, a high-performance scoring model for Sharp van der Heijde score using convolutional neural networks was constructed, and its clinical application was demonstrated. Comorbidities in patients with RA were investigated using IORRA database: international comparison of infections, malignancies, and major cardiovascular events across the large cohorts, longitudinal changes in incidences of malignancy and herpes zoster as well as the relevant risk factors, effects of chronic kidney disease on effectiveness and safety of RA treatment, and risk of osteoporosis. IORRA also revealed the changes in the numbers of overall and site-specific orthopedic surgeries for RA and disease activity at the time of surgery. Analyses of IORRA database showed that the less adequately treated rheumatoid arthritis is, the higher the cost of RA, and that the cost-effectiveness of biologics compared to methotrexate is acceptable. IORRA also demonstrated a better cost-effectiveness of abatacept when used as a first-line treatment compared to second-line treatment. Thus, the IORRA study has taken on a wide range of research issues from pre-onset to long-term prognosis of RA, and played an important role in establishing evidence for RA in Japan and abroad.

S17-3

The progress and establishment of RA therapy in clinical practice based on Tsurumai Biologics Communication

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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has made great progress in the past 20 years. Both of evidence from clinical trials of numerous biologics (Bio) and JAK inhibitors (JAKi) and validation by observational studies in real-world clinical practice have supported this progress. We have been continuing and disseminating information from a multicenter observational study (Tsurumai Biologics Communication Registry: TBCR, Mod Rheumatol 2012) on Bio/JAKi therapy conducted by the Department of Orthopaedic Surgery, Nagoya University and its affiliated hospitals. One of the keywords of the study is long-term treatment continuity, and the other is the significance of methotrexate (MTX) concomitant use in biologic and JAK inhibitor therapy. The learning curve for novel therapies can be seen from the improvement in Bio treatment continuity over time (Clin Rheumatol. 2016). It is thought that there is an improvement in recognition and knowledge of lung lesions and establishment of response to opportunistic infections such as TB and PCP. And, at the same time, possibly due to improvements in patient status over time with changes in treatment. MTX is considered an anchor drug for RA treatment, but in Japan, MTX dosage was limited to 8 mg/w when Bio therapy was approved in 2003, and the upper limit was raised to 16 mg in 2011. It had not been fully utilized in those days. In the TBCR, we have verified the relationship between MTX concomitant therapy and response to Bio treatment, the that between MTX concomitant use and persistence of Bio treatment, the persistence rate of Bio switch under low MTX doses, and the that between the frequency of arthroplasty and MTX concomitant use. The JCR RA guidelines, ACR, and EULAR treatment guidelines have been revised based on

information from many registries has supplemented the evidence. Although unmet needs remain, RA treatment is now well established. The process could be reviewed based on data from TBCR.

S17-4

Real-world evidence from the ANSWER cohort

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Conflict of interest: Yes

Real-world evidence is important to elucidate the clinical characteristics of patients with rheumatoid arthritis (RA) and to find out the optimal therapeutic options for individual patients whom we rheumatologists encounter in the daily clinical practice. We have established the ANSWER (Kansai consortium for well-being of rheumatic disease patients) cohort in which 150,000 longitudinal disease activity data from 10,000 RA patients are registered from seven universities and associated hospitals. We have presented the real-world evidences utilizing the ANSWER database. For example, we have determined the factors that was associated with the mortality risks in patients with RA complicated with interstitial pneumonia. We have also shown that persistent disease activity could deteriorate the kidney function utilizing the longitudinal data. We have also addressed which molecular targeted therapy is optimal for the patients who have particular clinical manifestations or serological markers utilizing the longitudinal disease activity or drug retention data. Such an evidence can be obtained only when we could utilize the qualified longitudinal big data. In this seminar, we will present the recent real-world evidences obtained from the ANSWER cohort. We also discuss the tips to establish and maintain the qualified big database.

S17-5

Tuning of the management of difficult to treat RA (D2T RA): from the real-world data of FIRST Registry

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Conflict of interest: Yes

Advances in molecularly targeted therapies have greatly improved the prognosis of rheumatoid arthritis (RA), and thus many patients have achieved clinical remission. On the other hand, there is a group of patients who remain symptomatic despite appropriate treatment. To better understand these patients, in 2020 EULAR defined difficult to treat (D2T) RA. Besides multidrug-resistant and refractory RA, which have received much attention, D2T RA also include conditions which have gathered less attention: non-inflammatory conditions (fibromyalgia, depression); impairment of treatment adherence; comorbidities/ complications. Importantly, patient representatives participated in the development of this definition, which seemingly encouraging rheumatologists to pay attention symptoms besides arthritis. In 2007, Japan became the first super-aged society in the world, and the aging rate still keep rising. Elderlies have the potential problems of: inadequate treatment due to comorbidities /complications; impaired treatment adherence due to depression, cognitive disorder, and polypharmacy; the high risk of bedridden due to polyarthritis. Elderly patients are also at high risk of adverse reaction to DMARDs, and thus are more likely to develop D2T RA. Together, elderly and D2T RA are non-separable, therefore rheumatologists in Japan are required to care those conditions at any time. Since D2T RA/elderlies comprise of multiple factors, treatment must be tailored to each condition; however specific approaches remain unclear. Under these circumstances, we have learned from FIRST Registry. In FIRST registry, 3233 patients have been registered 4716 times (as of November 2022). This session will address the findings from FIRST registry, (i) selection of bDMARDs for very elderly patients over 75 years old, (ii) prevention of infections during b/tsDMARDs treatment, (iii) usefulness of CT screening for malignancy, (iv) therapeutic strategies for refractory RA, and (v) the association between initial b/tsDMARDs therapy selection and future progression of D2T RA.

S18-1

Opening: The Role of Rheumatoid Orthopedic Surgeons in the Era of 100-Year Life -Proposals for the Future

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Conflict of interest: Yes

Drug therapy for rheumatoid arthritis (RA) has made great strides in recent years, with remission or low disease activity becoming a realistic goal. However, there are many problems in RA treatment that cannot be solved by drug therapy alone. The Rheumatoid Arthritis Clinical Practice Guidelines 2020 includes a non-pharmacological and surgical treatment algorithm, making it essential to understand and share this field. Even if the effects of drug treatment are obtained, if symptoms persist in minor joints, joint destruction occurs resulting in deformation or dysfunction, or if there are problems with appearance, brace therapy and intra-articular injection are included. Not only conservative treatment, but also surgical intervention considering the timing is important. Especially in today's age of 100-year lifespans, the situations in which patients are placed are diverse, and diversity is becoming a problem. In this symposium, we would like to have renowned rheumatoid arthritis orthopedic surgeons discuss the role of rheumatoid arthritis orthopedic surgeons in the era of 100-year lifespans from their respective standpoints, and to consider proposals for the future.

S18-2

Let's increase the number of rheumatoid arthritis specialist orthopedic surgeons! ~Efforts of Saga University Orthopedic Surgery~

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Conflict of interest: None

Rheumatoid arthritis patients are aging. Although the number of rheumatoid arthritis-related surgeries has decreased due to improved treatment results, the aging of rheumatoid arthritis patients will increase the number of cases requiring surgery for joints with degenerative changes. Therefore, the positioning of orthopedic surgeons who can accurately judge the indication and timing of surgery will become increasingly important in the future. As a result of young orthopedic surgeons becoming reluctant to participate in rheumatoid arthritis care, the percentage of orthopedic surgeons in the Japan College of Rheumatology is steadily declining. Many people become orthopedic surgeons because they want to perform surgery, but the real pleasure of RA treatment is that it involves not only surgical treatment but also drug treatment. Rheumatoid arthritis surgery that requires special attention should be performed by an orthopedic surgeon specializing in rheumatoid arthritis whenever possible. In recent years, there has been a conspicuous decline in the number of newly graduated doctors entering local university medical offices. Saga University Orthopedic Surgery is also having a hard time attracting new recruits. The ratio of female doctors is increasing year by year, but the ratio of female members of the Japanese Orthopedic Association is small. If the number of female orthopedic surgeons does not increase, the number of orthopedic surgeons will not increase. And the number of orthopedic surgeons specializing in rheumatoid arthritis will not increase. Rheumatoid arthritis treatment, which is mainly outpatient treatment, can be one of the subspecialties that can maintain a career for female doctors who are forced to change their work style due to life events.

S18-3

The role of rheumatic surgeons at university hospital in urban areas

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Conflict of interest: None

Recent remarkable advances in drug therapy for rheumatoid arthritis (RA) have changed the way orthopedic surgeons are involved in RA treatment. Recently, especially young orthopedic surgeons are moving away

from RA. Some possible reasons are as follows, 1) difficulty to catch up with new drugs, 2) decreasing appeal with decreased number of surgeries, and 3) feeling of difficulty to handle many joints at once. Treatment of RA patients requires not only the understanding of individual joints, but also the ability to grasp the patient holistically, including disease status, drug control, complications, rehabilitation, braces, social and psychological aspects, etc. The fact that it takes a considerable amount of time and effort to do so is also a factor that doctors dislike. However, the majority of patients complaining joint pain first visit an orthopedic surgeon, and orthopedic surgeons are best at examining bone and joint. Orthopedic surgeons are indispensable for RA treatment. One of the roles of university hospitals is education and training of human resources. Not all orthopedic surgeons need to be able to treat RA. However, all orthopedic surgeons should at least recognize that there are many opportunities to be the first touch in RA treatment, and be able to diagnose RA early and start appropriate treatment or hand over to a specialist so that patients can benefit from drug treatment. It is also necessary to continue training a certain number of rheumatic surgeons who can see RA joint lesions physically and over time. Providing advanced medical care and developing new medical technology is also one of the roles of university hospitals. Advances in drug therapy have reduced the number of surgeries for large joints, and have changed surgical needs to achieve higher ADL and QOL. Good control of disease activity and improvement of osteoporosis have made it possible to perform previously difficult surgical procedures, such as joint-sparing surgery and soft-tissue surgery, on RA patients. At university hospitals with experts in various fields, the collaboration between experts in each field and rheumatic surgeons makes it possible to update surgical procedures according to the changing times and provide feedback for them.

S18-4

Proposals for the future from the standpoint of the rheumatology center - Two important things to work on now -

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Conflict of interest: Yes

I would like to think of proposals for the future as proposals in 20 years before what it will be like in 20 years from now. Rapid advances in science and medicine are expanding the scope of medical care from patient to person, and now in 2023, we have entered an era in which prevention is considered at the healthy or pre-illness stage. The social system is also changing to support it, and the Apple Watch has already been approved as a medical device for electrocardiograph and heart rate monitor, and the option of removing cancer-free breasts and ovaries in patients with hereditary breast cancer ovarian cancer syndrome (HBOC) is in health insurance treatment. In addition, in order to prevent frailty and locomotive syndrome in the elderly, measures are being taken by focusing on lifestyle habits such as diet, nutrition, and physical activity, as well as living and social environments. Twenty years later, I believe that paradigm will have changed from the values and systems of medical care that are left untreated until a disease develops or dysfunction occurs to that avoiding it before onset of disease or disorder. So, what can be said as a proposal for the future is to focus on the pre-illness or early stage that the onset of disease or disorder can be prevented by surgical intervention, which is now left until onset or disorder. In case that there is already a surgical treatment, its spread and further improvement of technology will be promoted. In case that surgical treatment is still in development, its development will be promoted. For example, the treatment of rheumatoid foot deformity is the former, and cartilage regenerative medicine aimed at preserving joint structure and function is the latter. Rheumatoid foot deformity may not lead to a decrease in ADL or QOL due to compensation due to other bodily functions while young, but when compensatory ability decreases with age, physical activity decreases and frailty locomotive syndrome occurs. Regardless of whether it is the former or the latter, it is important to work on the promotion of preventive surgical intervention. And we should also work on the equalization of preventive surgical intervention, and its education for sustainable development.

S18-5

Treatment for Rheumatoid Arthritis by orthopedic rheumatologist in Akita Prefecture with a large elderly population

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Conflict of interest: None

Akita Prefecture has the highest population aging rate in Japan (38.8% in 2022) among the countries with the world's highest population aging rate (28.7% in 2021). In Akita Prefecture, orthopedic surgeons are responsible for the treatment of rheumatoid arthritis (RA) in large numbers, and there is an urgent need to improve the standard of RA treatment by orthopedic surgeons. Therefore, the Akita Orthopedic Group on RA (AORA) was established in 2010 with the aim of standardizing RA treatment and eliminating regional disparities. At the same time, registry (AORA registry) was started to visualize the level of treatment. The registry as a whole showed improvement in disease activity over time, but no improvement was observed in the group of patients aged 80 years or older. The elderly group had a high rate of pre-existing conditions and complications, a high rate and volume of PSL prescriptions, and inadequate MTX and b/tsDMARD prescriptions. Since 2017, we have been aiming for safe and high-quality RA treatment, and under the slogan of "Project to prevent the continuation of same drug use", we have been working to eliminate the randomization of NSAIDs and PSL administration, We aimed to introduce treatment of untreated osteoporosis. The AORA registry from 2017 was used for the study. The prescription rate of NSAIDs (including COX2 inhibitors) significantly decreased from 41.5% to 37.9%, and the prescription rate of acetaminophen and tramadol. The prescription rate of PSL decreased, and the prescribed dose significantly decreased. The treatment rate of osteoporosis increased over time from 39.5% to 47.1%, and the use of anti-RANKL monoclonal antibody drug increased. Discussion: The AORA registry has a high proportion of elderly patients, and it is important to protect renal function, avoid infectious diseases, and prevent osteoporosis. After the start of this project, there was no worsening of disease activity despite changes in prescribing trends. The presence of orthopedic surgeons who treat RA includes a thorough knowledge of joint examination, osteoporosis, and pain treatment. Pain in the elderly may be caused by factors other than RA, and there is no need to rely on NSAIDs. Physical therapy, rehabilitation, intra-articular injections, surgical treatment, and other treatments in which orthopedic surgeons have expertise may be safer and more effective than drug intensification for elderly RA patients. Thorough treatment of osteoporosis is also important.

S18-6

From the Rheumatology Clinic's Point of View

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Conflict of interest: None

The main role required for a clinic is "family doctor", which snuggle beside patients. Patients with RA must visit the clinic on a regular basis, the doctor checks for joint symptoms and adverse events, adjusts medications, and performs treatment. It is important to have a "family doctor" who can be consulted promptly in the event of exacerbation of joint symptoms or physical illness. In addition, it is also necessary to play the role of "Connecting" patients with RA to other medical institutions. It is a very important role to suggest possible surgical treatment and refer patients to appropriate medical institutions before their ADLs deteriorate. On the other hand, patients with RA may present with various complications such as infections or malignant diseases during treatment. It is essential for clinics to play a role of "Connecting" in protecting the lives of patients with RA by promptly referring them to the main hospital for close examination and treatment. Another role that clinics are expected to play is that of "Primary care". In rheumatology clinics, the role of "Primary care for joints" is fulfilled. Not all patients who come to the clinic complaining of stiffness or joint pain will be diagnosed with RA. Many patients present with joint symptoms due to a variety of factors, including musculoskeletal disease except RA, overuse, stress, menopausal symptoms, and psychiatric disorders. While the most important factor in providing appropriate medical care is to make an accurate diagnosis, it is also important to listen to the patient's complaints and seek solutions even in the absence of a clear diagnosis. It is the goal for all people to live a fulfilling 100-year life. Of course, patients with RA have the same goal, it is important to maintain energy and physical strength including maintaining disease control of RA. We are currently exploring what we can do to maintain and improve mindfulness and physical fitness, not only for patients but also for ourselves.

S19-1

COVID-19: Past and Future

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Conflict of interest: Yes

COVID-19 spread quickly around the world after being reported as a viral pneumonia of unknown cause in a seafood market in Wuhan, China, at the end of 2019. Initially, 5% of those infected became severely ill and the fatality rate exceeded 2% at one point. The government had issued a policy in the early stages of the epidemic that people who were not at risk of becoming seriously ill should seek medical institution if their symptoms persisted for four days. In the absence of a treatment option and vaccine, many patients became severely ill, leaving them with little choice. Three years after the pandemic, the mRNA vaccine has made a significant contribution to reducing the number of infected and seriously ill patients. In addition, although initially only severely ill patients were treated with dexamethasone and tocilizumab, gradually therapeutic agents were developed to prevent severe disease in mildly ill patients, and it became clear that early diagnosis and treatment could improve the prognosis. Thus, while great progress has been made in diagnosis, treatment, and prevention against COVID-19, SARS-CoV-2 has repeatedly mutated and changed its properties, acquiring abilities such as increased infectivity and immune escape. The effectiveness of conventional mRNA vaccines in preventing infection and disease onset has declined significantly, especially after the expansion of the Omicron variant, which infected many people; as of December 2022, one in four people in Japan is thought to have been infected with COVID-19 in the past, and a situation is gradually forming in which the spread of infection is becoming more difficult. In the future, the goal is to approach a situation where an epidemic is less likely to occur by slowly increasing the number of previously infected people while reducing the number of people who become seriously ill as much as possible and keeping the scale of the epidemic small.

S19-2

COVID-19 and Rheumatic Diseases; Similarities and Differences from an Immunological Perspective

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Conflict of interest: None

The coronavirus disease 2019 (COVID-19), caused by a novel corona virus named SARS-CoV-2, has emerged as a global pandemic. Although the early stage of the disease is characterized by the usual common cold symptoms, hyperferritinemia and liver damage suggestive of macrophage activation are observed in moderate to severe COVID-19, and the local and systemic "cytokine storm" are thought to be central pathogenesis of this disease. These pathogeneses are partly common among rheumatic musculoskeletal diseases including rheumatoid arthritis and adult Still's disease. When looking at COVID-19 from the perspective of lung injury with hyperferritinemia, the CT findings of rapidly progressive interstitial lung disease in anti-MDA5 antibody-positive dermatomyositis are similar to that in COVID-19. Interestingly, MDA5 is a virus recognition protein belonging to the RIG-1 family and is also known to be associated with coronavirus recognition, making the pathological similarities between autoimmune diseases and COVID-19. In addition to severe respiratory failure, one of the most characteristic features affecting the prognosis of COVID-19 is thrombosis, which occur in 30% to 50% of cases. it is well known that antiphospholipid antibodies such as lupus anticoagulants and anticardiolipin antibodies appear in those cases. On another front, the impact of these antiphospholipid antibodies on COVID-19 thrombosis and their association with prognosis varies from report, and many aspects remain inconclusive. The social impact of COVID-19 is indisputable; however, those autoimmune and inflammatory pathogenesis of COVID-19 had also given us an opportunity to reconsider the pathogenesis and pathophysiology of the rheumatic musculoskeletal diseases. In our session, we will review the relationship between COVID-19 and rheumatic diseases from an immunological point of view, as well as the effects of mRNA vaccination on the pathogenesis of autoimmune diseases.

S19-3

Advances in Vaccines and Medications Against COVID-19

Yasutaka Kimoto
Department of Rheumatology, Hematology and Metabolic Diseases, Kyushu University Beppu Hospital

Conflict of interest: Yes

The COVID-19 pandemic had a deep impact on the practice of rheumatic disease. In the early stages of the pandemic, the uncharacterized nature of the disease, the shortage of medical supplies, and the lack of therapeutic agents and treatment strategies caused a global confusion. Advancements in technology have provided a steady improvement in the healthcare circumstances. In December 2022, the following oral antiviral drugs were approved in Japan: molnupiravir, nirmatrelvir/ritonavir and ensitrelvir, as well as the injection drug remdecivir. Sotrovimab and casirivimab/imdevimab are approved as neutralizing antibody drugs, and dexamethasone, baricitinib, and tocilizumab as immunosuppressive and modulatory drugs. (including marketing authorization under the emergency approvals). For prevention, mRNA-based vaccine therapy has been successfully launched in clinical practice within a very short timespan. In patients with rheumatic diseases, the immunogenicity of vaccines may be reduced by drugs. For patients undergoing immunosuppressive therapy or chemotherapy who do not produce sufficient antibodies with vaccines, tixagevimab/cilgavimab, a long-acting antibody, is now available for use in the prevention of COVID-19. The pandemic has not yet resolved, with multiple waves of epidemics due to mutations in the genes of the virus. The pathogenicity and transmissibility of viruses and the efficacy of antibody therapies and vaccines have changed as a result of genetic mutations. vaccines against mutant viruses have already been introduced due to the rapid development of mRNA vaccines. Adequate use of the above drugs at appropriate timing is also desirable for patients with rheumatic diseases.

S19-4

Management of affected patients with the rheumatic diseases

Kenji Oku
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Conflict of interest: Yes

Rheumatic diseases put patients at risk for a variety of infectious diseases due to the immunosuppressive state induced by the underlying pathology and treatment. Infectious diseases often determine the prognosis of patients with rheumatic diseases and exacerbate the activity of rheumatic diseases, making it important to control the disease activity of both infections and rheumatic diseases. These are also evident in COVID-19 infection, and it is important to know how to continue or discontinue glucocorticoids, various immunosuppressive drugs, and molecular targeted therapies in the setting of infection. In some cases, the severity of illness may vary depending on the type and dosage of anti-rheumatic drugs, and treatment of infection should be adjusted accordingly. In this talk, I will review the management of patients with rheumatic diseases when COVID-19 is present, referring to the latest evidence.

S19-5

What rheumatologists can do to prepare for the next pandemic

Takuya Sawabe
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Conflict of interest: None

After the first official report of coronavirus disease 2019 (COVID-19) in Wuhan in December 2019, it spread worldwide in just a few months, leading to a pandemic. The wisdom of humanity has been concentrated to overcome this disaster, however, the pandemic has not ended by December 2022. These facts demonstrate the vulnerability of the current medical and social systems to a pandemic. Looking back, human history is also a history of battles against infectious diseases. Besides, there is a risk of pandemics of novel infectious diseases, such as highly virulent novel influenza viruses and drug-resistant bacteria. We need to use lessons learned from the COVID-19 pandemic to prepare for the next pandemic. Concerning the COVID-19 pandemic, many studies have been conducted, which made various recommendations. Clinicians are required to 1) identify and report infections which can be pandemic, 2) practice appropriate infectious disease care to prevent a pandemic, 3) block off transmission routes when an outbreak occurs, 4) collect updated information and provide appropriate medical care under the systematic medical system according to policy when a pandemic occurs, and 5) educate patient properly at all times. Rheumatologists should be aware of these requirements in their practice. Since physical examinations and laboratory test results are important in rheumatology practice, face-to-face medical consultation will remain the mainstream in normal times. However, telemedicine should be a powerful tool for dealing with outbreaks of infectious diseases, because the basic strategy for infection control is to block the route of infection. Therefore, it is necessary to explore a system of telemedicine which can provide appropriate rheumatology practice, and to shift promptly to the telemedicine system when an outbreak occurs. This presentation will summarize the lessons learned from the COVID-19 pandemic and discuss what rheumatologists can do to prepare for the next pandemic.

S20-1

Evaluation of the disease activity and therapeutic management of Takayasu arteritis

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Conflict of interest: Yes

Takayasu arteritis (TAK) is an autoimmune vasculitis mainly affecting aorta and its major branches. Although glucocorticoid (GC) is the mainstay for treatment of TAK, more than half of the patients with TAK relapse during tapering of GC. We conducted the TAKT study, a randomized, placebo-controlled, double-blind, phase 3 trial investigating the efficacy and safety of tocilizumab (TCZ), an anti-IL-6 receptor monoclonal antibody, for the treatment of refractory TAK. Although the primary endpoint was not met, the results suggested a benefit of tocilizumab over placebo in the time to relapse (Nakaoka et al. ARD 2018). After 96 weeks of TCZ treatment, the median glucocorticoid dosage was reduced to 0.105 (interquartile range 0.039-0.153) mg/kg/day, which was less than half that administered at the time of relapse before study entry. In addition, patients in the TAKT trial also reported clinically relevant improvements in patient-reported outcome measures (SF-36) with TCZ treatment (Nakaoka et al. Rheumatology 2020). In the post hoc analysis of the TAKT trial, we investigated whether TCZ treatment inhibited the progression of vascular lesions caused by TAK. Approximately 60% of patients with TAK did not experience progression in wall thickness within 96 weeks after initiation of TCZ. Few patients experienced progressed dilatation/aneurysm, or stenosis/occlusion. Wall thickness progression likely resulted from refractory TAK. Patients who experience wall thickness progression should be monitored regularly by imaging, and additional glucocorticoid or immunosuppressive treatment should be considered to avoid vascular progression (Nakaoka et al. Rheumatology 2022). In addition, I would like to touch on the topic regarding the alteration of gut microbiome in the patients with TAK, especially in relation to the vascular complication of TAK.

S20-2

Recent advances and challenges in the management of SLE

Eric F Morand
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Conflict of interest: Yes

Morbidity, quality of life, and mortality in patients with systemic lupus erythematosus (SLE, lupus) have changed little in the last 20 years. Recent approvals of medicines that address innate and adaptive immunity and local tissue pathology provide hope that outcomes will improve, but many challenges remain. The major advances in management of SLE can be compared to the paradigms learnt from rheumatoid arthritis, where clinical outcome studies and basic science discoveries converged to yield treat-to-target paradigms of care, and multiple highly effective new medicines. In SLE, operational definitions of low disease activity and remission have now been validated against damage accrual, low quality of life, and mortality, but formal treat to target intervention studies are needed to ensure that treatment escalation based on these endpoints is beneficial. Startling results of small uncontrolled studies of B cell targeting CAR-T cell therapy give hope that ‘new’ ways to address ‘old’ targets could yield major changes in lupus patient outcomes in the near future. In parallel, decades of study of human tissue which inform on the key role of type I interferons in lupus pathogenesis led to recent positive phase 2 and 3 trials of classical biological and small molecule drugs addressing ‘new’ targets in the innate immune system. Despite these advances, many challenges remain. Even targeted therapies are still notionally non-specific, as they target the healthy as well as the pathogenic function of the immune system. A future where only pathogenic autoimmune functions are targeted is emerging as technically achievable. For new medicines potentially available in the near future, patient selection for specific therapies remains a challenge. Finally despite improvements, clinical trials that do not yield clear results fail to inform on the value of the pathways targeted, and major changes in lupus trial methodology are needed.

S20-3

Recent advances and challenges in the management of systemic sclerosis

Vincent Cottin
Louis Pradel University Hospital and Claude Bernard University, France

S20-4

Recent advances and challenges in the management of dermatomyositis/polymyositis

Rohit Aggarwal
University of Pittsburgh Department of Medicine, Division of Rheumatology, Pittsburgh, USA

Conflict of interest: Yes

The idiopathic inflammatory myopathies (IIMs, also known as myositis), are rare, heterogeneous, autoimmune conditions leading to progressive muscle weakness, cutaneous manifestations, interstitial lung disease and several other manifestations. There are many contributory immunological pathways that are involved in the pathogenesis of myositis, leading to varying clinical phenotypic presentations, many of them associated with a specific myositis autoantibody. Targeting any one or several of these deleterious pathways with one or more therapeutic agent is reasonable, but there is a significant variability in response from patient to patient. Moreover, variable involvement of various extra-muscular organ, further complicates the management of myositis. There are very few large treatment clinical trials available to guide a uniform management approach, leading to heterogenous ways of treating myositis patients across the world. Recently, there have been significant advances in development of validated classification and outcome measures in myositis. Nevertheless, a multitude of immunosuppressive and immunomodulatory agents including steroid, methotrexate, azathioprine, mycophenolate, tacrolimus, cyclosporine is being used with variable success and significant side-effect due on reliance on high dose steroid for long period of time. Recently, regulatory agencies across the world approved 1st therapeutic agent i.e. IV immunoglobulin for dermatomyositis based on a phase 3 clinical trial. The emergence of biologic, small molecule, and other novel agents such as rituximab, abatacept, JAK/TYK inhibitors, anti-interferon therapy, etc, targeting potential pathogenic pathways offers hope for mitigating or curing this enigmatic group of diseases. However, these innovative approaches require careful examination of risk vs. benefit under well designed clinical trials with meaningful outcome measures.

S20-5

Recent advances and challenges in the concept and management of overlap syndrome including MCTD

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Conflict of interest: Yes

The etiology and pathogenesis of systemic autoimmune rheumatic diseases (SARDs) have not been clarified, and the development of diagnostic criteria has been pending for decades. Recent advances in the genome-wide association study elucidated the rather shared genetic predisposition among SARDs, which leads to the overlap syndrome in a portion of patients. The overlap of diseases may develop in the initial phase as well as in the later phases. Glucocorticoids have been the mainstay of the initial treatment of SARDs, although current recommendations encourage the concomitant use of immunosuppressive drugs or biological agents. Future proceeds in expanding indications of kinase inhibitors and biological agents may facilitate the use of those drugs in SARDs including overlap syndromes. Mixed connective tissue disease (MCTD) is a disease entity with characterized by overlapping clinical features of systemic lupus erythematosus, systemic sclerosis and polymyositis/dermatomyositis, as well as high titers of serum anti-U1 ribonucleoprotein antibody. In 2019, MCTD criteria have been revised by the Japan Research Committee of the Ministry of Health, Labor, and Welfare with identifying characteristic organ involvements such as pulmonary arterial hypertension, aseptic meningitis and trigeminal neuropathy, and the guideline for the management of MCTD has been published in 2021.

Special Symposium

SS1-1

Diversity in Medical care

Kyoko Tanebe
Women's Clinic We! TOYAMA

Conflict of interest: None

Japan's population will be approximately halved in the next 100 years. Japan will have no choice but to play all-hands-on-deck in securing the social security burden and labor force, and diversity and inclusion is not a mere joke, but an important policy for the survival of the nation. The success of a diverse workforce is a strength as a hedge against risk, and evolution occurs in the process of removing constraints that hinder their success. A typical example is gender equality, which is expected to promote gender equality as a human right, as well as to secure the labor force, economic growth, and a solution to the declining birthrate. The same is true in the medical field, where having a diverse workforce regardless of gender or age in an organization will lead to risk hedging, in other words, medical safety. In the Showa period, when medical care was based on doctors working long hours, personnel with time constraints due to child-rearing and other reasons have been marginalized. Unconscious prejudice can lead to a loss of motivation to work, conflict within the organization, loss of human resources, and a climate that makes medical accidents more likely to occur. Now is an opportune time to create an organization with high labor productivity by shifting from membership-based labor to job-based labor and aiming for all-hands-on-deck regardless of restrictions, as restrictions are being placed on working hours by force through reforms to the way doctors work. Specifically, unconscious biases and issues should be thoroughly visualized, learned, streamlined, and results shared within the organization. An open culture is essential to the effort, and managers with a strong will for reform are also needed. The Showa period is already over. Whether or not a hospital can survive as a vibrant organization with a diverse workforce depends on the mindset of its top management. Reforms in the way we work will not be possible without the centralization and focus of regional medical care, and the public will have to accept restrictions on access and the abolition of the primary care physician system, but on the other hand, it is also an opportunity to create new medical services and businesses that complement the concerns of the public. A change in thinking is required to ensure the viability and development of medical care as a form of social security.

SS2-1

Applying evidence to the practice of rheumatology in the Asia Pacific region: challenges and opportunities

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The Queen Elizabeth Hospital, Adelaide, Australia

Conflict of interest: None

The vast global burden of rheumatic diseases presents a particular challenge in the Asia Pacific region due to the diversity of disease prevalence, populations, languages, access to specialist care, and availability of therapeutic agents. In order to optimise evidence-based care, the best available evidence needs to be tailored to the unique local circumstances. Moreover, efficient systems to identify, appraise and collate the best evidence and implement it into practice are required to reduce redundant effort and enable the best use of scarce financial and human resources. The emergence and development of Living Evidence methodology in recent years allows for global evidence to be continuously appraised and summarised, and then applied to local clinical practice guidelines in a way that reduces redundancy and optimises the use of evidence in practice within different practice contexts. This presentation will describe living evidence methodology, the development of rheumatology living guidelines, and opportunities to further evolve this methodology within the APLAR region.

SS2-2

Genetic background in SLE - East Asian variants

Sang-cheol Bae
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Conflict of interest: None

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by diverse clinical manifestations with highly variable disease progression. A large heritability of up to 66% is estimated in SLE, with roughly 180 reported susceptibility loci that have been identified mostly by genome-wide association studies (GWASs) and account for approximately 30% of genetic heritability. For the last decade, large-scale, GWASs have efficiently scanned human disease genomes to identify the individual SLE loci in multiple ancestral populations, especially in Asian and European populations. Recently through the collaborative effort of the East Asian SLE genetics network, we newly genotyped 10,029 SLE cases and 180,167 controls and subsequently meta-analyzed them jointly with 3,348 SLE cases and 14,826 controls from published studies in East Asians. We identified 113 SLE susceptibility loci including 46 novel loci at genome-wide significance, with 169 association signals within non-HLA loci, now bringing the total SLE loci to ~180. A vast majority of risk variants reside in non-coding regions, which makes it quite challenging to interpret their functional implications in the SLE-affected immune system, suggesting the importance of understanding cell type-specific epigenetic regulation around SLE GWAS variants. The latest genetic studies have been highly fruitful as several dozens of SLE loci were newly discovered in the last few years and many loci have come to be understood in systemic approaches integrating GWAS signals with other biological resources. This talk will briefly summarize recent advances in our understanding of new SLE loci from East Asian studies, some critical variants, population-specific association heterogeneity, and variant-highlighted biology in SLE development and will touch examining polygenetic risk scores for SLE and their associations with clinical features.

SS2-3

A molecular approach to management of polygenic auto-inflammatory diseases

Ibrahim Almaghlouth
King Saud University, Riyadh, Saudi Arabia

Conflict of interest: Yes

Many of the adult onset autoinflammatory diseases are polygenic in nature. The complexity of their pathophysiology poses a potential challenge in their management. Commonly, treatment decision is based on available evidence that relies on the marginal effect on patients population. A complementary approach would include the available immunological abnormalities within individual patients. This presentation aim to shed light on the advancement in treatment strategy of common adult onset polygenic autoinflammatory diseases including adult onset still disease, SAPHO and Schnitzler's syndrome. A systematic search for the relevant articles addressing this topic for the last year will be conducted along with A case from our local practice. The presentation will focus on a molecular based approach and the available clinical evidence.

SS2-4

Takayasu arteritis (TAK) is not a young onset GCA - nor the vice versa

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Conflict of interest: None

Takayasu arteritis (TAK) is common in young Asians & GCA in older northern European ancestry with marked F: M in TAK. GCA specific features are polymyalgia, scalp tenderness, abnormal temporal artery, visual disturbance, constitutional & headache. TAK Specific features are carotidynia, claudication & other Stenotic symptoms, hypertension, pulse/BP discrepancy, bruit, aortic regurgitation. Angiographically, TAK & GCA differ in involvement of carotids, subclavian, vertebral, axillary & abdominal vessels. Six clusters of Imaging were noted in DCVAS - North American cohorts. Clusters 1, 2, & 3 i.e. Abdominal disease, symmetric arch disease & isolated left subclavian disease were TAK specific. While, cluster 6 in the North American and 5 & 6 in DCVAS cohort i.e. bilateral axillary disease and diffuse involvement without damage were GCA specific. Histopathologically, TAK has prominent inflammation of inner media & intima with excess adventitial fibrosis. Other differing features are fragmentation of internal elastic lamina, well circumscribed intimal, fibrocellular hyperplasia, focal aortic wall inflammation with 'skip lesions' & vessel wall thickness. Besides unique microbiota in TAK, mycobacterium tuberculosis (MTB) is implicated to trigger endogenous PRP- HSP65 interaction causing Ag presentation, T cell activation & recruitment in adventitia, giant cell granuloma formation in media & damage by cytokines from recruited cells in Intima & finally, vascular remodelling by VEGF and PDGF. In GCA, Burkholderia, Chlamydia pneumoniae & Varicella Zoster are suspected triggers leading to Th1 & TH17 activation at media & endothelium. There is no Gamma - delta T cell & NK cell recruitment unlike in TAK. Serum amyloid A, Pentraxins & recently reported apolipoprotein C2 & fibroblast growth factor 2 are biomarkers of disease / activity in TAK. Genetic associations of TAK include BW52, HLA B39, IL-6 & IL-12B (in Japanese), FCGR2A, LILR3B & PSMG1, while DR4 (HLA-DRB1*0401 and HLA-DRB1*0404), PLG, P4HA2 & PTPN22 are associated with GCA, suggesting GCA as MHC class 2 & TAK as class 1 associated disease. Benefit with Tocilizumab (TCZ) & steroids is clear in GCA & TAK, but it is modest to Methotrexate & Abatacept in GCA. TNFi failed in GCA &, Abatacept in TAK. Initial lower dose steroid, slower taper & upfront 2nd line immunosuppressant cause fewer relapse. TNFi > DMARDS / immunosuppressants > steroid alone, in that order, cause fewer new arterial lesions, maintain patency of revascularisation procedures. TNF & IL6 blockade with T2T using ITAS improve survival & delay relapse in TAK.

SS2-5

The APLAR 2021 Guidelines on the Management of Gout

Sami Salman
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Conflict of interest: None

The guidelines that will be presented in my lecture, are the output of the Asia-Pacific League of Associations for Rheumatology (APLAR) Task Force, that constitutes a joint undertaking of various APLAR nations.

I was elected to join the task force for setting these guidelines. The recommendations for each of the 20 prioritized clinical questions on gout are based on the synthesis and appraisal of the best available evidence, consideration of trade-offs between benefits and harms, accessibility, costs, appropriateness of therapeutic interventions, integration of patient values and preferences, and incorporation of different clinical practices.

SS3-1

Targeted therapies in rheumatoid arthritis: reality check

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Conflict of interest: None

Recent decades brought dramatic improvements in understanding of pathophysiology of rheumatoid arthritis (RA), leading to increasing recognition of the benefits of early treatment with disease modifying anti-rheumatic drugs (DMARDs), "treatto-target" approach, and discovery of an expanding range of innovative therapies targeting pathogenetically important pathways (i.e., inhibitors of tumor necrosis factor-alpha [TNFi], interleukin-6, Janus kinase [JAKi], etc.). Despite these advances in management, most patients with RA still don't fully benefit from available treatments and many suffer from chronic excessive inflammatory burden and adverse outcomes. Precise biomarkerdriven prediction of response to treatment in patients with RA is an area of active research but clinical implementation is lagging behind. In the meanwhile, "trial-and-error" approach for treatment of RA remains unchallenged. The objective of this talk is to discuss the current state of targeted therapies in improving outcomes in RA and to identify the key barriers for further improvement.

SS3-2

Advances in the Treatment of Systemic Sclerosis Associated Interstitial Lung Disease

Elizabeth R Volkmann

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Conflict of interest: Yes

Interstitial lung disease (ILD) affects the majority of patients with systemic sclerosis (SSc) and is the leading cause of SSc-related death. The therapeutic armamentarium for SSc-ILD has recently expanded. Treatments targeting diverse participants of inflammatory and fibrosing processes have demonstrated disease-modifying effects for SSc-ILD. These new treatments include mycophenolate, rituximab, tocilizumab, and nintedanib. However, questions remain regarding when to initiate therapy for SSc-ILD and how to personalize the treatment of SSc-ILD for the individual patient. Using a case-based format, this lecture will review recently published randomized controlled trials in SSc-ILD with a comprehensive discussion of the eligibility criteria, efficacy outcomes and safety profiles of current therapies. This lecture will also explain how to diagnose and monitor for progression of SSc-ILD using an evidence-based approach. The conclusion of the lecture will discuss emerging research in SSc-ILD, including the recent publication of an algorithm developed to predict progressive pulmonary fibrosis in this population.

SS4-1

Imaging in connective tissue diseases

Annamaria Iagnocco
Università degli Studi di Torino, Italy

Conflict of interest: None

Imaging is essential to the evaluation of organ involvement in patients with connective tissue diseases. The lecture “Imaging in connective tissue diseases” will present the state of the art on the role of imaging in connective tissue diseases and will discuss the potential of advanced imaging for assessing different organs in SLE, Systemic Sclerosis, Inflammatory Myopathies, and Sjogren Syndrome. The potential of imaging in advancing the field will be emphasized and new areas of research on imaging in the development of connective tissue diseases will be explored. Specific imaging applications for lung involvement, skin manifestations, salivary glands pathology, central nervous system abnormalities, and muscle lesions, will be presented with a particular focus on innovative imaging modalities. New imaging techniques that can detect disease in the early stage and continuously monitor its progression will be presented and discussed.

SS4-2

When Imaging meets clinical evaluation in RMDs: artifacts or reality?

Xenofon Baraliakos
Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Germany

Conflict of interest: None

The currently available imaging procedures have various possibilities to visualize or sometimes to predict the osteogenesis pathognomonic for axial spondylarthritis (axSpA). The individual imaging techniques of X-rays, computed tomography (CT) and magnetic resonance imaging (MRI) all have strengths and weaknesses in the diagnostics of axSpA. The generally easily available X-ray imaging rapidly provides information on the condition of large sections of the skeleton. In particular, it can depict the chronic stages with various structural alterations of the sacroiliac joint and syndesmophytes and ankylosis of the spine. The CT technique, which principally has the same contrast as X-rays, also shows pathological ossifications but without superimpositions, with better resolution of details and a higher dimensionality. The MRI technique has a superior soft tissue contrast so that acute inflammatory stages, such as bone marrow edema and erosion of the edges of vertebrae of the spine (shiny corners, Romanus lesions) or erosions and bone marrow edema of the sacroiliac joint are easily visible. Bony reconstruction processes can be visualized better in X-ray imaging and particularly in CT, which increases the evidential value of X-ray, CT and MRI techniques. The positions of conventional radiography and MRI are well-established in the diagnostic algorithm; however, low-dose CT of the spine is still in the experimental stage but the initial results look promising.

SS4-3

Remission criteria: do current definitions reflect a real remission?

Daniel Aletaha
Medical University of Vienna, Austria

SS4-4

Optimal treatment strategies in RMDs: is clinical guidance the best option?

Iain B McInnes
University of Glasgow, UK

Conflict of interest: Yes

The last two decades have brought remarkable advances in the range of modes of action in our therapeutics. This has lead to parallel improvement in the outcomes across a range of inflammatory arthropathies. The lecture will consider the additional value of strategic adjustment to the way in which different MOAs can be applied in the treatment of these chronic inflammatory conditions and will consider clinical paradigms, potential decision support from biomarkers and or imaging to further enhance the strategic approach to a patient throughout the disease trajectory.

Educational Lecture

EL1

Tuning of the management of difficult to treat RA (D2T RA): from the real-world data of FIRST Registry

Koshiro Sonomoto[1,2]
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Conflict of interest: Yes

Through the continuous and intensive effort for understanding the pathogenesis of rheumatoid arthritis (RA) and the development of new drugs, now we have 17 biologic/target-synthetic disease modifying anti-rheumatic drugs. A majority of the patients have benefited from these drugs and achieved clinical remission, while there is a certain group of patients who remain symptomatic despite appropriate treatment. To better understand this group, EULAR multidisciplinary taskforce comprised of physicians, patients, psychologists, and occupational therapist described the definition of D2T RA in 2020. Besides refractory RA, which have been the major research focus, the definition encompasses a wide range of conditions: non-inflammatory conditions (e.g., fibromyalgia, depression); impaired treatment adherence; comorbidities/complications. It is stated that this definition is not for research but for clinical practice, thus the definition seemingly encouraging the rheumatologists to pay attention to such conditions, which has not gathered much attention. Of note, above-mentioned components are shared between D2T RA and elderlies. Therefore, rheumatologist in the aged-countries always need to consider a variety of conditions when manage RA. However, due to its diversity, there is no single approach. Evidence should be accumulated to describe specific approaches to patients with a variety of conditions. In August 2003, we launched a registry of RA patients receiving b/tsDMARDs: FIRST registry. A total of 3233 patients from 27 medical institutions in 9 municipalities have been registered for 4716 times (as of November 2022). From FIRST registry we learned: (i) selection of bDMARDs in patients aged 75 years or older, (ii) prevention of infectious adverse events during b/tsDMARDs therapy, (iii) advantage of CT screening for malignancy compared to regular screening, (iv) treatment strategies for multidrug-resistant RA, and (v) the correlation of the 1st b/tsDMARDs and future progression of D2T RA. This session will discuss better practices in RA management using FIRST registry.

EL2

Synovial fluid analysis in rheumatic diseases

Naoto Yokogawa
Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

The 3C's (Cell count, Culture, Crystal) are essential in synovial fluid (SF) analysis: cell count, gram stain and culture, and crystal examination for monosodium urate (MSU) and calcium pyrophosphate (CPP). The gold standard for the diagnosis of crystal-induced arthritis is the identification of crystals by compensated polarized microscopy. Compensated polarized microscopy is not available in Japan but a polarizing device called U-GAN® is commonly used alternatively. We prospectively validated the crystal identification methods in 30 patients with knee joint effusion. We evaluated the non-centrifuged SF by three methods: ordinary microscopy, U-GAN®, compensated polarized microscopy, and compared the results with those obtained by a commercial laboratory (evaluation of sediment after centrifugation using U-GAN®). The results of the laboratory and our compensated polarized microscopy evaluation were in perfect agreement. The sensitivity of the ordinary microscopy evaluation was 73%, and the sensitivity of the evaluation using U-GAN® was 80%. In daily clinical practice, evaluation by ordinary microscopy without centrifugation is considered sufficient. As ultrasound-guided arthrodesis techniques becomes popular, we can obtain a very small amount of SF, which can be evaluated by rheumatologists if they know the procedure. Musculoskeletal ultrasound (MSUS) is helpful but cannot make a differential diagnosis of septic arthritis, gout, or pseudogout. We retrospectively reviewed of the findings of 16 patients who had MSUS among 30 hospitalized patients with crystal-proven gout. Only 7 patients had US findings consistent with gout. SF analysis was recently approved by national insurance in Japan but is still not available for clinics yet. It is urgent to establish the access to the testing. SF analysis should be included in the curriculum of rheumatology training.

EL3

An up-to-date on adult-onset acquired autoinflammatory diseases including VEXAS syndrome

Yohei Kirino
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Conflict of interest: Yes

Clonal hematopoiesis of indeterminate potential (CHIP) are found in approximately 5% to 10% of elderly healthy individuals and have been associated with various common diseases including cardiac disease and osteoporosis. The VEXAS syndrome, reported in 2020, is characterized by polychondritis, generalized skin rash, pulmonary infiltrates, high fever, arthritis, and myelodysplastic syndrome, and is caused by an acquired somatic variant of *UBA1*, a gene involved in E1 ubiquitination, in hematopoietic stem cells. Based on overseas reports, about 8,000 potential cases are expected in Japan. The clinical presentation of VEXAS syndrome is diverse, and it is often treated in rheumatology, dermatology, hematology, and general medicine departments. Most cases require high to moderate doses of steroid therapy for treatment, and steroid reduction results in flare-ups of fever, skin rash, and other symptoms, and many patients die from opportunistic infections. Other drugs such as methylation inhibitors, biologics, and molecular-targeted agents are being tried. From 2021, about 100 cases of suspected VEXAS syndrome will be collected from about 50 facilities in Japan for *UBA1* screening, and clinical characteristics of the positive cases are being identified. In this talk, I will present an overview of adult acquired autoinflammatory diseases including VEXAS syndrome and the latest findings.

EL4

Recent Clinical Research Topics ~time-dependent confounding and Directed Acyclic Graph (DAG)~

Nobuyuki Yajima[1,2,3]
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Conflict of interest: None

In this session, I will discuss my recent clinical research topics: time-dependent confounding adjustment and DAG. You may not adjust for confounding factors that change over time, but use baseline confounding information, but you may not be able to adjust for confounding adequately. If we can adjust for time-dependent confounding, we can broaden the scope of your study. G-estimation, marginal structural models (MSM), and other methods are used to deal with this problem. Next, we will introduce DAG (Directed acyclic graph). In recent papers, I have seen it attached as a figure. It is a graphical representation of causal relationships by connecting cause and effect with arrows. It is not only useful for extracting confounding factors, but also for sharing the same understanding among researchers and with reviewers. Terms such as conditioning, collider, and confluence will be explained and introduced with examples from the paper.

EL5-1

Diagnosis and Management of Psoriatic Arthritis

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Conflict of interest: Yes

Psoriatic arthritis (PsA) is associated with decreased quality of life. As delayed diagnosis may lead to progressive joint destruction and long-term disability, the key clinical features of PsA should be recognizable to a wide range of clinicians to facilitate early diagnosis. In addition to assessment and identification of skin and nail lesions, which occur in up to 85% of those with musculoskeletal manifestations, clinicians should be aware of both the peripheral and axial manifestations of musculoskeletal disease reviewed here. Peripheral joint disease includes polyarticular, oligoarticular, distal, arthritis mutilans subtypes, and cognizance of these patterns of disease, as well as periarticular manifestations, including dactylitis and enthesitis, is useful for swift diagnosis of PsA. Axial psoriatic arthritis (axial PsA), also known as the spondylitis subtype, may be limited to the spine and sacroiliac joints, but may also affect peripheral structures. Meticulous history-taking and physical examinations, and familiarity with appropriate imaging studies is often necessary to distinguish axial-PsA from other differential diagnoses. Swift diagnosis and treatment are necessary to both control PsA disease, and to mitigate the risks of the many associate comorbidities that may accompany it. In addition, T2T strategies such as assessing disease activity and background characteristics (presence or absence of co-morbidities) of individual patients should be taken into consideration when determining treatments, and all patients should be able to select appropriate drugs, including biologic agents, based on drug characteristics. In particular, I would like to discuss the mechanism of action of therapeutic agents, their efficacy and safety, including a review of clinical data.

EL5-2

Axial Spondyloarthritis in Japan

Tetsuya Tomita
Morinomiya University of Medical Sciences

Conflict of interest: Yes

Axial Spondyloarthritis (ax SpA) is a group of diseases that cause inflammation of the sacroiliac joint, which is the axial joint, and the ligament attachment of the spine. Sometimes peripheral arthritis also occur. It presents with various extra-articular symptoms such as anterior uveitis, cardiovascular disease, inflammatory bowel disease, and psoriasis. Ax SpA is defined by the classification criteria of the International Society for Evaluation of Spondyloarthritis (ASAS) in 2009, and is classified into radiographic ax SpA that meets the modified New York (NY) criteria and non-radiographic ax SpA. A typical disease of r-ax SpA is ankylosing spondylitis; AS). AS basically develops under the age of 45 and is more common in men. It is believed that ankylosis of the whole spine occurs in 30-40%. It has been strongly associated with HLA B-27 and is considered to be a rare disease in Japan, where the prevalence of HLA B-27 is extremely low. The axSpA National-wide Epidemiological Survey in Japan, first conducted in 2018, estimated that there were 3,200 patients with AS. Nr-ax SpA was considered to be a precursor or mild case of AS, but recent reports indicate that the disruption of the axial joint structure on images does not progress over time, but the clinical burdens are no different from AS. In Japan, the number is estimated to be 800. Nr-ax SpA is more common in women, and the proportion of carriers of HLA B-27 is lower than that of AS. TNF inhibitors and IL-17 inhibitors have been approved for AS since 2010, and JAK inhibitors have been approved in 2022, and treatment options are increasing. On the other hand, there are increasing cases of inappropriate use of therapeutic drugs due to mis-diagnosis and over-diagnosis. Psoriatic arthritis is one of peripheral spondyloarthritis, Previously, it was reported that only 5% of patients had axial disease, but recent surveys have shown that about 30% of patients have axial disease.

EL6

Responding to Patient Harassment and Patient Violence

Giichiro Oiso
Hamamatsu University School of Medicine

Conflict of interest: None

Patient violence is a problem in health and care settings around the world. This situation led to the 2012 WMA Statement on Violence by Patients and Related Persons in the Healthcare Sector, which states, “The State has an obligation to ensure the safety and security of patients and physicians and other healthcare workers. Violence in the workplace includes both physical and non-physical (psychological) violence. Given that non-physical abuse, such as harassment and intimidation, can have serious psychological consequences, a broad definition of workplace violence should be used. National medical associations should encourage each medical institution to develop and implement protocols to address acts of violence. Protocols should include the following:” and a “zero-tolerance policy toward violence in the workplace”, among other things. In response to these social conditions, the provisions of the revised Medical Care Law regarding the improvement of the working environment of medical institutions went into effect in 2014. At the same time, the “Guidelines for Management Systems to Improve the Working Environment of Medical Institutions” (Ministry of Health, Labor and Welfare Notice No. 376, September 26, 2014) was issued, requiring the introduction of a management system to improve the working environment, including a systematic response to violence and harassment. On the other hand, even if a patient has been subjected to violence or harassment, the fact remains that the patient still needs to be examined and treated, and the question arises as to how the refusal of further medical treatment based on such violence or harassment should be considered in relation to the duty of invitation (Article 19, Paragraph 1 of the Medical Practitioners Act). According to the “Guidelines for appropriate responses to requests for medical examination and treatment, including the obligation to be invited” (Medical Policy Bulletin 1225, No. 4 December 25, 2019), a patient’s disruptive behavior is considered to be “a case where the relationship of trust that forms the basis of medical treatment is lost in light of the manner in which the disruptive behavior occurred or is occurring during medical treatment or medical care”. The refusal to provide new medical treatment is justified such as in cases where the patient continues to make repeated complaints that have nothing to do with the medical treatment itself. In this presentation, I will introduce some cases of patient violence and harassment, and then discuss what kind of cases can justify refusal of medical treatment.

EL7

Autoinflammatory disorders up to date 2023

Hidenori Ohnishi
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Conflict of interest: Yes

Autoinflammatory disorders (AID) are classified as a category in the International Union of Immunological Societies (IUIS) classification of Inborn Errors of Immunity (IEI). The 2022 edition of the IEI registers 485 diseases, 56 of which are AIDs, an increase of 14 diseases from the 2019 edition. The basic pathogenesis of AID is the overproduction of IL-1beta due to the excess activation of the NLRP3 inflammasome, but recently diseases have been discovered that cause abnormal inflammasome activation based on NLRC4 or Pyrin, which are sensor molecules as well as NLRP3. Although these diseases are basically chronic inflammatory diseases caused by an excess of the innate immune system, the concept of these diseases has been expanding with the recent discovery of a number of new diseases that are associated with immunodeficiency and autoimmune diseases. A group of diseases in which inflammatory cytokines other than IL-1beta form the primary pathogenesis have also been identified, with type I interferonopathy being a representative one. In addition, a new disease concept, late-onset AID caused by somatic mosaic mutations, was reported in 2020 as VEXAS syndrome, an adult-onset systemic autoinflammatory condition caused by somatic mutation of UBA1 gene. The number of case reports in Japan suggests that VEXAS syndrome is a highly prevalent disease. There have been reports of cases of late onset of autoinflammatory pathology caused by somatic mosaic mutations in NLRP3, NLRC4, and MyD88 genes, and it is thought to be a disease etiology that will attract more attention in the future. The research group for autoinflammatory disorders funded by the Ministry of Health, Labour and Welfare is currently preparing guidelines for the management of these diseases, and the recent information will be reviewed in this session.

EL8

Introduction to Statistical Data Analysis Involving Realworld Data

Ayumi Shintani
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Conflict of interest: None

Randomized controlled trials are considered to have the highest level of evidence for clinical research. This is because randomization allows to have a similar backgroup between the comparison groups which allows direct comparison of outcomes. However, interventional studies such as randomized controlled trials have the disadvantage that the inclusion criteria are rigid, it is difficult to reflect actual clinical practice, and subjects with a strong desire to get better are included, making it more likely that the prognosis will be better than in actual clinical practice, and the effect of the therapeutic agent is less likely to be seen. On the other hand, in observational studies (e.g., registry studies) using actual clinical results, treatments are selected based on various patient backgrounds, making direct comparison of outcomes difficult because of differences in patient characteristics between the treated and untreated control groups. Ignoring this difference in the analysis often leads to unexpected results, such as no effect or even harm from the treatment under study, since the treated group is often sicker than the control group. This incorrect analysis of the effect of treatment due to differences in patient background between comparison groups is called "confounding" and is a problem in many real-world data analyses. The ability to prevent this confounding is an important point to improve the science of research using real-world data. In order to prevent confounding, statistical models called multivariable regressions and Propensity scome methods are commonly used to adjust for background data discrepancies. In this lecture, I will explain the importance of utilizing real-world data in clinical research, its analysis methods, interpretation of results, and cautions for its use.

EL9

The pathophysiology and management of osteoporosis in patients with rheumatic disease

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Conflict of interest: None

It is well known that patients with rheumatoid arthritis (RA) are more likely to have osteoporosis. The cause is related to the disease activity of RA, the decrease in physical activity associated with joint destruction, the postmenopausal osteoporosis, and the use of steroids. Since RA is a disease that causes joint destruction, it is not difficult to imagine that osteoclasts are activated locally in the joints, but it has a great effect on bone metabolism not only joints but also whole body. Inflammatory cytokines and osteoclast activation are closely related, and it is possible that controlling inflammation and disease activity may be effective for osteoporosis in RA. The control of disease activity in RA has improved dramatically. Controlling the disease activity can be prevented the decrease of bone density, but it cannot be expected to significantly increase bone density. Therefore, for osteoporosis associated with RA, it is necessary to use therapeutic drugs for osteoporosis in combination with anti-rheumatic drugs. To date, the concept of difficult to treat RA, in which disease activity cannot be well controlled, has been proposed, and the definition of difficult to treat RA includes the patients that glucocorticoid cannot be reduced. It is well known that glucocorticoid use is a risk factor for osteoporosis, but since osteoporosis due to glucocorticoid is also associated with deterioration of bone quality that cannot be evaluated by bone density. It is necessary to evaluate the risk by using the scoring in the management and treatment guidelines for glucocorticoid-induced osteoporosis and use appropriate osteoporosis therapeutic drugs in RA patients with glucocorticoid use. RA cannot be cured, so it is necessary to continue treatment, and it is also necessary to continue treatment for osteoporosis. In this session, you can learn the pathophysiology, and the points of treatment strategies for osteoporosis in RA.

EL10

ABC in muscle pathology

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Conflict of interest: Yes

Muscle fibers should be evaluated with attention to their distribution within or by the fascicles. Endomysium and perimysium should be clearly differentiated. A perivascular cuffing in the perimysium, albeit often seen in myositis, is essentially nonspecific and the diagnose of myositis should not be made based upon this finding. The endomysial cytotoxic T cells infiltration, surrounding and invading into non-necrotic fibers, is diagnostic of polymyositis (PM) and inclusion body myositis (IBM). However, in the early 2000s, it was pointed out that most clinical PM cases pathologically show necrotizing myopathy while only few cases show pathological PM and most of them evolve into IBM. IBM is pathologically characterized by rimmed vacuoles or p62 and TDP-43 aggregates, in addition to endomysial lymphocyte infiltration. Clinically, IBM is characterized by muscle weakness and atrophy in the quadriceps and finger flexors in elderly patients. It is now increasingly believed that there is no such disease that fulfills the pathological criteria of PM. Necrotizing myopathy, typically seen in cases with clinical PM, is now recognized as a subtype of myositis, immune-mediated necrotizing myopathy, for which C5b-9 deposition on the sarcolemma is considered to be diagnostic. Perifascicular atrophy is a well known finding of DM. In 2005, Greenberg et al. reported that the genes induced by type I interferon (IFN1) are highly expressed in DM muscles, and DM is increasingly recognized as a type I interferonopathy. On muscle pathology, the expression of MxA, an IFN1 marker, can be confirmed by immunohistochemistry, which is more useful for the diagnosis than perifascicular atrophy. Antisynthetase syndrome (ASS), serologically characterized by the presence of anti-ARS antibodies, is often diagnosed clinically as DM or PM, but have recently been classified as a new subtype of myositis. Pathologically, ASS is characterized by perifascicular necrosis and perimysial pathology.

EL11

Utilization and Future Prospects of AI and IoT in Rheumatology

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Conflict of interest: Yes

There are high expectations for the application of artificial intelligence (AI) and IoT (Internet of Things) to medicine, including the management and operation of big data, the construction of information databases, and the integration of a wide range of advanced research results. The Japan College of Rheumatology (JCR) formed the Committee AI and was entrusted with the GSK medical education project subsidy in 2018 held for four years. The themes of the four-year symposium were basically divided into "AI research-oriented" and "IoT research-oriented". In 2019, we focused on the world's most advanced "Microsoft's latest technology", "cancer genomic medicine" and "computer-aided diagnosis of medical images" from three keynote lectures. From 2020, we have set a key theme for each year, incorporating content that is close to social implementation, and adding research results from JCR and related academic members. In 2020, the keynote lectures were "AI-based real-time endoscopic diagnosis support system for colorectal tumors" and "Research and development for the realization of personalized cancer medicine" as well as the two presentations from JCR members regarding to "Utilization of images, AI and IoT in rheumatology medical practice". In 2021, the keynote lectures were "Application of machine learning in immunogenetic research" and "Application of deep learning technology to renal biopsy pathological images". "Diagnostic support for IgG4-related diseases based on machine learning" and "Spinel surgery and digital transformation" were introduced by the two academic members. In 2022, we selected "the interpretation of joint X-ray images using AI", "the use of AI in functional genetics", and the progress of research from two members who once made presentations in 2019. Through these four years of educational symposiums, we have experienced rapid technological innovation, and in this lecture, we will summarize these findings and discuss future prospects.

EL12

Outcome Measures in Systemic Sclerosis

Dinesh Khanna
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Conflict of interest: None

Systemic sclerosis (scleroderma, SSc) has seen a substantial progress in the development and validation of outcome measures over last decade. This presentation will discuss the outcome measures ready for clinical trials in SSc, including recent work by the NIH funded White Paper initiative to provide regulatory approvable outcome measures. The presentation will focus on skin, lungs, and composite endpoints, including the ACR CRISS and Revised CRISS, which are the global outcome measures to assess stabilization/ improvement. In addition, I will present preliminary outcome measures that are endorsed by the NIH funded White Paper initiative for Raynaud's phenomenon, digital ulcers, and biomarkers.

EL13

Novel aspects of immunological memory revealed by SARS-CoV-2 virus

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Conflict of interest: None

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viruses highlights the importance of vaccine for counteracting the threats by emerging and re-emerging infectious diseases. Rapid development of vaccines with new modalities accelerated the immunization into populations with multiple backgrounds, and lead to the clinical studies on COVID-19 vaccinees and convalescent individuals. Immunological memory is a phenomenon behind the vaccine-elicited protective immunity, but the dysfunction may also lead to the pathogenesis of autoimmunity. High-dimensional profiling of antibodies and memory lymphocytes against SARS-CoV-2 viruses revealed that they are more diverse and flexible in the antigen specificity than previous appreciated. Indeed, the repeated vaccination by ancestral vaccine strain expanded the breadth of specificity in elicited antibodies to be effective against antigenically diverse variants, instead of being more specific to the ancestral strain. The phenomenon greatly contributed to the vaccine strategy to provide protective immunity against Omicron variants with dramatic shift in the antigenicity. However, it also needs to be optimally regulated as the dysfunction increases the risk for autoimmunity. Here, I will introduce novel aspects of immunological memory which were shown by the studies on COVID-19 convalescent and vaccinated individuals.

EL14

Patient Safety

Yoshimasa Nagao
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Conflict of interest: Yes

In Japan, patient safety activity has started due to the some severe malpractices which occurred in 1999. After that, various measures have been performed. From 2015 to 2016, in a scientific research supported by the Ministry of Health, Labor and Welfare, we classified the patient safety activity which should be performed in hospital to "emergency phase" and "usual phase", and showed a picture of works in one schema (The loop of patient safety activity). In "emergency phase", we need the following works. 1. Treatment cooperation which crossed departments. 2. Open-disclosure to a patient. 3. Judgement of necessity of a report to a medical accident investigation center. 4. Medical accident investigation and making on a report. 5. Explanation the result of investigation to the patient family. Some measures for recurrence preventive are leaded from the investigations. Failure of initial action in "emergency phase" leads the hospital to huge risk. In "usual phase", we need the following works. 1. Collection on incident reports. 2. Root cause Analysis and search of a problem. 3. Reconsideration of rules or procedures. 4. Training and education. 5. Patrol in a site. The validity of the quality control technique in the hospital is pointed out. Appropriate utilization of a mathematical method is useful to lead a good outcome. "Usual phase" is connected with "emergency phase" complementarily. It's necessary to recognize the patient safety activity as core action, not an option, and build governance appropriate to make these something useful. I'd like to explain the picture of patient safety activity introducing some recent topics.

EL15

How to Write an Acceptable Medical Paper

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Conflict of interest: None

All the thinking, all the analysis, all the experiment, and the data gathering are nothing until we write them up. In the world of scholarship, we are what we write. Many researchers find it difficult to write a paper. They feel difficulty in summarizing the results of observations and experiments that they have worked so hard on, and they are reluctant to write a paper. However, no job is finished until the paperwork is done. We should write papers for peer-reviewed journals, especially original articles. An original article is (1) the first publication of original research results, (2) written in a format that allows the reproduction of experiments and analyses and verification of results and conclusions, and (3) published in a peer-reviewed journal and cited by readers. In this lecture, I will explain the iron-clad rule of "fool-proof English", a writing technique that can be used by non-native English speakers and that eliminates all redundant and ambiguous expressions. I will also explain several writing skills: how to use verbs, adjectives, and adverbs that frequently appear in scientific papers and how to connect sentences. Furthermore, I will explain how to write papers with a strong focus on logic and organization. Writing procedures for each part of an original paper (Introduction, Methods, Results, Discussion, Abstract, Title) will be explained. Finally, I will also outline how to respond to peer review comments.

EL16

IgG4-related disease, idiopathic multicentric Castleman disease, and TAFRO syndrome. An update

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Conflict of interest: None

IgG4-related disease (IgG4-RD) is a newly recognized systemic disease, which can affect almost any organ in the body, and it mainly affects elderly men. The most frequently involved organs are the salivary glands, lacrimal glands, retroperitoneum/periaorta, kidneys, and pancreas. Although the lymph node (LN) is a frequently affected organ in IgG4-RD, differentiation between LN lesions of IgG4-related lymphadenopathy and those of idiopathic multicentric Castleman disease (iMCD) is sometimes very difficult. In such cases, the presence of lacrimal or salivary glands or pancreatic lesions will support the diagnosis of iMCD. On the other hand, retroperitoneal fibrosis or IgG4-positive plasma cell-rich tubulointerstitial nephritis is a common feature between these two diseases, and the presence of these lesions may lead to misdiagnosis. In addition, elevated serum IgG levels or elevated serum IgE levels can be seen in some patients with IgG4-RD. However, persistently elevated serum C-reactive protein levels or an incomplete response to the glucocorticoid therapy will support the diagnosis of iMCD, and these two diseases are easily differentiated by these features. TAFRO syndrome is a subtype of iMCD, but its clinical course is very different from iMCD. TAFRO syndrome ischaracterized by thrombocytopenia (T), anasarca (A), fever (F), reticulin fibrosis or renal insufficiency (R), and organomegaly (O). Histopathological findings of the lymph nodes of TAFRO syndrome is quite similar to those of iMCD. In TAFRO syndrome, the size of lymphadenopathy is not so large, and serum IgG levels are usually mildly elevated. Recently, it has been revealed that thrombotic microangiopathy is a typical histopathological feature of affected kidneys by TAFRO syndrome. In this lecture, I will focus on recent advances in the understanding of IgG4-RD, iMCD, and TAFRO syndrome.

EL17

Musculoskeletal MR imaging of rheumatological diseases

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Conflict of interest: None

Imaging is one of the indispensable tools for the diagnosis and treatment of rheumatic diseases. Radiographs are the basis. In the appendicular skeleton, the usefulness of ultrasonography has been widely recognized, and it has come to be used as well as a stethoscope in actual clinical practice. While, in the axial skeleton, MRI, which does not expose the patient to radiation, is still the main examination because there are many restrictions on the observation range of ultrasound in this area. In this session, I will focus on spondyloarthritis (SpA), which mainly involves the axial skeleton, allied disorders of SpA such as SAPHO syndrome, and crystal-induced arthritis in the axial skeleton. I will outline the characteristics of MRI sequences, how to interpret imaging findings, and important findings for differentiating other diseases. In the appendicular skeletons as well, I plan to explain MRI findings and pitfalls while presenting images of rheumatoid arthritis, polymyalgia rheumatoid arthritis, crystal-induced arthritis, and myositis. In recent years, the development and evolution of hardware for both MRI and CT have been remarkable. Due to the application of artificial intelligence (AI) technology, the accompanying software also continues to evolve remarkably. We are living in an era where even radiologists cannot keep up with these evolution without annual updates. Therefore, in this presentation, I will include a future forecast of what can be done with the MR imaging method now and what it will be possible in the future. I would also like to mention MR sequences that are useful in diagnosis in daily clinical practice or clinical research.

EL18

Clinical update on vasculitis syndrome

Ken-ei Sada
Clinical Epidemiology, Kochi Medical School

Conflict of interest: Yes

Vasculitis syndromes are classified by the Chapel Hill Classification 2012 as large, medium, or small vessel vasculitis, mainly based on the size of the affected vessels. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis is classified as small vessel vasculitis and includes three diseases: microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA). New classification criteria were proposed by EULAR/ACR in 2022, weighting differences in ANCA types, interstitial lung disease, and type of upper respiratory improvements. These criteria contribute to reduce unclassifiable patients in the Japanese population than the previous epidemiologic classification algorithm. In treatment, new evidences have been added, such as rituximab in maintenance therapy, mepolizumab for EGPA, glucocorticoids reduction regimen, and the position of plasma exchange. Additionally, avacopan, an inhibitor of the complement C5a receptor, is expected to improve safety and reduce chronic damage in the patients with MPA or GPA. A revised guideline for the treatment of ANCA-associated vasculitis, incorporating these new evidences, is scheduled for publication in 2023. Clinical evidence has limited for polyarteritis nodosa, which is classified as medium-sized vessel vasculitis, the Research Committee of Intractable Vasculitis Syndrome of Ministry of Health, Labour and Welfare has proposed a treatment recommendation based on current available evidence from a systematic review in 2020. For Takayasu's arteritis and giant cell arteritis, which are classified as large vessel vasculitis, the combination of glucocorticoids and tocilizumab has reported as a useful treatment option, based on the results of the TAKT study conducted in Japan for refractory Takayasu's arteritis and GiACTA study in western countries for refractory giant cell arteritis, respectively. In 2017 Japanese Circulation Society guidelines on Management of Vasculitis Syndrome, concomitant tocilizumab use is recommended for refractory cases. Although monitoring of disease activity is sometimes difficult in the patients under tocilizumab treatment because C-reactive protein turn into negative, PET-CT is now available for evaluation of disease activity of large vessel vasculitis. Clinical trials are currently underway to evaluate the efficacy of JAK inhibitors in both Takayasu's arteritis and giant cell arteritis.

EL19

How will informatization (medical DX) change/alter medical practice?

Kensuke Yoshimura
Chiba University Hospital

Conflict of interest: None

The Basic Policies for Economic and Fiscal Management and Reform, issued in June 2022, stated the establishment of a Headquarters for Promoting Medical DX, and its first meeting was held in October of the same year. We would like to provide a basis for discussion on how this will affect daily medical practice based on the contents of the policy.

EL20

Neurological examination and neurological diseases: tips and updates for rheumatologists

Noriko Isobe
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Conflict of interest: Yes

Neurological examination and detailed interview from patients are very important and fundamental to diagnose neurological diseases. There are various underlying etiologies of neurological diseases; e.g. degenerative, inflammatory, infectious, vascular, metabolic, toxic, compressive, and functional ones. The anatomical diagnosis includes central or peripheral nerve systems and muscle, which are further subcategorized based on the distribution of neurological findings. In this talk, I focus on the diseases that rheumatologists often see in their daily clinical practice and introduce some neurological examinations useful for diagnosis and differentiation from other diseases with similar clinical characteristics. In detail, general information on types of peripheral neuropathy, common peripheral neuropathy observed in each autoimmune disease, how to diagnose peripheral neuropathy by presenting tips of neurological examinations and their interpretation. Additionally, I also introduce characteristic central nerve system involvement observed in rheumatoid or collagen diseases, as well as tips to diagnose them both anatomically and clinically. I hope that the talk will be useful for the future clinical practice of rheumatologists.

EL21

What should rheumatologists know about chest physical examination and respiratory diseases?

Hiroshi Mukae
Department of Respiratory Medicine, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: Yes

Rheumatic disease is known to be associated with a variety of respiratory diseases. The disease can be divided into lung lesions caused by rheumatic disease itself, complicated lung infections, and drug-induced lung injury. Pulmonary lesions due to rheumatic disease itself consist of interstitial lung diseases (ILD), airway diseases, pleural diseases, and vascular diseases. Since each condition is related to the treatment of rheumatic disease itself and to life prognosis, its management is very important, and depending on the condition, collaboration with other departments, such as respiratory physicians, may be necessary. However, early detection is often left to the rheumatologists, and it is essential to treat patients with an understanding of their individual conditions and treatments, and to anticipate possible respiratory diseases. Although chest examination tends to be neglected in the practice of respiratory diseases, it plays a significant role in the early detection and follow-up of respiratory diseases. Among pulmonary lesions, ILD are the most frequent and have the greatest impact on life outcome. ILD can have a variety of presentations, from rapidly progressive cases to chronically progressive cases associated with RA and SSc. Among these, the antifibrotic agent has been shown to be effective in the treatment of "progressive fibrosing ILD (PF-ILD)", but there are issues to be clarified, such as its effectiveness in each connective tissue disease and in combination with immunosuppressive drugs. Pulmonary infections are also an important complication due to the presence of airway involve-

ment and opportunistic infectious conditions associated with the use of steroids, immunosuppressive drugs, and biologic agents. In this lecture, I would like to outline the chest examination and respiratory diseases that a rheumatologist with collagen disease should know from the standpoint of a respiratory physician, including my own experience.

EL22

Effect of glucocorticoids on metabolic diseases

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Conflict of interest: None

Under normal conditions, 10 mg of cortisol (approximately 2.5 mg of prednisolone equivalent) is secreted per day. When cortisol binds to the glucocorticoid receptor (GR), GR changes its conformation and translocate into the nucleus. Through interaction with transcription coactivators, it binds to several genes and regulates the metabolism of glucose, lipids, bones, etc., and maintains the homeostasis of the body. On the other hand, steroids also bind to GR, and GR translocated into the nucleus inhibits the activation of transcription factors such as AP-1 and NF-κB. Since these transcription factors induce the transcription of various inflammatory proteins including cytokines such as TNF-α, their inhibition exerts a strong anti-inflammatory action, which is the pharmacological action of steroids. So steroids have potent anti-inflammatory and inhibitory actions on immunocompetent cells, and are widely used for the treatment of various diseases. In particular, steroids therapy for collagen disease contributes in the improvement of prognosis. However, there is increased awareness of the many adverse effects of long-term use of glucocorticoid. Administration of synthetic GC induces an imbalance in internal cortisol levels and leads to a number of significant side effects, including diabetes, weight gain, hyperlipidemia, skin thinning, opportunistic infection, cataract, hypertension, psychoses, and osteoporosis. These complications, especially osteoporosis and cardiovascular complications, have a significant impact on the patient's prognosis and healthy life expectancy. It is important that we should carefully consider the indications for steroid administration and use the minimum amount of steroids successfully.

EL23

Pulmonary hypertension: how is the future of connective tissue disease-associated pulmonary hypertension following the revision of European guideline?

Masaharu Kataoka
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Conflict of interest: None

Connective tissue disease-associated pulmonary hypertension can be fatal from right heart failure and is important in managing connective tissue disease. Connective tissue disease-associated pulmonary is a complex disease that requires accurate evaluation of the pathophysiology on a case-by-case basis, because it includes group 2 and group 3 factors of pulmonary hypertension as well as group 1 pulmonary arterial factor. In particular, scleroderma-associated pulmonary hypertension is accompanied by elements of pulmonary venous capillary fibrosis, so it has a more complex pathophysiology. A recent big topic in the field of pulmonary hypertension is that the European guideline of pulmonary hypertension was announced in the summer of 2022 after a major revision. In this revision, the value of mean pulmonary arterial pressure at rest for the diagnosis was lowered from 25 mmHg to 20 mmHg, and the diagnostic criteria during exercise stress was added. Thus, patients with connective tissue diseases occupy an important position, and patients with pulmonary hypertension will probably be diagnosed much more frequently than before. Therefore, it should be focused how to early and properly diagnose pulmonary hypertension in patients with connective tissue diseases. Furthermore, over many years, our team has stored DNA/RNA from the patients with pulmonary hypertension and constructed a sample bank. We succeeded in identifying a new onset causative gene in pulmonary hypertension patients and in identifying a specific cause of onset in Japanese patients, which is not found in Westerners. This educational training lecture will comprehensively organize the current status and future of pulmonary hypertension, including molecular genetical knowledges.

EL24

Clinical manifestations of respiratory viral infections and infection control for clinicians

Jiro Fujita
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Conflict of interest: Yes

In order to understand the clinical manifestations of respiratory viral infections, it is first necessary to consider the receptors of individual viruses. The receptor for hemoagglutinin, one of the proteins on the surface of influenza virus, is sialic acid, which is mainly distributed in the respiratory tract. There are two types of sialic acid: sugar chains with sialic acid-terminal α2,6-linked galactose are distributed in the upper respiratory tract, and sugar chains with sialic acid-terminal α2,3-linked with galactose are distributed in the lower respiratory tract. Human influenza binds to the former and avian influenza to the latter. On the other hand, SARS-CoV-2, which is the causative virus of coronavirus infectious disease 2019 (COVID-19), has a spike protein present on the surface of the virus that binds to the angiotensin-converting enzyme 2 (ACE2). ACE2 is widely distributed not only in the upper and lower respiratory tract but throughout the body. Since vascular endothelial cells also have receptors, the frequency of complications with vasculitis increases. COVID-19 until August 2021 (5th wave) and COVID-19 caused by Omicron strain after January 2022 were very different. As a pathological condition, the mutated spike protein binds more tightly to ACE2 in the Omicron strain, and as a result, it proliferates mainly in the upper respiratory tract and is less likely to enter the lower respiratory tract. As the frequency of pneumonia complications decreased, the frequency of viremia also decreased. For this reason, it is less likely to become a systemic infection, and the course of the disease is relatively mild. Since the Omicron strain has changed to an infectious disease that mainly affects the upper respiratory tract, it has become difficult to distinguish between influenza and COVID-19. Infection control measures for respiratory viral infections are droplet control measures, aerosol control measures, and contact control measures.

EL25

Histopathological classification and latest findings of renal biopsy in lupus nephritis

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Conflict of interest: None

Lupus nephritis is one of the most important and frequent organ involvements among patients with systemic lupus erythematosus, resulting in increased morbidity. To evaluate pathological findings of lupus nephritis, the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification was proposed in 2003 and had been widely used. Recently, a working group for lupus nephritis classification updated the ISN/RPS classification in 2018 based on the previous evidences, that includes changes in definition of mesangial hypercellularity or crescents (Bajema et al. 2018). Several validation studies of the new 2018 revised ISN/RPS classification have already been performed and its usefulness has been emphasized. In this classification, glomerular lesions are classified into mesangial lesions defining class I and II LN, active and chronic lesions defining class III and IV LN, and membranous lesions defining class V LN. Moreover, the 2018 revised classification includes a description of tubulointerstitial lesions and evaluation of a modified NIH activity/ chronicity index additionally to 2003 classification. The revised classification will further clarify the role of tubulointerstitial lesions in therapeutic response of LN in the future. In this session, I will describe the histopathological findings of LN -each glomerular, tubulointerstitial, and vascular lesion- and how to assign the ISN/RPS classification. In addition, I would like to discuss the key points of the 2018 revised classification and how to

measure the modified NIH activity/ chronicity index. The latest findings in histopathology in LN, such as the usefulness of exotosin (EXT) 1/2 in LN V and new disease concept including lupus podocytopathy, will also be mentioned. I hope that this lecture would help rhuematologists who treat patients with LN to be able to classify the histopathology of their own LN patients, and reflect the results in their therapeutic strategy.

EL26

DPC and its utilization that rheumatologists should know

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Conflict of interest: None

Big data currently available to researchers in Japan include DPC and receipt data, as well as case databases collected by academic societies. The presenter has been involved in the utilization of DPC data and the NDB, which is an archive of national-level receipt data. In this symposium, I would like to express my personal opinion on the current status and issues of rheumatoid arthritis medicine using these two big data. In the DPC survey, Form 1, EF file, detailed data during hospitalization is collected. Form 1 is medical record information, including medical institution information, basic patient information (age, gender), diagnosis information, and surgery information are entered as mandatory items. In addition, some items are also registered such as cancer stage (TNM classification), Japan Coma Scale, Hugh-Jones classification, NYHA classification, etc. The E file is a file that records the subtotal of the billed amount for each medical treatment procedure, and the points for each patient and the order of a series of procedures are recorded by day and classified into procedure fees, drug fees, and material costs. The F file is a file that records the details of medical care. By analyzing the E file and F file, it is possible to understand the drugs and specified insurance medical materials used, and the examinations and treatments performed by day. becomes possible. By using these data, it is possible to visualize, for example, the selection status of rheumatism drugs according to patient characteristics and facility characteristics. In the case of NDB, there is no clinical information equivalent to Form 1, so the content that can be analyzed regarding the process is limited compared to DPC, but for cases other than hospital admission to DPC hospital, long-term medical treatment status and prognosis, including nursing care, can be analyzed. In this educational lecture, I will introduce an example of perioperative process evaluation using these two data.

Meet the Expert

MTE1

Better understanding of rehabilitation and custom orthotic interventions in treatment of patients with rheumatoid arthritis useful or rheumatologist of physician

Jun Hashimoto
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Conflict of interest: Yes

Treatment modalities for rheumatoid arthritis (RA) that contains education for understanding the disease and managing daily living, pharmacological treatment, surgical treatment, rehabilitation and care should be timely informed and performed to patients with RA. There are several important notes for rehabilitation and custom orthotic interventions. The first is having both viewpoints of joint protection/energy conservation and improvement of physical activity. Joint protection/energy conservation is to remove the burden on inflamed/damaged joint. Typical examples are using a wrist orthosis for joint stabilization or using proximal large joints and both extremities for heavy physical work. It is important to restrict a use of cane in case of walking disability, since it could cause the physical destruction in wrist and shoulder joints of non-weight bearing joint. Walking disability of patients with RA should be treated with accurate diagnosis of disturbance in gait and surgical intervention if necessary. This is the time for rheumatologist of physician to consult the rheuma-foot and ankle surgeon, spine surgeon or joint surgeon. As to improvement of physical activity, ring splint for swan-neck or button-hole deformity of finger, and adjustment of footwear and insole interventions for forefoot deformity are helpful. The second is that rehabilitation and custom orthotic interventions are standard approach for improvement of physical activity of the patients with RA through his/her life-span. EULAR recommendation mentioned that physical activity interventions are standard care and include the behavioral change techniques self-monitoring, goal setting, action planning, feedback and problem solving with strength of recommendation A and category of evidence 1A. Recently SARAH randomized controlled trial showed that a tailored exercise regimen for hand and upper limb is effective in restoration and retaining of hand function. The third is improvement and reinforcement for provision of information regarding surgical intervention for physical activity improvement. Multidisciplinary information could provide the patients with informed and voluntary decision making from several therapeutic alternatives and contribute his/her long life-plan in the era of centenarians.

MTE2

Rheumatoid hand/foot deformity

Hajime Ishikawa
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Conflict of interest: None

While the joints of the human hand and foot are anatomically homologous, they are functionally different. Common causes of deformity of the hands and feet affected by rheumatoid arthritis include (1) weak supporting structures (joint capsule, ligaments, and tendons) due to synovitis; (2) imbalance between extrinsic and intrinsic muscles due to muscle spasm, myostatic contracture, and muscle atrophy; (3) malalignment at the proximal joints; and (4) asymmetrical joint structure. Conversely, differences in causes related to the deformity of hands and feet are as follows: (1) in the hands, prehension and dexterous movements by the thumb and fingers, which have delicate sensations, work mainly on the flexion side, while in the feet, the load is applied to the entire sole, and when kicking out during walking, the toes move in the extension side; (2) in the hands, extrinsic muscles (FDP and FDS) and intrinsic muscles flex the MCP joint, and extrinsic muscles (EDC, etc.) extend the PIP and DIP joints, while in the foot, due to the sling mechanism, extrinsic muscles (FDL) does not flex the MTP joint, extrinsic muscles (EDL) does not extend the PIP and DIP joints) and only the intrinsic muscles are functioning; (3) in the hands, spreading and closing of the fingers occurs centering on the middle finger, while in the foot, these movements occurs centering on the second toe due to anatomical differences in interosseous muscles. Similar deformities in the hands/ feet include boutonnière deformity of the fingers/ hammer toe

deformity, ulnar deviation of the fingers/ fibular deviation of the toes, and boutonnière deformity of the thumb/ hallux valgus deformity. All of these are caused by imbalance between intrinsic and extrinsic muscles. With a thorough understanding of the mechanism underlying deformity, balancing surgery at adequate timing can restore the shape of the hands and feet, eliminate pain, and improve patients' quality of life and activities of daily living.

MTE3

Current Status and Future Prospects of Behçet's Disease-New Issues Revealed from Clinical Practice Guidelines-

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Conflict of interest: None

Behçet's disease is a recurrent inflammatory disease of unknown etiology, for which diagnosis is based on a combination of typical symptoms of the disease and exclusion of similar diseases. In recent years, multiple disease susceptibility genes have been identified, but no findings beyond the known link to *HLA-B*51* have emerged and no serum markers linked to disease diagnosis have been found. Among patients meeting the diagnostic criteria for Behçet's disease, the prognosis varies greatly depending on complications, and this makes it necessary to consider the treatment strategy individually. The Japanese Society for Behçet's Disease has published the "Behçet's Disease Clinical Practice Guidelines 2020" for intractable rare diseases, based on accumulated knowledge and discussion among experts. These guidelines have established certain helpful directions for treatment. Here, we introduce findings that are more difficult to include in guidelines, such as the approach of specialists involved in treatment of Behçet's disease.

MTE4

State of the Art of the Diagnosis of FUO/FUI in 2023 - approach to the difficult, seronegative, periodical cases -

Noboru Hagino
Division of Rheumatology, Teikyo University Medical Center in Chiba

Conflict of interest: None

We rheumatologists have many opportunities to take care of patients with fever/inflammation of unknown origin. In most of the cases, basic medical skills (exclusion of infections and malignancies, identification of typical presention of rheumatic diseases/syndromes) will make the diagnosis, but rarely, we encounter a group of cases that are very difficult to diagnose. Even in these cases, careful follow-up can lead to the diagnosis of a specific disease or syndrome, but the rapid progression of organ damage may make therapeutic intervention inevitable, thus obscure the clinical picture itself. In this "Meet the Expert", I would like to unravel cases of FUO/IUO, which are difficult for rheumatologists to diagnose, using sample cases. In the past few years, autoinflammatory syndromes such as VEXAS syndrome have emerged as a disease concept among "seronegative seronegative" and "periodic" unexplained fevers and inflammations. At the same time, it has become clear that myelodysplastic syndromes/ myeloproliferative disorders (MDS/MPD) are often diagnosed during follow-up of patients with unknown fever and inflammation in the rheumatology clinic. Despite sophisticated serological testing and imaging, these diseases/syndromes are still often troublesome to clinicians. I hope this lecture will provide an opportunity to think together about how to approach difficult cases so as not to compromise the patient's tomorrow.

MTE5

Key points in the diagnosis and treatment of IgG4-related diseases

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Conflict of interest: Yes

IgG4-related disease (IgG4-RD) has been established in the 21th century as a novel systemic disease which is characterized by elevated levels of serum IgG4 and various lesion formation consisting of dense infiltration of IgG4-positive plasmacytes with fibrosis. The most common sites for IgG4-RD are the lacrimal glands, salivary glands, and pancreas. In addition, multiple organ involvement, including kidney, bile duct, and retroperitoneum, et al. form diverse clinical features in synchronous and metachronous course. Thanks to increased awareness of IgG4-RD as a new disease concept, it is easy to diagnose an IgG4-RD in a case presenting with bilateral swelling of the lacrimal and salivary glands and elevated levels of serum IgG4. In fact, even if there is no histopathological finding, it is devised so that a definitive diagnosis can be made In a typical case according to the 2019 ACR/EULAR Classification Criteria for IgG4-RD. On the other hand, it is often difficult to diagnose in a case with lesions not frequently affected organs. Inflammatory factors such as fever, elevated CRP, and severe weight loss are not characteristic of IgG4-RD. Patients with such clinical features are rare except for IgG4-related hypophysitis / periaortitis, and are strongly suspected of IgG4-RD mimickers. In this lecture, I would like participants to understand the basic clinical pictures of IgG4-RD. Next, participants should learn how to use Japan's comprehensive diagnostic criteria and ACR / EULAR classification criteria. Finally, I would also like to mention the points that distinguish IgG4-RD mimickers. It is often difficult to determine the treatment indication and the timing of treatment start because of the synchronous and metachronous course and the spontaneous remission. I would like to discuss the actual treatment referring to the findings of long-term observations in our department.

MTE6

Risk management of infectious diseases in view of clinical immunology and rheumatology

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Conflict of interest: None

Risk management for infectious diseases is one of the most important issues in clinical practice of Rheumatology. Infectious diseases not only directly lead to poor life prognosis, but also often become obstacles to adequate anti-rheumatic/immunosuppressive treatment. Therefore, it is necessary to understand adequate risk management methods for infectious diseases. In my opinion, understanding of clinical immunology is required for better infectious disease risk management. In this lecture, I would like to outline the overview, methods, and practice to infectious disease risk management based on an understanding of clinical immunology. As a contemporary topic, I also provide some information on COVID-19 risk management in patients with rheumatic diseases.

MTE7

Introductory course of statistical genetics

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Conflict of interest: None

Statistical genetics is a research field that evaluates causality of human genetic variations on diseases, using statistical and bioinformatics approaches. Recent developments of sequencing technologies have provided human disease genome data of hundreds of thousands of the subjects, and successfully identified comprehensive catalogues of genetic susceptible loci. Genetic backgrounds contribute to onset and prognosis of rheumatic diseases (= high heritability), and genome-wide association studies (GWAS) have identified a number of disease risk loci. However, little is known regarding how to develop methodology to integrate large-scale human genome data with diverse biological resources, to which statistical genetics should contribute. We have developed such methods and applied to a pioneering example of large-scale genetic association studies on a variety of human complex traits, including immune-related diseases, clinical biomarkers, and past medical records. Tran-layer omics analysis identified the cell types and microbiomes implicated in disease biology. Recent advance

in single cell sequencing technologies introduce novel insights in the field of rheumatology. Network analysis between the disease risk genes and the drug target genes could identify novel candidates of drug repositioning. Integration of cell type-specific gene expression profiles estimated from GWAS with compound perturbation databases can pinpoint novel therapeutic targets and compounds. Further, we demonstrated utility of deep learning in human population genomes, such as in silico estimation of HLA gene variants. These results should empirically show the value of statistical genetics to dissect disease biology, novel drug discovery, and personalized medicine. Finally, we would like to introduce our activity on young researcher developments ("Summer school of statistical genetics").

MTE8

A primer of statistical analysis for clinical researches using RStudio

Hisashi Noma
The Institute of Statistical Mathematics

Conflict of interest: None

In modern medical researches, many advanced statistical techniques have been commonly used, e.g., logistic regression, Cox regression and propensity score analyses, and we cannot understand clinical evidence from these research papers unless we have sufficient knowledge about these methods. In addition, we cannot write clinical research papers if we cannot use statistical software properly. However, most of these software packages require certain programming skills and expensive charges. In this session, I conduct a hands-on seminar using a statistical software RStudio (https: //www. rstudio. com/), which can be used without usage charges. R is a well-known statistical software that has been widely used in clinical researches published in international medical journals, and has rich and reliable functions for data analyses. RStudio enables all statistical analyses using R and involves useful supportive tools for the analyses of R. In addition, I will provide a short tutorial of standard statistical analyses for clinical studies.

MTE9

The knack in physical examination of children including juvenile idiopathic arthritis patients

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Conflict of interest: None

"Physical examination" is an important procedure for physicians to understand patient's conditions by looking at, touching, and listening with a stethoscope. Although the same is true for pediatric rheumatologists, we value physical examination much more. Children may be unable to express themselves due to young age or fear of examination. In juvenile cases, the informant in medical interviews may be a patient's guardian. Guardians cannot feel a patient's pain as same as they can their own. For this reason, pediatric rheumatologists determine a patient's medical condition by physical examination and make a diagnosis by adding information from guardians. Hence, I would like to share with you some tips about how pediatric rheumatologists examine pediatric patients.

MTE10

Total elbow arthroplasty; how to use Unlinked or Linked for lifelong strategy

Mitsuyasu Iwasawa[1], Masashi Naito[1], Tetsuro Yasui[2], Sakae Tanaka[3]
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Conflict of interest: None

The destruction of large joints in rheumatoid arthritis (RA) is decreasing with the progress of drug therapy. There is a concern that it will be difficult to acquire adequate treatment and surgical techniques of upper limbs in the future, because the number of total joint arthroplasty of the upper limbs is extremely small compared to that of the lower limbs. Total elbow arthroplasty (TEA) is an effective mean to achieve therapeutic goals for range of motion, pain relief, and stability. Surgical techniques are more diverse than those of other joint arthroplasties. In many models, the radiohumeral joint, which is the main load transmission in the extended position, is not constructed, so it has been required to devise measures against joint instability and difficulty in applying the load. Although the Linked type does not cause joint instability, it requires a longer stem length, humeral anterior flange and cement fixation due to its higher constraint, and the stem shape and structure have also been improved to avoid breakage and loosening. On the other hand, the Unlinked type is small size due to its low stress, but due to its low constraint, it is necessary to ensure stability by soft tissues. In Unlinked type, accurate implant fixation and reconstruction of soft tissues are required more than those in Linked type. Lifelong strategy with an eye on revision surgery is required in TEA, especially for younger patients. It is desirable to use the Unlinked type, which allows more bone preservation in the primary surgeries, than the Linked type. We believe that it is important to make TEA a general surgery that is not limited to experienced surgeons. In this lecture, appropriate surgical indications and surgical techniques will be explained.

MTE11

Essential basic knowledge for clinical use of ultrasound examination ~Including live demonstration~

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Conflict of interest: None

Recently, the usefulness of ultrasonography has been widely recognized in the management of rheumatoid arthritis. The ultrasound examination is useful in all situations such as diagnosis, the evaluation of treatment efficacy and management under remission, but the most useful is at the time of early diagnosis and differential diagnosis. However, it is also true that the ultrasonography is an examination whose result may be affected by the settings of the equipment and the sonographer's skills. In order to maximize the potential of ultrasound examination, it is necessary to understand the standard settings such as frequency of the probe in grayscale and power Doppler, gain and focus. An most important scanning skill is to take an image while keeping the gel layer without pressing the probe against the skin, particularly in a shallow part from the body surface such as a peripheral small joint or a tendon enthesis. This skill is very important in order not to underestimate synovial thickening and power Doppler signals that increased inside and/or outside of the joint. Furthermore, pathological findings in ultrasonography are not only intra-articular synovitis, but also include multiple findings including tendon and ligament enthesitis, tenosynovitis and calcification in the cartilage and cartilage surface. It is essential knowledge for differential diagnosis to understand how these pathological findings are seen in which disease, and that it may or may not be diagnosed only by ultrasound findings. In order to understand these things efficiently, this seminar is planned to give a lecture with live demonstration by using real ultrasound machine. I would be pleased that who want to start ultrasonography from now join this seminar.

MTE12

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 the majority of patients with rheumatic diseases such as rheumatoid arthritis and psoriatic arthritis and sustained remission facilitates prevention of joint damages and physical dysfunction, by the treatment with biological disease-modifying antirheumatic drugs (bDMARDs) or targeted synthetic (tsDMARDs) such as Janus kinase (JAK) inhibitors in addition

to methotrexate. As various molecular targeted drugs are used for many immune and infectious diseases, 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 bDMARDs 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.

MTE13

Pathogenesis of osteoporosis in rheumatoid arthritis patients

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Conflict of interest: Yes

Osteoporosis is known to be a common complication in patients with rheumatoid arthritis (RA). Osteoporosis in RA presents a complex picture of coexisting localized periarticular that occurs early in the course of the disease and systemic osteoporosis. Periarticular osteoporosis is manifested early in the disease in the form of subchondral trabecular bone loss, but bone atrophy is not necessarily limited to the inflamed joints. The causes of periarticular osteoporosis in RA patients have been postulated to include steroid use, decreased exercise load due to pain, in addition to accelerated bone resorption and suppression of bone formation around the joints by inflammatory cytokines. It is also possible that bone marrow edema reflects the progression of periarticular osteoporosis. Systemic osteoporosis may also be related to inflammation, glucocorticoid use, and immobility. In addition to this, a high rate of vitamin D deficiency has also been reported in RA patients, which may lead to an increased risk of osteoporosis and fractures via calcium malabsorption and increased risk of falling. RA treatment has changed significantly over the past 20 years. The advent of biologics has greatly improved disease activity in RA patients, resulting in improved ADL and quality of life. However, the aging of patients is causing various problems associated with aging. Osteoporosis in RA patients, in particular, has become a major problem due to the high frequency of complications and the deterioration of ADL and QOL caused by fractures. Despite improvements in disease activity, biologic agents have been shown not to alter fracture frequency. It is hoped that new treatment strategies will be developed to improve both disease activity and bone fragility.

MTE14

Complementology that rheumatologists should know

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Conflict of interest: None

Any clinician knows that complement is an important immune system competent in defending against infection. On the other hand, however, complementology is an unfamiliar field, and even a weak one, for most clinicians. I don't think I would have had the opportunity to step into this field if I hadn't been unexpectedly involved in basic research on complement while studying abroad. To put it in extreme terms, until now, clinicians didn't have much trouble even if they didn't know enough about complementology. This is because examination methods are limited, and above all, there are no therapeutic drugs specific to complement. But what about the future? In recent years, drugs that specifically inhibit complement activation have been developed one after another, making it possible to effectively treat various intractable immune diseases. In Japan, the "first in class" anti-complement drug, eculizumab, was launched in 2010 as an anti-C5 humanized monoclonal antibody. Since then, a total of four anti-complement drugs has been approved. Indications for these anti-complement drugs include microscopic polyangiitis, granulomatous polyangiitis, atypical hemolytic uremic syndrome, and autoimmune neurological diseases, which are familiar with rheumatologists. Understanding complementology is important in order to deliver appropriate treatment to patients. In this lecture, I would like to outline the basics of complementology that rheumatologists should know, and introduce the role of complement in diseases, the effects and mechanisms of action of anti-complement drugs, and the side effects to be aware of. The "old" complementology, which was discovered more than 100 years ago is transforming into a "new" complementology over time. It would be my great pleasure if I could share with you the recent remarkable progress on complementology through my talk.

MTE15

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

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

Conflict of interest: Yes

As of December 2022, there are 13 synthetic anti-rheumatic drugs, including 5 JAK inhibitors, and 8 biologics that can be used for rheumatoid arthritis in Japan. On the other hand, in juvenile idiopathic arthritis (JIA), the former has only methotrexate and the latter only 5 agents, and the disparity is extremely large. The common causative factors of the inflammatory pathology of arthritis are inflammatory cytokines, and recently monoclonal antibodies, specific receptors directed against individual inflammatory cytokines, have been formulated as therapeutic agents to inhibit the function of single inflammatory cytokines. In JIA, various inflammatory cytokines are produced, and the mutual induction mechanism has also been clarified, but there is actually a leading cytokine specific to the disease, and blocking that cytokine can end inflammation. Systemic JIA requires long-term, high-dose steroid use for strong systemic inflammation, and suffers from side effects. Tocilizumab (TCZ), an anti-IL-6 inhibitor, was the first in the world to be approved as an anti-IL-6 inhibitor in biologic therapy after undergoing clinical trials. Canakinumab, which has a proven anti-IL-1 inhibitory effect in Europe and the United States, was also approved in Japan, demonstrating efficacy for TCZ-ineffective patients. In addition, anti-TNF therapeutic agents such as etanercept (ETN) and adalimumab (ADA) are used for the type in which arthritis persists even after systemic symptoms have improved. On the other hand, for articular JIA, in addition to ETN, ADA and TCZ, abatacept, which inhibits co-stimulatory signals between antigen-presenting cells and T cells, is also approved in Japan. Recently, it obtained indication approval as a result of clinical trials. In this presentation, I will outline the drugs that can be used in JIA, their dosage forms, and how to use them in clinical settings, focusing on the differences from RA.

MTE16

Pitfalls of management of systemic sclerosis

Masataka Kuwana
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Conflict of interest: None

Systemic sclerosis (SSc) remains an intractable condition with poor functional and survival outcomes. This is primarily due to the physicians' unawareness of its natural disease course, which largely differs from rheumatoid arthritis and systemic lupus erythematosus. As a result, in clinical practice, some patients are left untreated without being referred to specialized centers, and others receive unnecessary, inappropriate treatment. It is meaningless to discuss the treatment indications and their efficacy without a full understanding of the unique features of this disease. A number of global randomized controlled trials have been conducted or are ongoing, and potential "disease-modifying therapies" are already available in clinical practice. In addition, early interventions have been shown to be more effective than delayed intervention. Fundamental knowledge of SSc management required for introduction of 'appropriate' treatment for 'appropriate' cases at 'appropriate' timing will be discussed in this session.

MTE17

Interaction of environmental, individual, and genetic factors in rheumatoid arthritis: prevention, early diagnosis, and early treatment

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a systemic autoimmune disease that causes chronic inflammation of the joints. In recent years, with the advent of various disease-modifying anti-rheumatic drugs, remission has become a realistic treatment goal. However, even when remission criteria are met, there are still many cases with unmet needs that are difficult to treat. It has also been pointed out that even with current drug therapy, there is a certain subgroup of patients with progressive joint destruction who require surgery. RA is an abnormal autoimmune disease caused by a complex interaction of genetic and environmental factors. More than 100 RA susceptibility loci, including HLA-DRB1, have recently been identified by genome-wide association studies (GWAS) and GWAS meta-analyses. Big data approaches using GWAS have identified important information on susceptibility genes, pathways, and cell types that contribute to pathogenesis. However, individual susceptibility genes are thought to have small effects, and allelic combinations are essential for RA pathogenesis, along with the effects of these susceptibility genes on the specific pathways affected. Therefore, to understand the role of genetics in RA pathogenesis, it is important to understand the physiological significance of each susceptibility gene associated with RA. It is also necessary to analyze the pathogenic mechanisms involving environmental and individual factors such as smoking, infections, mental stress, sleep deprivation, age, childbirth, gender, diet, and obesity as non-genetic factors in the mechanism of RA development. Understanding these risk factors for RA may contribute to early diagnosis of the disease and, if the factors are modifiable, may be useful in preventing or delaying its onset. The major challenge for the future is how to improve Patient Reported Outcomes (PROs), which requires prevention efforts, early diagnosis, and initiation of appropriate therapy to prevent refractory RA.

MTE18

Imaging of axial spondyloarthritis

Yuho Kadono
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Conflict of interest: Yes

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

MTE19

Practice for appropriate diagnosis and treatment of axial spondyloarthritis

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Conflict of interest: Yes

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

MTE20

Basic knowledge for diagnosis of arthritis and arthralgia

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Conflict of interest: None

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

MTE21

Osteoimmunology

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Conflict of interest: None

Osteoimmunology deals with the interaction and shared mechanisms of the bone and the immune system. In particular, osteoimmunology is important for understanding the pathology of bone destruction associated

with rheumatoid arthritis, in which osteoclast-mediated bone destruction is caused by the activation of T cell-mediated autoimmune inflammation. Accumulating evidence indicates that IL-17-producing T cells have profound effects on bone by inducing RANKL and stimulating osteoclast precursor cells in addition to promoting the local inflammation mediated by inflammatory cytokines such as TNF and IL-6. These studies helped understand the mode of action of drugs such as cytokine blockers and JAK inhibitors and establish the use of anti-RANKL antibody for bone damage in arthritis. Many immunomodulatory molecules were shown to be involved in the regulation of bone metabolism. In addition, bone cells and immune cells share the same microenvironments in the bone marrow, communicating through various factors. Osteoblasts, osteoclasts and osteocytes do not only metabolize the bone but also play distinct roles in the immune regulation, suggesting the importance of effect of bone on immunity. Thus, the osteoimmunological point of view became essential for understanding the pathogenesis of rheumatic diseases and other osteoimmune diseases. Here I will review the recent advance in the field of osteoimmunology and its relevance in bone loss associated with inflammation as well as other physiological and pathological conditions.

MTE22

Diagnosis and Treatment of Foot and Ankle Disorders in Rheumatoid Arthritis

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Conflict of interest: Yes

The foot is most frequently affected by rheumatoid arthritis. Even if activity of rheumatoid arthritis is well controlled by biologics, activity of daily living in some patients is severely limited by foot pain. Mild foot deformities or synovitis in few joints causes pain at a walk. The benefit has a big not only patient satisfaction but also medical care economy without increasing drugs if we can operate patients with minimum invasive surgery. Recent advancement of orthopedic surgery in the foot and ankle field will be mentioned in this lecture. For the forefoot, we treat patients aiming at joint preservation as much as possible. Our study showed that morphological characteristic in rheumatoid hallux valgus are similar to general hallux valgus. Therefore, osteotomies should be indicated for rheumatoid hallux valgus, if articular cartilage did not much affected. For the midfoot and hindfoot, we can treat lesions using arthroscopic or endoscopic approach with benefit of progress of the arthroscope technology. Although synovectomy is performed less frequently, it is a minimally invasive procedure that may be considered. On the other hand, terminal stage of foot deformities are difficult to be treated by drugs even if the paradigm shift of the treatment occurs. There are lesions to require arthrodesis or total ankle replacement still more. Partial tarsal fusions are selected for limited parts of tarsal joints. In addition, ankle fusion or total ankle arthroplasty is chosen for the ankle in terminal stage. When both the ankle joint and subtalar joint are affected and there is significant deformity and instability, simultaneous arthrodesis of both joints can be performed, and when alignment is good, satisfactory results can be expected with total ankle arthroplasty using total talar prosthesis (combined TAA). A balanced treatment system of orthopedics treatment and systemic control by drugs is necessary for patient satisfaction.

MTE23

How to proceed the diagnosis of autoinflammatory diseases

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

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

MTE24

MTE: RA Hand Surgery

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Conflict of interest: Yes

In recent years, drug treatment for rheumatoid arthritis (RA) has changed dramatically and made remarkable progress in biologics. These changes have highlighted and widely recognized the importance of RA tight control towards the goal of achieving remission or low disease activity. As a result, joint destruction associated with RA is also suppressed, and there is a possibility that it will be repaired, so orthopedic surgery is also changing, and small joint surgery such as wrist joints and finger joints is attracting attention, and interest in joint-sparing surgery is also increasing. This time, I would like to consider the surgery of the RA hand while presenting the case. With RA drug treatment, inflammation may remain in some joints even if disease activity is controlled, and neglect of such inflammation causes joint destruction and progression of deformity. For joint synovitis remaining, if the effect of conservative treatment such as intra-articular injection is insufficient, synovectomy should be considered before deformity or joint destruction appears. This is also important from the viewpoint of joint preservation, and it can also prevent tendon rupture in the wrist joint, so the timing of surgical intervention is important. Also, even if the inflammation seems to subside, joint destruction may progress. In such cases, it is important to determine the indication for operative treatment. If characteristic deformation of the RA finger has already occurred, after understanding the cause, consider the surgical method depending on the situation. In the wrist joint, it is important to consider surgery according to the progress of joint destruction. In anticipation of joint destruction repair effect, joint-preserving surgery is performed if possible. In relatively young people, where joint destruction has not yet progressed and the degree of deformity is mild, it is important to consider whether joint-preserving surgery can be indicated. The significance of RA hand surgery is expected to increase in the future, but while it is important to perform it under tight control, it is necessary to pay attention to infection due to the increased use of immunosuppressants. In any case, since RA hand surgery is often used as an affected area, it is likely that the range of its contents will expand and become more sophisticated, and it is likely to change including rehabilitation. We will continue to provide drug treatment as aggressively as possible, and we will also treat RA hand surgery with an "aggressive" attitude.

MTE25

How to select treatments for ANCA-associated vasculitis

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Conflict of interest: Yes

In anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), ANCA, neutrophils, complement, neutrophil extracellular traps, and cytokines form a vicious cycle. Therapeutic drugs for AAV have been developed with the goal of blocking the pathway contributing to the pathogenesis. Treatment of AAV is composed of remission induction phase and remission maintenance phase. For microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA), glucocorticoids (GCs), cyclophosphamide (CY), rituximab (RTX), and avacopan are mainly used for remission induction therapy in Japan. Clinical trials have shown that RTX is non-inferior and has similar safety profile to CY in remission induction therapy for patients with MPA/GPA. LoVAS trial conducted in Japan revealed that the reduced-dose GC regimen was non-inferior to the standard-dose GC regimen when used in combination with RTX. PEXIVAS study enrolled MPA/GPA patients with non-severe renal involvement or pulmonary hemorrhage, and showed non-inferiority of the reduced-dose GC regimen to the standard-dose GC regimen in terms of death or end-stage kidney disease. In ADOVOCATE trial, the phase III clinical trial of avacopan, demonstrated non-inferiority of avacopan + RTX/CY to GC + RTX/CY for achieving remission at week 26 and superiority for maintaining remission at week 52. Clinical practice guidelines from Japan and overseas state recommendations about these drugs. In a clinical setting, however, there is a certain range of treatments chosen in each individual case, and it is expected that opinions will often diverge even among specialists. For remission maintenance therapy, RTX has been shown to have a better efficacy to other drugs, but there are many areas where evidence is still insufficient such as treatment intervals, treatment duration, and order of drug discontinuation. In this session, I would like to discuss with the participating doctors about how to utilize evidence from clinical trials in the treatment of MPA/GPA.

MTE26

Treatment Strategy for the patients with rheumatoid arthritis

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Conflict of interest: Yes

For the drug treatment of rheumatoid arthritis (RA), extreme progress has been made during recent ten years. In addition to biological DMARDs, targeted synthetic DMARDs were introduced into the clinical practice, the choices of the treatment are those acting on five targets with more than 10 products globally. It is also true for methotrexate (MTX), an anchor drug in RA treatment, different route of administration can be utilized by the recent approval of subcutaneous MTX product in Japan, along with the longer experience with the oral MTX products. In considering the standardized treatment strategy, recent updates of the recommendation/guidelines, limitations, gaps between global and Japan, and future perspectives may be discussed in this lecture.

MTE27

Essentials of basic and clinical aspects of methotrexate

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Conflict of interest: Yes

Methotrexate is an anchor drug for treatment against rheumatoid arthritis even in the present era of various biologic disease modifying antirheumatic drugs (DMARDs) and JAK inhibitors are available. The reason is that methotrexate has the balanced effectiveness and safeness and advantage of cost effectiveness. In the daily practice, methotrexate is used about 60% of rheumatoid arthritis patients who are treated with any DMARDs. Adverse events sometimes occur even when the patients get into and being sustained remission awing to methotrexate. That makes the physician feel sad and discouraged as to think that 'I will never use methotrexate anymor'. Nevertheless, we need to use methotrexate in several occasions. To know the basis of methotrexate is helpful in management of rheumatoid arthritis and adverse events of methotrexate. Methotrexate is a reduced folate developed in 1940s and inhibit strongly proliferation of cells by binding to dihydrofolate reductase in S phase. Methotrexate also inhibit thymidylate synthetase and increase adenosine release. In these days, the divergent effects of polyglutamated methotrexate are actively investigated. In clinically, physicians should be pay attention to the occurrence of adverse events such as lymphoproliferative disorders, drug induced interstitial lung disease, myeloid suppression, infection and liver dysfunction and so on. To suppress the avoidable adverse events, we need explain patients not to take methotrexate when they feel sick, we need to educate physicians and pharmacists to avoid everyday prescription of methotrexate, and we need to explain physicians to know the difference of bland name and generic name. In this lecture, the essence of basis and the clinics of methotrexate will be introduced to improve daily practice.

MTE28

Interleukin 6: from bench to bedside

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Conflict of interest: Yes

The first stage of research into the application of new technologies to humans is called translational research. The benefit of medical doctor-initiated research is their knowledge about the needs in a medical setting, but the research should fully reflect the features of the seeds as a result of basic research. IL-6 is a cytokine involved in regulation of biological functions such as immune response, inflammation, proliferation and differentiation of various cell types. IL-6 plays an important role in maintaining the homeostasis. But IL-6 overproduction leads to symptoms such as fever and malaise, laboratory abnormalities including increased APPs, and appearance of autoantibodies, resulting in organ damage. Therefore, IL-6 blockade could solve the unmet medical needs of various inflammatory diseases in which IL-6 overproduction is pathologically involved. Tocilizumab (TCZ), the first antibody drug in Japan, has been used to treat Castleman's disease, RA, JIA, AOSD, and cytokine release syndrome, a side effect in CAR-T cell therapies, TA, GCA, and severe pneumonia associated with COVID-19. In addition, pH-dependent binding humanized anti-IL-6R monoclonal antibody satralizumab was approved for Neuromyelitis optica spectrum disorder associated with anti-aquaporin 4 antibody. In this session, following items will be discussed. I. IL-6 discovery and IL-6 receptor system II. IL-6-producing cells and various physiological actions III. The effect of IL-6 blockade in animal models IV. Immunopharmacological features of TCZ V. Advantages and disadvantages of anti-IL-6R antibodies VI. Development of clinical evidences of IL-6 blockade VII. Current status and future prospects of IL-6 blockade Notably, in order to develop clinical evidence, it is necessary to prove not only safety and efficacy, but also the concept of therapy resulting in clarification of the mechanism of the drug efficacy. I will explain the importance of designing clinical trial protocol to protect human rights.

MTE29

To support rheumatic disease patients who hope to become mothers

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Conflict of interest: Yes

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. Tight control strategies based on "treat to target" have enabled many patients to control their disease activity. This advancement has brought much good news to rheumatic disease patients who have the desire to become mothers. Until now, patients with rheumatic diseases who wanted to be mothers tended to avoid having their babies born for various reasons. The high frequency of adverse pregnancy outcomes such as miscarriages and premature births, as well as problems such as infertility, are also major reasons for this. However, the aforementioned major advances in treatment and practice strategies have made it possible

for patients with rheumatic diseases to aspire to become mothers. However, the aforementioned major advances in treatment and practice strategies have made it possible for patients with rheumatic diseases to 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 conducted in all patients, not only women with rheumatic diseases who plan to conceive soon, especially before pregnancy. The goal should be to provide a better state of fertility for future life events such as pregnancy, lactation, and child rearing. This seminar will outline the particularities of patients with rheumatic diseases who hope to become mothers. By reconfirming treatment strategies based on these special characteristics, we would like to consider "supporting rheumatic disease patients who hope to become mothers at all costs", with a focus on rheumatoid arthritis and systemic lupus erythematosus mainly.

International Concurrent Workshop

ICW1-1

Successful treatment with tofacitinib in rheumatoid arthritis patient with inflammatory lung nodule and interstitial lung disease

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Conflict of interest: Yes

We report a case with rheumatoid arthritis (RA) with inflammatory lung nodule and interstitial lung disease (ILD) was successfully treated with tofacitinib (TOF). A 74-year-old man with a history of longstanding uncontrolled RA with ILD suffered with multiple arthritis, cough, suptum and dyspnea on exertion. He had 3.4 cm sized large cavitary lung mass and ILD. Two biopsies performed 6 months apart showed no malignancy or granuloma, and results suggesting chronic inflammation, however fungal infection, cancer, and necrotizing pneumonia were not differentiated. Infection was not excluded, and he suffered from ILD, so we could not use methotrexate (MTX) and could only use sulfasalazine (SSZ) and steroids, and arthritis were not controlled. The size of the lung nodule increase even after anti-fungal treatment with itraconazole and the symptoms of arthritis were getting worse. With the consent of the patient, TOF 5 mg bid administration was started with a chest imaging study close follow up decision. The size of the inflammatory nodule was gradually reduced and the arthritis symptoms improved. TOF is selectively inhibits signaling downstream of janus kinase (JAK) 1 and 3 for the treatment of RA. Therefore, we proposed TOF which allowed us to control joint involvement, stabilize pulmonary inflammation improving respiratory symptoms, may be a treatment option for treating symptomatic lung disease in RA patients.

ICW1-2

Diffuse Alveolar Hemorrhage: A Rare Fatal Complication of Systemic Lupus Erythematosus (A Report of Two Cases)

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Conflict of interest: None

We report two Filipino women with systemic lupus erythematosus (SLE) who developed diffuse alveolar hemorrhage (DAH), a rare, life-threatening complication associated with a high mortality rate. DAH should be suspected in patients with SLE presenting with new pulmonary infiltrates, a decline in hemoglobin, hemoptysis, dyspnea, and persistent desaturation. The first patient is 23 years old and was diagnosed with SLE 8 years ago; initially presenting with malar rash, oral ulcers, nephritis, and positive antinuclear antibodies (ANA). She had a poorly controlled disease and was admitted for facial and bipedal edema due to lupus nephritis. She was given 1 gram of methylprednisolone intravenously (IV) for three consecutive days. She then became tachypneic producing bloody secretions, with desaturation and sudden decline in hemoglobin. She was given cyclophosphamide 1 gram IV and referred for plasmapheresis but eventually succumbed. The second patient is 56 years old with generalized body weakness. Laboratory workup showed nephritis, anemia, ANA, low C3, and high anti-dsDNA titers. Pulse methylprednisolone 1000 mg was initiated. However, there was new-onset hemoptysis and desaturation and the patient was intubated. Bronchoscopy revealed diffuse bleeding on the right middle lobe and she eventually expired. Both patients with active SLE nephritis presented in this study died within days of DAH diagnosis. Hence, aside from early recognition to improve outcomes we should anticipate its possible occurrence in patients with high disease activity.

ICW1-3

Hemophagocytic lymphohistiocytosis presenting as b symptoms in a young female with systemic lupus erythematosus, in remission: a case report

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Conflict of interest: None

[Objective] We aim to highlight the case of Hemophagocytic Lymphohistiocytosis, a life-threatening and severe systemic inflammatory syndrome, presenting as B Symptoms of fever, drenching night sweats, and weight loss in a young female with Systemic Lupus Erythematosus, In Remission. [Methods] We present the case of a 33 year old female with Systemic Lupus Erythematosus, who initially presented with cyclic chills, fever of Pel-Ebstein pattern, night sweats, and unintentional weight loss. She had multiple lymphadenopathies on physical exam, and on Whole Abdominal Computed Tomography, a right suprarenal mass was incidentally detected. Adrenalectomy was done which showed that the mass was benign. Meanwhile, serial complete blood count monitoring showed worsening pancytopenia. [Results] A bone marrow aspiration biopsy showed hemophagocytic features. H Score for Hemophagocytic Lymphohistiocytosis was then estimated to be at > 90%. Chemotherapy comprised of Etoposide and Dexamethasone was started. Febrile episodes resolved, and pancytopenia improved. Disease activity by SLEDAI consistently showed that SLE is in remission. [Conclusions] Our study shows that although uncommon, Hemophagocytic Lymphohistiocytosis in the background of Systemic Lupus Erythematosus, In Remission may occur. Prompt recognition is warranted to avoid fatal complications from the disease.

ICW1-4

Successful Treatment of Refractory Thrombocytopenia With Rituximab Plus Eltrombopag In A Post-Splenectomy Lupus Patient: A Case Report

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Conflict of interest: None

Objective: To present a case of a 33-year-old Filipino female with a known case of SLE including the treatment and outcome following Rituximab + Eltrombopag due to severe thrombocytopenia refractory to corticosteroids and splenectomy. **Case:** A 33-year-old Filipino female presented at the emergency room with low levels of platelet (29 g/L) and diagnosed with SLE for 11 years and was maintained on prednisone and hydroxychloroquine. Interim revealed patient had persistent thrombocytopenia despite chronic treatment of corticosteroids and hydroxychloroquine. She was referred to a hematologist who started with Eltrombopag and eventually underwent splenectomy. Patient still had decreasing levels of platelets post-splenectomy hence, patient was advised admission for Rituximab infusion. Unfortunately, patient became positive for COVID 19 causing a delay on her treatment. After 1 week, she was admitted with a platelet of 35 g/L and had Eltrombopag, methylprednisolone pulse therapy, and Rituximab. Her 2nd infusion of Rituximab with Eltrombopag was done after 12 days which resulted to increasing platelet counts thereafter. **Conclusion:** Rituximab combined with Eltrombopag can be effective in patients with refractory severe thrombocytopenia post splenectomy. Rituximab can be an alternative regimen instead of giving contraindicated immunosuppresant agents.

ICW2-1

Colchicine in treatment of cardiovascular outcomes in patients with calcium pyrophosphate crystal deposition disease

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Conflict of interest: None

Objectives: To assess the effect of colchicine, hydroxychloroquine, and methotrexate on cardiovascular outcomes (CVO) in CPPD pts. **Methods:** The study included 305 pts with CPPD. Among the factors influencing CVO were considered: gender, age, smoking, alcohol intake ≧20 standard doses/week, hypertension, history of cardiovascular disease (CVD): (ischemic heart disease (CHD), acute myocardial infarction myocardial infarction (AMI), acute cerebrovascular insufficiency (ACV), chronic heart failure (CHF) >3 grade, NYHA, diabetes mellitus (DM), cholesterol >5.1 mmol/l, GFR <60 ml/min/1.73 m^2, uric acid >360 μmol/l, CRP >2 mg/l, phenotypes of CPPD, taking COLCH, HCQ and MTX, GCs, NSAIDs. The causes of death were determined on the patient's death certificate, and then classified according to the ICD-10. newly developed cases of non-fatal cardiovascular events were identified on the basis of medical documentation. **Results:** The mean age at inclusion was 58.9±12.5 yrs. 264 patients were available for follow-up. Any of the studied cardiovascular events were registered in 79 (29.9%) pts. 46 (17.4%) pts died; 35 of 46 (76.1%) pts died because of CVD; 11 (23.9%) pts died due to other causes. Non-fatal cardiovascular events were registered in 44 (16.7%) pts. The risk of cardiovascular events was higher for ps aged >65 years, serum cholesterol level ≧5.1 mmol/l, GFR <60 ml/min/1.73 m^2, history of CVD. Colchicine therapy was associated with the lower risk of cardiovascular events (OR 0.20, 95% CI 0.11-0.39). Therapy with MTX and HCQ did not exert an influence on opportunity of CVO. **Conclusion:** Adverse CVD outcomes in CPPD pts are associated with age, hypercholesterolemia, CKD, and a history of CVD. The intake of colchicine, but not methotrexate and hydroxychloroquine, by patients with CPPD is associated with decline of risk of cardiovascular events.

ICW2-2

A Retrospective Single-Center Study of the Efficacy and Safety of Canakinumab in Patients with Colchicine-Resistant Or -Intolerant Familial Mediterranean Fever: A second report

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Conflict of interest: None

[Objective] The data of canakinumab (CAN) toward familial Mediterranean fever (FMF) patients in Japan is very limited. In this regard, we previously reported the post-marketing experience of 13 patients with colchicine-resistant or -intolerant familial Mediterranean fever (crFMF) treated with canakinumab (CAN) at our institution. This is a second report trying to clarify the real-world efficacy and safety of CAN toward crFMF patients. [Methods] We recruited 29 crFMF patients treated with CAN at our institution between 2017 and 2022. We analyzed their clinical background, including *MEFV* gene mutations/variants, CAN retention rates, frequency of febrile attacks, incidence of side effects, and reasons for discontinuation. [Results] The median age of 29 patients (typical FMF was 17 whereas 12 atypical) was 42 years old. None of the patients had exon 10 mutations of *MEFV* gene whereas considerable patients expressed *MEFV* gene polymorphisms. Colchicine responsiveness before the introduction of CAN was intolerable in 16 cases, no effect in 7 cases, and insufficient effect in 6 cases. Median follow-up period of CANwas 21 months, and the number of febrile attacks decreased from a median of 1/month at the time of administration to 0.27/month at 6 months after treatment. Three patients had complete resolution of attacks during the observation period, and 12 patients showed a 50% or greater reduction in attack frequency during the treatment of CAN. None of the factors such as typical or atypical cases, age of onset, or MEFV variants were significantly associated with the efficacy of CAN. The reasons for discontinuation were inadequate efficacy in 3 cases, ileal ulcer in 2 cases, persistent fever attacks in 2 cases, worsening abdominal pain in 1 case, and cellulitis in 1 case. [Conclusions] This study has confirmed the efficacy and safety regarding CAN in patients with crFMF in a real-world clinical setting in Japan.

ICW2-3

Generation and Pathophysiological Analysis of Knock-in Mice of M694I Variant of Human MEFV Gene

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Conflict of interest: None

[Objective] There are no model mice for the M694I variant of the MEFV gene, a disease-related gene important for FMF in Japan. We aimed to generate knock-in mice of the human MEFV gene M694I variant and to examine whether they have the pathogenesis of FMF. [Methods] Oligo of the exon10 region of the human MEFV gene was inserted into fertilized eggs of C57BL/6N mice using CRISPR/cas9, and the DNA sequence of mice was confirmed by the Sanger method. Backcrosses were performed twice using mice with confirmed insertions and C57BL/6N mice to create homozygous M694I mutant/ wild type (WT). Macrophages were injected with 5% thioglycollate medium into the abdominal cavity of M694I KI/ WT mice, and macrophages were collected to examine macrophage activation in response to LPS+ATP or LPS+C3toxin stimulation by protein expression analysis and cytokine/chemokine levels in the culture supernatants. We also collected CD4-positive macrophages from the spleen. CD4-positive T cells were isolated from the spleen to induce Th subset differentiation. [Results] The survival rate was significantly lower in the M694I group. Growth curves showed significant poor body weight gain at 15 weeks of age, increased neutrophils and activated macrophages in the M694I group, elevated serum G-CSF, IFN-γ, IL-6, TNF-α and other pro-inflammatory cytokines in the M694I group, and induction of T cell differentiation in vitro. In addition, the percentage of IL-17-producing cells was significantly increased in the M694I group. [Conclusions] Knock-in of the MEFV gene M694I induced FMF-like chronic inflammation. The involvement of Th17 cells in the background of inflammasome hyperactivity is suggested.

ICW2-4

The Ragulator complex activates the NLRP3 inflammasome through interactions with HDAC6 in acute gout arthritis

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Conflict of interest: None

[Objective] The activation of the NLRP3 inflammasome is spatiotemporally orchestrated by various organelles. Lamtor1/p18 forms pentameric Ragulator complex to mobilize the mTORC1 on the lysosomal membrane. There has been a series of important reports regarding the relationship between the Ragulator complex and pyroptosis, a type of inflammatogenic caspase-1 dependent cell death. However, the involvement of the Ragulator complex in inflammasome activation has not been elucidated. [Methods] We established conditional knockout (KO) mice lacking Lamtor1, an essential component of the Ragulator complex, in macrophages. We evaluated the role of Lamtor1 in a monosodium urate (MSU)-induced acute gouty arthritis model. We next evaluated the role of Lamtor1 in NLRP3 inflammasome activation by using Lamtor1 deficient BMDMs and Lamtor1 KO THP-1 cell lines. Mechanistically, we searched for proteins with which Lamtor1 interacts by performing quantitative proteomics and also performed a screening using a library of natural compounds to identify a negative regulator of the Ragulator complex. [Results] Myeloid-specific Lamtor1 KO mice showed marked attenuation of the severity of MSU-induced arthritis. Deficiency of Lamtor1 abrogated NLRP3 inflammasome activation in BMDMs and Lamtor1 KO THP-1 cell. Mechanistically, Lamtor1 interacted with HDAC6, and this interaction augmented the subsequent interaction between the Ragulator complex and NLRP3. Lack of HDAC6 attenuated the interaction between Lamtor1 and NLRP3, resulting in insufficient NLRP3 inflammasome activation. We found that DL-all-rac-α-tocopherol inhibited the Lamtor1-HDAC6 interaction, resulting in diminished NLRP3 inflammasome activation in vitro and in acute gouty arthritis model. [Conclusions] The Ragulator complex plays a critical role in inflammasome activation by interacting with NLRP3 via HDAC6. The therapeutic applications targeting the interaction between the Ragulator complex and HDAC6 may be effective for acute gout flare.

ICW2-5

Dysfunction of Tankyrase causes autoinflammation through activation of the TLR2 signaling pathway

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Conflict of interest: None

[Objective] Toll-like receptors (TLRs), which recognize PAMPs and activate the innate immune system and cytokine production, are associated with the pathogenesis of rheumatic diseases including autoinflammatory syndrome and systemic lupus erythematosus. Here, we have provided the genetic evidence showing that Tankyrase, a poly (ADP-ribose) polymerase (PARP) family member, negatively controls TLRs signaling and autoinflammation. [Methods] We generated Tankyrase conditional knockout (KO) mice in which endogenous Tankyrase was deleted in the myeloid/ monocytic lineage to examine the role of Tankyrase for the in vivo immune system. Mass spectrometry, IHC, Co-IP, pulse-chase, FACS, antigen microarrays to detect autoantibodies, luc assay, ubiquitin assay and ELISA were performed to investigate the molecular mechanisms in this study. [Results] We show that Tankyrase KO mice displayed severe systemic inflammation due to elevated inflammatory cytokine production. Tankyrase KO mice suffered from colitis, hepatitis and pneumonitis due to infiltration of macrophages and reactive recruitment of lymphocytes into multiple organs. We provide mechanistic evidence showing that TLR2 is tyrosine phosphorylated and activated in Tankyrase KO macrophages and that phosphorylation of tyrosine 647 within the TIR domain in TLR2 by SRC and SYK kinases is essential for activation of the TLR2 signaling pathway. We further generated mice lacking both Tankyrase and 3BP2, an adaptor protein which is required for SRC and SYK activation and negatively regulated by Tankyrase, and found that systemic inflammation observed in Tankyrase KO mice was completely rescued in Tankyrase/3BP2 double KO mice. [Conclusions] Our observation that dysfunction of Tankyrase causes autoinflammation through activation of the innate immune system in a 3BP2 level-dependent manner expands the concept that 3BP2 could be a therapeutic target for rheumatic diseases caused by dysregulation of the TLRs signaling pathway.

ICW3-1

Oral delivery of delta-9-tetrahydrocannabinol provides symptom and disease modification in mouse models of knee osteoarthritis

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Conflict of interest: None

Objectives: Osteoarthritis (OA) is a joint disease that affects chondrocytes from cartilage and fibroblast-like synoviocytes (FLS) from synovium. Some OA patients use cannabis to alleviate pain. Delta-9-tetrahydrocannabinol (THC), a prominent phytocannabinoid, signals in joint cells. We investigated the effects and mechanisms of action of THC on pain and joint degeneration in pre-clinical models of knee OA. **Methods:** Destabilization of the medial meniscus (DMM) and monosodium iodoacetate (MIA; 0.5 mg) mice were given THC (0, 5, or 10 mg/kg) orally 5 days/ week for 9 or 3 weeks, respectively. Von Frey tests were used to evaluate mechanical allodynia (pain). DMM mouse joints were evaluated for cartilage degeneration/synovitis (OARSI scoring) and Ki67/αSMA expression [immunohistochemistry (IHC)]. FLS and chondrocytes from human OA synovium and cartilage were treated with 0-10 μM THC for 48h. Flow cytometry was used to detect Annexin V^+ cells. RNA sequencing was performed on OA FLS to determine differentially expressed genes (DEGs) and DEG-enriched pathways. **Results:** 10 mg/kg THC reduced pain in DMM (n=15/group) and MIA (n=5/group) mice. In DMM mice, all THC doses reduced cartilage degeneration, with 10 mg/kg THC reducing synovitis (n=9-10/group) and decreasing αSMA but not Ki67 synovial expression (n=6/group). In vitro, THC increased Annexin V^+ OA FLS (n=5) at 2.5 μM. RNA sequencing identified 73 DEGs in OA FLS (n=4) treated

with 1 μM THC. Extracellular matrix (ECM) organization pathways were enriched in 35 upregulated genes, while cholesterol biosynthesis pathways were enriched in 38 downregulated genes. **Conclusions:** 10 mg/kg THC reduced pain, cartilage degeneration, synovitis, and synovial αSMA expression in DMM/MIA mouse knee joints. Non-cytotoxic THC treatment of human OA FLS modified gene expression associated with ECM organization and cholesterol biosynthesis. Our next studies will focus on identifying the signaling mechanisms of THC in joint cells.

ICW3-2

Foxp3+ Treg educated Dendritic cells have dual function for each different antigen

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Conflict of interest: None

[Objective] Foxp3 Treg cells are known to suppress antigen presenting cells such as dendritic cells. The function of dendritic cell can be evaluated by an ability to stimulate effector T cells. However whether DC interacted with antigen specific Foxp3 Treg cells have equal suppressive function with every responding T cells is not known. [Methods] (1) Tnaive cells specific to peptide antigen A (OVA) or to antigen B (LCMV), dendritic cells presenting both antigen A and antigen B were transferred into recipient mice intravenously together with Treg cells specific to either antigen A or antigen B. Transferred cells were collected on day 3 from the splenocytes of the recipient mice. Cell proliferation of the transferred two T cell populations was separately evaluated and suppressive function of DCs in vivo were assessed. (2) Dendritic cells presenting both A and B peptide were cultured with Treg cells specific to A or B. DCs isolated from the culture and Tnaive cells specific to A or B were co-cultured in the second culture in the absence of the initial Treg cells. Cell proliferation of the Tnaive cells in the second culture was assessed and the Treg treated DC function was evaluated. [Results] (1) Tnaive cells specific to the same antigen as co-transferred Treg cell recognize were suppressed, while Tnaive cells specific to the other antigen were not suppressed. (2) DCs interacted with Treg-A suppressed T cells specific to A, while the same DC still remained their stimulatory function to T cells specific to B peptide. [Conclusions] DCs are thought to mediate suppressive function of Treg cells in vivo. DCs interacted with Treg cells become suppressive only for the same antigen as Treg recognize, while they remain to have stimulatory function for the T cells specific to irrelevant antigen which Treg cells do not recognize.

ICW3-3

An endogenous metabolite, itaconate ameliorates collagen-induced arthritis

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Conflict of interest: None

[Objective] Various drugs are used to treat patients with rheumatoid arthritis (RA); however, many patients do not achieve remission. Moreover, increased susceptibility of treated patients to opportunistic infections has not been settled yet. Thus, new therapies with a low risk of infection are awaited. Itaconate (ITA) is an endogenous metabolite with anti-inflammatory, antiviral, and antimicrobial effects. Fibroblast-like synoviocytes (FLS) are critical players in the inflammation and destruction of the joint. This study aimed to identify the effect of ITA on FLS and its potential to treat RA. [Methods] FLS were isolated from synovial samples from patients with RA. Tumor necrosis factor α (TNFα)-treated FLS were cultured with ITA or phosphate-buffered saline (PBS). The proliferation potency of these FLS was evaluated by tetrazolium/formazan and BrdU assay. Cell migration was measured by *in vitro* scratch assay. We performed RNA sequencing and metabolomics using TNFα-treated FLS with or without ITA. Finally, intraarticular injections of ITA or PBS into ankle joints were performed on rats with type II collagen-induced arthritis (CIA). Bone erosion scores were assessed by micro-CT. [Results] The proliferation of FLS measured by tetrazolium/formazan assay ($p<0.01$), as well as BrdU assay ($p<0.01$), was reduced by ITA. ITA also inhibited the cell migration of FLS ($p<0.05$). The results of RNA sequencing and metabolomics indicated that ITA altered FLS metabolism, including glycolysis, which is involved in the migration of FLS. Intraarticular injection of ITA reduced the ankle diameter ($p<0.01$) and clinical arthritis score ($p<0.01$) in the CIA model (two-way ANOVA test). The bone erosion score was reduced in the ITA-treated group (mean; 1.6 vs. 0.1, $p<0.01$). [Conclusions] ITA inhibited the proliferation and cell migration of FLS, and ameliorated disease activity and bone destruction in the CIA model. ITA could be a novel therapeutic agent with a low risk of infections for RA.

ICW3-4

Airway smooth muscle cells activate fibroblast and promote peribronchial fibrosis via TNFSF14 (LIGHT) - LTβR signaling

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Conflict of interest: None

[Objective] Airway remodeling is an indicator of severe asthma and contributes to therapeutic resistance. There remains uncertainty about the factors that regulate airway remodeling, particularly peribronchial fibrosis, in asthma. We have previously shown that the inflammatory cytokine TNFSF14 (LIGHT), which is produced during asthma and viral infection of the airways, promotes airway hyperresponsiveness by enhancing airway smooth muscle (ASM) hypertrophy and contractility. Mice specifically lacking the LTβR, a receptor for LIGHT, on smooth muscle cells exhibited a reduced airway hyperresponsiveness in house dust mite (HDM)-induced chronic asthma, with reduced ASM mass. Interestingly, in addition to smooth muscle changes, peribronchial fibrosis was also reduced in ASM- LTβR deficient mice. The aim of this study was to investigate the possibility that ASM activated by LIGHT-LTβR signaling may promote airway fibrosis via activation of fibroblasts (FBL). [Methods] HDM-induced chronic asthma in ASM-LTβR deficient mice was assessed for peribronchial FBL infiltrations. Transcriptomic analysis of human ASM and FBL after LIGHT stimulation was performed using RNAseq. Proliferative and migratory function of FBL was analyzed in vitro. [Results] ASM-LTβR deficient mice showed reduced peribronchial FBL infiltration and collagen deposition. LIGHT stimulation enhanced the expression of CCL2, CXCL12, BMP, and FGF, which are known to be involved in FBL migration and activation, in an ASM-specific manner. FBL cultured in supernatants containing soluble factors from LIGHT-stimulated ASM had significantly enhanced proliferative and migratory capacities compared to those cultured in PBS-stimulated ASM supernatants. [Conclusions] ASM activated by LIGHT may contribute to airway remodeling via promoting lung fibroblast proliferation and migration. Elucidating the cross-talk between fibroblasts and smooth muscle may be important for the control of fibrotic diseases of the lung.

ICW3-5

Semaphorin 7A promotes Neutrophil extracellular trap formation

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Conflict of interest: None

[Objective] Although semaphorin molecules were identified as a regulator of neuronal growth, they play essential roles in the inflammatory

response. A previous study showed that semaphorin 7A (SEMA7A) is a potent promotor of neutrophil migration during hypoxia. However, the effect of SEMA7A on the other neutrophil functions remains unclear. The purpose of this study is to investigate the role of SEMA7A in neutrophil activation. [Method] Peripheral blood neutrophils were isolated from healthy donors by using magnetic cell sorting (MACS). The expression of SEMA7A and its receptors, integrinβ1 and Plexin-C1, on neutrophils or vascular endothelial cells was detected by flow cytometry. For neutrophil extracellular trap (NET) formation assay, recombinant SEMA7A-Fc proteins or control-Fc proteins were pre-coated onto a 96-well plate. Isolated neutrophils were primed with or without 5 ng/ml human TNF-α for 30 minutes and seeded onto the plate. Hoechst-33342 and SYTOX green dye were then added to non-fixed live cells so that extracellular DNA would be detected. Fluorescence images were acquired on a BZ-X810 microscope (Keyence). Reactive oxygen species (ROS) were measured by using Fluorimetric Hydrogen Peroxide Assay Kit (Sigma-Aldrich). [Result] SEMA7A was not expressed on steady-state neutrophils or endothelial cells. TNF-α induced the expression of SEMA7A on endothelial cells. Plexin-C1 is expressed on neutrophils. Direct interaction between neutrophils and recombinant SEMA7A proteins significantly increased neutrophil ROS production and NET formation. Priming with TNF-α was necessary for this effect. By using an anti-Plexin-C1 antibody, SEMA7A-induced NET formation was significantly reduced. [Conclusion] Under TNF-α primed condition, SEMA7A activates neutrophils via its receptor Plexin-C1. This impact can be involved in the pathogenesis of rheumatic diseases such as autoimmune vasculitis.

ICW3-6

Leveraging the Japanese microbial genome database to identify rheumatic diseases-crAss-like phage associations

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Conflict of interest: None

[Objective] The human gut microbiome interacts with the host's body via the immune system and contributes to autoimmune diseases. In gut microbiome studies, the genomic sequences of the individual microbes are important resources. However, current gut microbial databases do not sufficiently cover the Japanese-specific bacterial genomes and overall viral genomes, hindering us from a comprehensive understanding of the gut microbiome-autoimmune diseases associations in Japanese, especially for virome. [Methods] We developed a pipeline to recover microbial genomes from gut metagenome shotgun sequencing data and applied it to the data of 787 Japanese individuals. We evaluated whether the recovered microbial genomes contained the features of the Japanese gut microbiome. Based on the expanded gut virome database, we performed clustering of the crAss-like phage genomes and annotated sub-family and genus-level taxonomy. Then, we evaluated the associations between the crAss-like phages and autoimmune diseases including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). We predicted the bacterial hosts of the crAss-like phages. [Results] We reconstructed 19,084 prokaryotic and 31,395 viral genomes from 787 Japanese gut metagenomes as Japanese Metagenome Assembled Genomes (JMAG) and Japanese Virus Database (JVD). Enrichment of the *Bacillus subtilis* and β-porphyranase among the JMAG could derive from the Japanese traditional foods natto (fermented soybeans) and nori (laver), respectively. Multiple crAss-like phage clades, including αγ and ζ crAss-like phages, were decreased in RA and SLE and positively associated with gut bacterial diversity. The crAss-like phages mainly infected *Bacteroidota*, but also infected *Firmicutes*. [Conclusions] Our expanded Japanese microbiome catalog enabled us to identify the autoimmune disease-associated changes of the gut virome with fine taxonomic resolution. JMAG and JVD are publicly available (https: //github.com/ytomofuji/JMAG_JVD).

ICW4-1

The short-term clinical outcome of upadacitinib in patients with rheumatoid arthritis from Niigata University Orthopedic Surgery Rheumatoid Arthritis Database

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Conflict of interest: None

[Objective] To clarify the clinical outcome of upadacitinib (Upa) in patients with rheumatoid arthritis (RA). [Methods] Twenty cases (15 women and 5 men) with RA were registered from NOSRAD. The average age on administration of Upa was 68 years old (47 to 85 years old). The average RA duration was 10 years (4 to 30 years). Difficult to treat RA was 11 cases (55%). Methotrexate was treated in 6 cases and its dose was 6.7 mg /week on average. Prednisolone was treated in 6 cases and its dose was 3.4 mg/ day. The administered daily doses of Upa were 15 mg in 9 cases, and 7.5 mg in 11 cases. The clinical outcome and the adverse events were examined. [Results] The average DAS28-ESR was 3.9 on the administration, and significantly decreased to 2.2, 2.0, and 2.4 on 1, 3, and 6 months after the administration ($p<0.01$). The average CDAI was 15 on the administration, and significantly decreased to 7.3, 5.0, and 5.9 on 1, 3, and 6 months after the administration ($p<0.01$). White blood cell count was significantly decreased from 6588 on the administration to 6171 on 1 month after the administration ($p<0.05$), but showed no significant change after 3 months. Lymphocytes count was significantly elevated from 1425 on the administration to 1730 on 1 month after administration ($p<0.05$), but showed no significant change after 3 months. For adverse events, herpes zoster, fever up, and cough was detected in 1 case each. Upadacitinib was decreased from 15 mg to 7.5 mg in daily doses for the latter 2 cases. All the 3 cases were retained for Upa. The retention rate was 100% by the end of observation period (6 months). [Conclusions] Upa demonstrated rapid decrease of the disease activity of RA and good efficacy even in difficult to treat RA cases although the observation period in this study was only 6 months without severe adverse events.

ICW4-2

Clinical observation of Tofacitinib in the treatment of difficult-to-treat rheumatoid arthritis: a retrospective study

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Conflict of interest: Yes

[Objective] To explore the clinical efficacy and safety of Tofacitinib in the treatment of difficult-to-treat rheumatoid arthritis (D2T-RA). [Methods] Sixty patients with D2T-RA who had received therapies with Tofacitinib for 24 weeks were included into this study. The improvements of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), visual analogue score (VAS), swollen joints count, tender joints count, interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10), γ-interferon, tumor necrosis factor α (TNF-α), anti-cyclic citrullinated peptide antibody (CCP), anti-keratin antibody (AKA), and antinuclear antibody (ANA), and the changes of blood routine, liver function and kidney function before and after treatment were observed prior to treatment initiation and at weeks 4,12, and 24 after Tofacitinib treatment. [Results] After 4,12 and 24 weeks of Tofacitinib treatment, RF, CRP, ESR, swollen joints count, tender joints count and VAS were significantly decreased ($P<0.05$). ESR, CRP, RF, IL-2, IL-4, IL-6 and IL-10 were significantly decreased. The positive rates of CCP, AKA and ANA decreased. One patient developed diarrhea after 4 weeks, 2 patients developed herpes zoster after 24 weeks, 2 patients developed a mild increase in transaminase after 4 weeks, 6 patients developed a mild increase in transaminase after 12 weeks, 6 patients developed a mild increase in transaminase after 24 weeks. No serious adverse reactions such as leukopenia, thrombocytopenia, cardiac insufficiency and allergy occurred in all patients. [Conclusions] Tofacitinib in the treatment of D2T-RA was effec-

tive, can **significantly** improve the clinical symptoms, signs, disease activity and other indicators of patients, and with high safety, is a alternative choice for the treatment of D2T-RA.

ICW4-3

Baricitinib chronotherapy targeting cytokine secretions in rheumatoid arthritis: A multicenter prospective study

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Conflict of interest: None

[Objective] Cytokines, such as TNF-α and IL-6, exhibit a circadian rhythm that peaks from midnight to early morning in patients with rheumatoid arthritis (RA). We previously reported that baricitinib (BAR) administration combined with cytokine secretion improved collagen-induced arthritis in mice. Therefore, we evaluated whether the nighttime administration of BAR is effective in RA patients. [Methods] This 24-week, prospective, open-label trial included patients who received disease-modifying antirheumatic drugs (DMARDs) or biological DMARDs at stable doses for ≧12 weeks and had not reached clinical disease activity index (CDAI) remission. A total of 102 patients were assigned to one of four doses: BAR 2 mg morning, 2 mg evening, 4 mg morning, or 4 mg evening. The primary outcome was the response to treatment in each group using the ACR20 at week 12. The secondary outcome was the change in CDAI. [Results] The participants, who were followed up to 12 weeks, included 26, 24, 23, and 23 patients from 2 mg morning, 2 mg evening, 4 mg morning, and 4 mg evening groups, respectively. Biologic-naive patients were 63.2% and 31.8% in 2 mg and 4 mg groups, respectively. There were no other differences in patient background in all groups. The ACR20 response rate at week 12 was 50% and 85.7% in the 2 mg morning and evening, respectively (P<0.05). The average reduction in CDAI at week 12 was -8.6±10.6 and -13.5±7.4 in the 2 mg morning and evening, respectively, with no significant differences between them. However, CDAI was reduced in the evening group at week 4 (P<0.05). In the 4 mg groups, the ACR20 response rate at week 12 was 57.9% and 83.3% in the morning and evening, respectively (P=0.08). Additionally, the average reduction in CDAI at week 12 was -9.6±9.0 and -16.4±9.9 in the morning and evening, respectively (P<0.05). Furthermore, CDAI improved in the evening group at weeks 4 and 8 (P<0.05). [Conclusions] BAR therapy targeting cytokine secretion was effective in treating RA.

ICW4-4

Effect of JAK1 inhibition on bone erosion repair in rheumatoid arthritis: a pilot study

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Conflict of interest: Yes

[Objective] To evaluate whether inhibition of JAK1 could lead to erosion repair in patients with active RA. [Methods] This was a 24-week, single-centered, non-randomized pilot study. We enrolled 20 adult patients with active RA (DAS28-CRP > 3.2) and ≧1 bone erosion on HR-pQCT. They were given upadacitinib 15 mg once daily for 6 months. HR-pQCT of the 2-4 MCP head was done at baseline and 6 months. The primary outcome was the change of erosion volume on HR-pQCT. Erosion regression was defined as decrease in volume exceeding the smallest detectable change. [Results] Of the 20 patients, 11 (55%) patients had failed to respond to 3 or more csDMARDs. At 24-week, there was significant improvement in mean DAS28 (-1.75, p<0.001). Erosion regression was seen in 8 (40%) patients on HR-pQCT. Although no significant change in overall median erosion volume before and after upadacintinib (0.07 [-0.90-0.76] mm3, p=0.904) was noted, the deterioration was less obvious compared to a historic cohort of 20 patients with similar age and disease activity on csDMARDs (median erosion volume change in 6 months: 0.67 mm3). When patients were stratified according to whether or not they had failed multiple csDMARDs, significantly high proportion of patients in the non-multiple-DMARDs failure group had volume regression in at least one erosion compared to those in the failure group (75% vs 25%, p=0.04). There was improvement in mean total erosion volume in the non-failure group (-0.33±1.33 mm3), whereas mean erosion volume in the failure group worsened (2.09±7.62 mm3). One patient developed chest infection requiring hospitalization and withdrew from the study. [Conclusions] The results of the study suggest JAK1 inhibition is clinically efficacious in refractory RA disease and can retard erosion progression. Regression of erosion is possible, particularly in those with limited csDMARDs exposure. Whether early JAK1 inhibition could lead to better structural outcome warrants further investigations.

ICW4-5

The effect of perioperative Janus kinase inhibitor withdrawal on surgical site infection and relapse of rheumatoid arthritis in orthopedic surgery: a multi-center observational study

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Conflict of interest: None

[Objective] Although new guidelines recommend three days of preoperative withdrawal of Janus kinase inhibitors (JAKi), the optimal timing and duration of JAKi interruption in patients with rheumatoid arthritis (RA) undergoing orthopedic surgery are still unclear. By contrast, a balance between reducing the risk of surgical site infection (SSI) and preventing relapse of RA must be reached. We conducted a multi-center observational study to investigate the effect of perioperative JAKi withdrawal on surgical site infection (SSI) and relapse of RA in orthopedic surgery. [Methods] RA patients who visited six tertiary care centers between 2018 and 2021 and took JAKi before the orthopedic surgery were included. We defined SSI based on the United States Centers for Disease Control criteria and relapse as the clinician-assessed reappearance of joint tenderness or swelling. [Results] Of thirty-one patients, two patients (6.5%) developed SSI. Both patients had multiple risk factors for SSI other than JAKi, including advanced age, diabetes mellitus, and the use of a glucocorticoid. Although the rare incidence of SSI hampered the assessment of the risk factors for SSI, any trends of characteristics in patients without SSI were not identified in terms of the type of JAKi used, timing and duration of preoperative JAKi withdrawal, or invasiveness of surgery. Seven out of thirty-one patients relapsed (22.6%). The postoperative withdrawal period of JAKi was significantly associated with relapse (odds ratio [OR] for >14 days compared to ≦7 days: 8.5, 95% confidence interval [CI]: 0.97 - 74.4, p = 0.048). On the contrary, the preoperative withdrawal period was not associated with relapse (OR for >4 days compared to ≦1 day: 1.2, 95% CI: 0.39 - 17.5, p = 0.33). [Conclusions] Except for patients with multiple risk factors, no JAKi users developed SSI. During the perioperative period, a shorter postoperative withdrawal period of JAKi may be important to prevent relapse of RA.

ICW4-6

The Risks of Cancer, Infection, and MACEs Associated with Tofacitinib and Baricitinib Are Comparable: Results of a Multi-center Cohort Study in Japan

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Conflict of interest: None

[Objectives] The risks of real-world adverse events such as herpes zoster (HZ) and malignancies associated with tofacitinib and baricitinib treatment for rheumatoid arthritis (RA) are unclear. To compare the incidence of infectious diseases, HZ, major cardiovascular events (MACEs), and malignancies in RA patients treated with tofacitinib or baricitinib in a real-world setting. [Methods] We enrolled 296 RA patients treated with tofacitinib (n=192) or baricitinib (n=104). The incidence rates (IRs) of infectious disease and HZ and the standardized incidence ratio (SIR) of malignancies were determined. We investigated factors related to infectious diseases. After adjusting the clinical characteristic imbalance by propensity score weighting, we compared the incidence of adverse events between tofacitinib and baricitinib. [Results] The IRs were: infectious diseases other than HZ, 15.63 per 100 patient-years (PY); serious infectious diseases other than HZ, 8.36/100 PY; HZ, 13.00/100 PY. Multivariable Cox regression analyses revealed independent following risk factors: the glucocorticoid dose in infectious diseases other than HZ and older age in HZ. Two MACEs and 11 malignancies were identified. The SIR for overall malignancies was higher compared with the general population (1.59/100 PY, 95%CI: 0.79-2.85), but not significant. There were no significant differences between tofacitinib and baricitinib in these adverse events' IRs. [Conclusions] We demonstrated higher IR of infectious diseases in RA patients treated with tofacitinib and baricitinib with comparable risk between these two Janus kinase inhibitors in daily clinical practice. The incidence of malignancies was numerically high but not significant compared with general population in Japan.

ICW5-1

Serum biomarkers for distinguishing infections from flares in systemic lupus erythematosus patients presenting with fever

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Conflict of interest: None

Objectives*: Fever in* SLE patients is difficult to differentiate. Therefore, the aims of this study are to determine biomarkers; ESR, CRP, ESR: CRP ratio, serum complement, anti-dsDNA antibody, Neutrophil-to-Lymphocyte ratio (NLR), Immature Granulocyte percentage (IG%), IG-cells, and Platelet-to-Lymphocyte Ratio (PLR), to discriminate causes of fever in SLE patients between infection and active disease. **Method:** The cross-sectional study was performed at the inpatient and outpatient department of the Faculty of Medicine, Chiang Mai University, between 2020 and 2022. Blood samples for biomarkers from SLE patients with fever (three groups: patients with infection, inactive disease; I-IA; patients with non-infection, active disease; NI-A; and patients with infection and active disease; I-A) were performed prior to therapy. SLE patients with no fever, no infection and inactive disease (NI-IA), were asked for blood sample. **Results:** A 62 SLE patients (13 I-A, 17 I-IA, 14 NI-A and 18 NI-IA), including 56 females, 90.32%, with a mean age of 44±13 years, were included. SLE patients in NI-A group had higher proportion of elevated anti-dsDNA antibody >100 IU/ml than patients in I-IA group (94.31% vs. 41.18%, p<0.01). Biomarkers showed sensitivity, specificity, and area under the curve (AUC) to discriminate cause of fever between I-IA and NI-A groups; NLR>6.3 (59%, 86%, 0.72), ESR: CRP ratio<1.14 (71%, 86%, 0.78) and between patients with infection (I-A, I-IA) and patients with non-infection (NI-A, NI-IA); NLR>6.3 (53%,91%,0.72), ESR: CRPratio <1.14 (63%, 94%, 0.79), IG >0.6% (73%, 75%, 0.74), IG cell>40 cell/mm3 (70%, 78%, 0.74). **Conclusion:** The NLR>6.3 and ESR: CRP-ratio<1.14 may useful in differentiating causes in SLE patients presented with fever between infection and active disease. Whereas NLR>6.3, ESR: CRP-ratio<1.14, IG>0.6% and IG cells>40 cell/mm3 may useful for discriminating between SLE patients with infection and without infection. Further studies need to confirm.

ICW5-2

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

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Conflict of interest: None

[Objective] As conventional currently-used laboratory tests for systemic lupus erythematosus (SLE) are not sufficient to reflect disease activity, this study aimed to explore novel biomarkers for SLE. [Methods] Sera were collected from 34 patients with SLE and 10 healthy controls (HC), and a total of 368 inflammation associated proteins were analyzed. Peripheral blood mononuclear cells were isolated from the same 34 patients and 15 HC. The proportion of 47 peripheral immune cell types was evaluated by flow cytometry. Clinical data, including SLE Disease Activity Index (SLEDAI), were collected and correlation analyses were performed. [Results] Of 34 patients, 31 were females and the median age was 40 years old. The median SLEDAI was 6.0 and 11 had lupus nephritis. From the protein profile, 82 proteins showed significant differences between SLE and HC. Among them, 14 had positive (r>0.4) and 4 had negative correlations (r<-0.4) with SLEDAI. The frequency of Th17 (p<0.01), type 17 CD8 T (Tc17, p<0.05), type 17 follicular helper T (Tfh17, p<0.01), type 17 peripheral helper T (Tph17, p<0.01), activated CD4 (p<0.01) and CD8 (p<0.01) T cells were increased in SLE compred with HC. The frequency of activated CD4 (r=0.40), Tfh (r=0.37) and Tph (r=0.45) were correlated with SLEDAI. From these results, we focused on C-type lectin domain family 7 member A (CLEC7A). CLEC7A functions as a pattern-recognition receptor for glucans and plays a role in innate immune response. Serum CLEC7A levels were upregulated in SLE, correlated with SLEDAI (r=0.48), and higher in the patients with lupus nephritis than in those without. Interestingly, serum CLEC7A levels were correlated with the frequency of activated CD4 (r=0.76), activated CD8 (r=0.52), Tfh17 (r=0.37) and Tph17 (r=0.50), as well as serum TNF (r=0.82), IL-6 (r=0.66) and IFNγ (r=0.51) levels. [Conclusions] Serum CLEC7A levels were upregulated in SLE and positively correlated with SLEDAI. CLEC7A could be a potential novel biomarker in SLE.

ICW5-3

Strong Interferon alfa expression in renal tissue predicts high activity and poor prognosis in active lupus nephritis

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Conflict of interest: None

[Objective] Lupus nephritis (LN) is a major organ involvement of SLE which aggravates renal mortality. Instead of non-specific immunosuppressive therapy, new biologic agents targeting IFNα, IL-12 and BAFF have been expected to improve its prognosis. The aim of our study is to clarify whether the immunohistochemical expression of these morecules in LN kidney tissue is associated with LN clinicopathological findings and prognosis. [Methods] Fifty cases of active LN (ISN/RPS class III and IV), five of LN class II, IgA nephropathy and idiopathic hematuria assigned as controls were enrolled. Immunohistochemistry (IHC) for CD3, CD20, IFNα, IL-12/p40, and BAFF were performed. The IHC score was calculated by scoring the number of positive cells/ area of cortex. Active LN cases were grouped by the highest expression of IFNα, IL-12/p40 and BAFF,

then clinicopathological features were compared among three groups. [Results] Clinical data of active LN included 43 female, 43.5 y.o. (mean), urinary protein 2.2 g/day, anti-ds-DNA antibody 200.9 IU/ml, CH50 21.9 U/ml, SLEDAI 19.8 points. Histologically, 13 cases with class III, 27 cases with class IV and 10 cases with class III/IV+V were included. LN cases were classified into IFNα (n=17), IL-12 (n=16), and BAFF group (n=17) by IHC score. Control groups had low IHC score compared with active LN. Hypocomplementemia and glomerular endocapillary hypercellularity were significantly increased in IFNα group, while chronic lesions such as tubular atrophy in renal tissue were significantly higher in IL-12 group ($p<0.05$). IFNα group had a poorer renal prognosis than BAFF group in treatment response after 52 weeks. [Conclusions] The IHC of IFNα, IL12 and BAFF for active LN enabled to group active LN. Especially, IFNα and IL-12 group showed different clinicopathological features and renal prognosis. The results indicate the possibility of stratifying cases according to the IHC of target molecules, which might lead to precision medicine in the future.

ICW5-4

The presence of CD28null T Cells is Associated with Increased Risk and Severity of Pneumonia in Systemic Lupus Erythematosus Patients

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Conflict of interest: None

[Objective] Patients with systemic lupus erythematosus (SLE) are prone to the risk of infection, including pneumonia. This study aimed to determine the association between the $C28^{null}$ T cells with the risk and severity of pneumonia in patients with SLE. [Methods] This cross-sectional study recruited fifty-one female SLE patients aged 16-45 years old who were admitted to Saiful Anwar General Hospital, Indonesia. All subjects were monitored for the clinical, laboratory, radiographic findings, and the outcome during admission. Patients were diagnosed with pneumonia based on clinical, laboratory, and radiological characteristics. CURB65 score was used to assess the clinical severity of pneumonia among subjects, and patients were classified as mild-moderate and severe pneumonia. $CD28^{null}$ T cell percentages were measured by flowcytometry from blood, counted as $CD4^{+}CD28^{null}$ and $CD8^{+}CD28^{null}$. [Results] Twenty-one SLE patients were diagnosed with pneumonia during admission. Subjects with pneumonia had higher percentages of $CD4^{+}CD28^{null}$ ($4.6 \pm 3.1\%$ vs. $0.7 \pm 0.3\%$; $p<0.001$] and $CD8^{+}CD28^{null}$ ($17.2 \pm 7.1\%$ vs. $12.6 \pm 7.7\%$; $p=0.034$) T cells, compared to non-pneumonia. Percentages of $CD4^{+}CD28^{null}$ and $CD8^{+}CD28^{null}$ were positively correlated with CURB65 score ($r=0.649$, $p=0.001$; $r=0.685$, $p<0.001$) and patient's length of stay ($r=0.410$, $p=0.033$; $r=0.372$, $p=0.048$). Subjects with pneumonia who passed away during admission (n=3) also had higher percentages of $CD4^{+}CD28^{null}$ ($12.3 \pm 5.6\%$ vs. $3.4 \pm 2.1\%$; $p=0.000$) and $CD8^{+}CD28^{null}$ ($24.4 \pm 3.8\%$ vs. $16.0 \pm 6.8\%$; $p=0.030$) compared to survivors. In the multivariate analysis, $CD4^{+}CD28^{null}$ was significantly associated with the incidence of pneumonia ($p=0.001$) and severe pneumonia ($p=0.004$). [Conclusions] The presence of $CD28^{null}$ T cells was associated with higher incidence and more severe pneumonia in SLE patients. $CD28^{null}$ T cells might propose a new pathogenesis in the development of infection in SLE.

ICW5-5

The association of fecal calprotectin levels and clinical characteristics in patients with connective tissue diseases with gastrointestinal symptoms: A retrospective cohort study

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Conflict of interest: None

[Objective] To investigate the association of fecal calprotectin (FC) levels and clinical manifestations in patients who have connective tissue diseases (CTDs) and gastrointestinal symptoms. [Methods] This is a single-center retrospective cohort study conducted at Hiroshima University Hospital. Patients who had been diagnosed with CTDs and examined FC (SRL Inc., Tokyo, Japan) when they had gastrointestinal symptoms from January 2019 to August 2022 were consecutively registered. [Results] A total of 16 patients were reviewed whose median age was 41.5 years old, with a female ratio of 87.5%. Among them, nine patients had been diagnosed with systemic lupus erythematosus (SLE), three with systemic sclerosis (SSc), and the remaining four with polyarteritis nodosa, Behcet's disease, peripheral spondyloarthritis and autoimmune-associated protein-losing enteropathy. In nine SLE patients, five patients were diagnosed as having lupus enteritis. In the overall populations, the median FC levels (interquartile range) were 159.0 (79.0 - 663.0) μg/g, while those of SLE and SSc were 136.0 (85.5 - 496.0) μg/g and 71.0 (42.0 - 142.0) μg/g, respectively. In SLE, patients with lupus enteritis tended to show higher levels of FC than those without (446.0 (88.7 - 624.0) μg/g vs. 107.5 (76.8 - 160.0) μg/g, $p=0.07$). In two patients with lupus enteritis who followed FC, elevated FC levels decreased after immunosuppressant treatment. [Conclusions] FC levels were associated with disease types and subtypes in patients with CTDs. In patients with SLE, elevated FC levels can be one of the diagnostic clues for lupus enteritis.

ICW5-6

Activation of CD8+ T cells in peripheral blood is related to disease activity and resistant to treatment in patients with Systemic Lupus Erythematosus -LOOPS registry/FLOW study-

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Conflict of interest: None

[Objective] We investigated the relationship between peripheral blood CD8+ T cells and the pathogenesis of SLE. [Methods] The study consisted of 211 SLE patients (mean age, 42.3 years; female ratio, 89%; mean disease duration, 112.8 months) who were first admitted to the hospital and enrolled in the LOOPS registry between November 2012 and December 2018 and 62 age-sex matched healthy controls (HC). Based on peripheral blood comprehensive immunophenotyping according to the NIH/FOCIS protocol, $CD8^{+}$ T cells were classified into naïve ($CD45RA^{+}CCR7^{+}$), central memory (CM) ($CD45RA^{-}CCR7^{+}$), effector memory (EM) ($CD45RA^{-}CCR7^{-}$), and EMRA ($CD45RA^{+}CCR7^{-}$) cells for cluster analysis. [Results] (1) Activated $CD8^{+}$ T cells (a$CD8^{+}$ T: $CD38^{+}HLA\text{-}DR^{+}$ $CD8^{+}$) and activated cytotoxic T cells (aTc1: $CXCR3^{+}CCR6^{-}$ $CD38^{+}HLA\text{-}DR^{+}$ $CD8^{+}$) in peripheral blood were increased in SLE compared with HC ($p<0.01$). In addition, they were correlated with anti-ds-DNA antibodies ($rs=0.338/0.256$, $p<0.01$) and CH50 ($rs=-0.329/-0.295$, $p<0.01$), and significantly increased in patients with active lupus nephritis (renal BILAG≧B) ($p<0.01$). (2) SLE patients were classified into three subpopulations by cluster analysis of $CD8^{+}$ T cell phenotypes (ward's method). SLE patients in the cluster with high a$CD8^{+}$ T/aTc1 had high disease activity and a high rate of active lupus nephritis and were treated with intensive immunosuppressive therapy. (3) At 24 weeks after the intervention, the active $CD8^{+}$ T cell group (a$CD8^{+}$ T cells/Peripheral Blood Mononuclear Cells (PBMC) ≧4.52% (HC 95% tile) had a higher percentage of active BILAG (A≧1 or B≧2) (17.9% vs 0%; $p<0.01$) and higher SLEDAI score (4.8 vs 1.8; $p=0.01$) compared to the normalized $CD8^{+}$ T cell group (a$CD8^{+}$ T cells/PBMC <4.52%). [Conclusions] Activated $CD8^{+}$ T cells in the peripheral blood were significantly correlated with disease activity of SLE and complication rate of lupus nephritis, additionally involved in the resistance to treatment.

ICW6-1

Efficacy and safety of the second-generation JAK inhibitors for rheumatoid arthritis: a single-center retrospective case-control study

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Conflict of interest: None

[Objective] Because of their selective inhibition of Janus kinase (JAK) 1 than other JAK subtypes, upadacitinib (UPA) and filgotinib (FIL) are sometimes called the second-generation JAK inhibitors (JAKi). We investigated whether the efficacy and safety of the second-generation JAKi for rheumatoid arthritis (RA) are affected by the history of other JAKi use. [Methods] A single-center retrospective case-control study of RA patients treated with the second-generation JAKi between January 2021 and September 2022. Patients were divided into two groups who cycled from a different kind of JAKi (JAK cyclers) and who have not previously been treated with JAKi (JAK naïve) and compared efficacy and safety of the second-generation JAKi. Clinical information was collected from medical records. Disease activity was evaluated at the time of the second-generation JAKi, at 1, 3, and 6 months after. Log-rank test was used to compare the continuation rate, which was recognized as a composite measure of efficacy and safety in real-world clinical practice. [Results] 59 RA patients treated with the second-generation JAKi (UPA and FIL were 39 and 20, respectively) were included in the study. There was no significant difference in 1-year continuation rates between UPA and FIL (p = 0.13). JAK cyclers and JAK naïve patients were 29 and 30, respectively. There was no significant difference in patient backgrounds; however, the rate of using methotrexate was significantly lower in JAK cyclers (34.5% vs. 73.3%, p = 0.04). Both groups showed similar efficacy after 1 to 6 months of starting the second-generation JAKi; the achieved low disease activity of DAS28-CRP at one month was 78.6% in JAK cyclers and 80.0% in JAK naïve. There was no significant difference in the continuation rates between the two groups (median time; 18.2 months in JAK cyclers, 16.2 months in JAK naïve, p = 0.54). [Conclusions] The second-generation JAKi may be practical for JAK naïve patients and for JAK cyclers.

ICW6-2

Comparison of efficacy and safety of upadacitinib and other Janus kinase inhibitors in rheumatoid arthritis using inverse probability weighting with propensity score: From the FIRST registry

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Conflict of interest: None

[Objective] Five JAK inhibitors (JAKinibs) are currently approved for the treatment of rheumatoid arthritis (RA). In this study, we investigated the differences in efficacy and safety of upadacitinib (UPA) compared with other JAKinibs in a registry of RA patients who received molecular-targeted agents at our department and related institutions (FIRST registry). [Methods] Patients with RA who received JAKinibs for at least 6 months between July 2013 and March 2022 were enrolled. Selection bias was minimized by propensity-score based inverse probability weighting (PS-IPTW). The primary endpoint was a comparison of CDAI at six months after induction of UPA (n=52) or other JAKinibs (n=307; tofacitinib, baricitinib, peficitinib, filgotinib). Secondary endpoints were a comparison of continuation rates and adverse events until six months. [Results] After adjustment by PS-IPTW, CDAI at six months after induction of JAKinibs was significantly lower in the UPA group than in the other JAKinibs group (UPA vs. other JAKinibs=4.7±5.8 vs. 7.5±8.5, p<0.05). There was no difference in the rate of continuation and adverse events between the two groups. In a multivariate analysis, the factors associated with CDAI remission at six months in the UPA group were identified as " the history of treatment by fewer molecular-targeted agents before the induction of UPA". Although the UPA group achieved CDAI remission more than the other JAKinibs group in patients who had treated with less than two prior molecular-targeted agents (UPA vs other JAKinibs=74.6% vs. 41.4%, p<0.01), both groups had similar CDAI remission rates in patients who had treated with two or more molecular-targeted agents (UPA vs other JAKinibs=32.9% vs 30.5%, p=0.80). [Conclusions] All JAKinibs showed high efficacy against difficult-to-treat RA (D2TRA); however, UPA may be more effective in the pre-D2T phase, when the patients have been treated with fewer molecular-targeted agents.

ICW6-3

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

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Conflict of interest: None

[Objective] The aim of this multicenter, retrospective study was to clarify the impact of rheumatoid factor (RF) or anti-cyclic citrullinated peptide antibody (ACPA) titer on retention rate of biologics and JAK inhibitors (JAKi) in patients with rheumatoid arthritis. [Methods] Patients were as follows; females, 83.5%; age, 60.2; DAS28-ESR, 4.3; treatment course with either TNF inhibitors (TNFi; N=2704), anti-interleukin-6 receptor antibody (aIL-6R; N=1218), CTLA4-Ig (N=903) or JAKi (N=487). Patients were classified into three groups according to their serum RF (IU/mL) and ACPA (U/mL) titer: negative (RF<15 and ACPA<4.5), low positive (15≦RF<100 and 4.5≦ACPA<100), or high positive (100≦RF and 100≦ACPA), respectively. The reasons for drug discontinuation were classified into four major categories (lack of effectiveness, toxic adverse event, non-toxic reasons, and remission). The drug retention rate was estimated at 24 months using the Kaplan-Meier method and adjusted for potential confounders (age, sex, disease duration, concomitant oral glucocorticoid or methotrexate, etc.) by Cox proportional hazards modeling. [Results] The discontinuation rates of TNFi, aIL-6R, CTLA4-Ig and JAKi for the corresponding reasons were as follows, respectively; lack of effectiveness (36.2%, 21.4%, 30.4% and 27.1%; Cox P<0.001), toxic adverse events (13.3%, 12.5%, 12.1% and 14.6%; Cox P=0.369). When grouped by ACPA, discontinuation rates due to ineffectiveness were listed in ascending order as follows, respectively; ACPA negative (aIL-6R, 20.9%; TNFi, 28.8%; JAKi, 30.7%; CTLA4-Ig, 43.4%; Cox P<0.001), low positive (aIL-6R, 19.2%; JAKi, 26.4%; CTLA4-Ig, 27.3%; TNFi, 33.6%; Cox P<0.001) and high positive (aIL-6R, 23.1%; JAKi, 25.6%; CTLA4-Ig, 29.7%; TNFi, 35.2%; Cox P<0.001). [Conclusions] Regarding ineffectiveness, aIL-6R showed highest continuation rates regardless of RF/ACPA titer. CTLA4-Ig and JAKi showed higher continuation rates in ACPA-positive cases regardless of their titer levels.

ICW6-4

Safety and Efficacy of Upadacitinib in Patients with Rheumatoid Arthritis and Inadequate Response to Conventional Synthetic DMARDs: Results Through 5 Years From the SELECT-NEXT Study

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Conflict of interest: Yes

[Objective] In the phase 3 SELECT-NEXT study, we evaluated the efficacy and safety of upadacitinib (UPA) up to 5 yrs in a long-term extension (LTE). [Methods] Patients (Pts) received UPA 15 mg (UPA15) or 30 mg (UPA30) once daily or placebo (PBO) for 12 wks, with csDMARDs. Pts randomized to PBO were switched to UPA15/30 in a pre-specified manner at wk 12. From wk 12, pts were able to enter a blinded LTE for up to 5 yrs. The blinded extension remained until dose switching from UPA30 to UPA15 with the earliest switch occurring at wk 168. [Results] Of the 661 pts at baseline, 611 (92%) completed wk 12 and entered the 248-wk LTE. In total, 271 (41%) pts discontinued study drug during the LTE due to adverse events (16%), withdrawal of consent (10%), loss to follow-up (3%), lack of efficacy (3%), or other reasons (9%). Clinical outcomes continued to improve or were maintained through wk 260, as demonstrated by 51% and 43% of CDAI remission and 75% and 66% attaining DAS28 (CRP) <2.6 with UPA15 and UPA30, respectively (AO). Physical function and pain improved similarly with UPA15/30 at wk 260; the mean change from baseline was -0.86/-0.78 for HAQ-DI and -44/-44 mm for pain (AO). Through 5 yrs, treatment-emergent adverse events (TEAEs) and AEs of special interest were consistent with previous study-specific analyses. Numerically higher rates of any AE (250.4, 295.6), serious AEs (16.1, 22.5), any infection (78.0, 95.6), serious infections (3.2, 7.2), herpes zoster (2.7, 7.0), NMSC (0.4, 2.7), and neutropenia (1.9, 4.9) were observed with UPA30 vs UPA15. While malignancies (excluding NMSC; 1.0, 1.7) and MACE (0.4, 0.9) were rare, numerically higher rates were also observed with UPA30 vs UPA15. [Conclusions] UPA 15 demonstrated sustained efficacy across multiple RA disease activity measures through the 5-yr study period. The safety profile was consistent with earlier time points and with an integrated phase 3 safety analysis of UPA in RA.

ICW6-5

Treatment strategy in patients with rheumatoid arthritis and inadequate response to Janus kinase inhibitors from the FIRST registry

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Conflict of interest: None

[Objective] Janus kinase inhibitors (JAKi) are effective in patients with rheumatoid arthritis (RA); however, some patients show an inadequate response to JAKi (JAKi-IR). This study aimed to clarify the clinical characteristics of RA patients with JAKi-IR and molecular targeted drugs suitable for these patients. [Methods] The study included 398 RA patients to whom JAKi was introduced at our department. The trajectory of CDAI was analyzed using Growth Mixture Model (GMM). The clinical characteristics of JAKi-IR patients were analyzed. The efficacy and safety of switched molecular-targeted drugs were analyzed six months after switching treatment in JAKi-IR patients. [Results] CDAI trajectories using GMM were divided into three groups, one of which did not achieve low disease activity (LDA) 1 year after JAKi introduction -defined as JAKi-IR (n=75). The factors associated with JAKi-IR were identified the number of previously used biologics (OR 1.4, 95%CI 1.2-1.7), and the inability to use sufficient dose of JAKi (OR 2.3, 95%CI 1.1-5.2) by multiple logistic regression analysis. Out of 75 JAKi-IR patients who switched to another molecular-targeted drugs (TNFi, 16; non-TNFi, 29 (IL-6 receptor inhibitor, 22; CTLA4-Ig, 7); JAKi, 30), 32 patients achieved CDAI-LDA. No significant difference was observed in the patient background at the time of change of molecular targeted drugs and the retension rate among the 3 groups. The percentage of patients who achieved LDA (TNFi/non-TNFi/JAKi [%]=19/34/63, p<0.01) was significantly higher in the group switched to other JAKi. The factors associated with CDAI-LDA in JAKi-IR patients were identified switching to a different JAKi (OR 4.3, 95%CI 1.6-11.4) by logistic regression analysis. [Conclusion] The extracted factors related to JAKi-IR were identified the number of previously used biologics and the inability to use sufficient dose of JAKi Selection of different JAKi might help improve the disease activity in RA patients with JAKi-IR.

ICW7-1

The association of serum biomarkers with joint destruction in patients with rheumatoid arthritis treated by certolizumab pegol, from the FIRST registry

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Conflict of interest: None

[Objective] Certolizumab pegol (CZP) has immediate efficacy in active rheumatoid arthritis (RA) patients with inadequate response to methotrexate (MTX-IR), indicating that it may predict early treatment response. However, the factors that predict the efficacy of CZP in reducing radiographic progression are unknown. In this study, we investigated the relationship between clinical response to CZP and serum biomarkers and the effect of CZP on the inhibition of joint destruction. [Methods] One hundred MTX-IR RA patients treated with CZP were enrolled. The primary endpoint was the changes in the modified total sharp score (mTSS) at 52 weeks (ΔmTSS). Secondary endpoints were changes in CDAI, persistence rate, adverse events at week 26, and rate of achievement of radiographic remission (RR, ΔmTSS≦0.5). [Results] The continuation rate after 52 weeks of CZP introduction was 80%. CZP was discontinued due to adverse events in 3 cases. CDAI at week 52 was significantly improved (25.5±12.9→7.4±9.7 (mean±SD), p < 0.0001), and 83% of patients achieved low disease activity (LDA) or remission. mTSS at baseline was 14.2±35.22, ΔmTSS at week 52 was 0.94±3.572, and 82% of patients achieved RR. Univariate and multivariate logistic regression analyses found lower serum TNFα levels at 24 h after administration of CZP as the factor associated with CDAI remission at week 12 (OR 0.41, 95%CI 0.16-1.04). A receiver operating characteristic (ROC) analysis yielded a cut-off value of 0.87 pg/mL (lower patients (n=54): higher patients (n=33) =48.8%:27.2%, p=0.0481). Subsequently, low serum TNFα levels at week eight were identified as the factor that contributed to RR (OR 0.48, 95%CI 0.24-0.93). Similarly, a ROC analysis detected a cut-off value of 2.81 pg/mL (lower patients (n=56): higher patients (n=27) =94.2%:68.0%, p=0.002). [Conclusions] Serum TNFα levels after CZP administration could be a predictive marker for CDAI-remission and radiographic remission.

ICW7-2

The impact of the first universal biosimilar switching policies for inflammatory arthritis in North America on uptake and spending

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Conflict of interest: None

Objective To quantify the impact of mandatory and new-start innovator biologic to biosimilar switching policies on uptake and spending on biosimilar infliximab and etanercept in British Columbia (BC), Canada. **Methods** We used administrative claims data for all individuals in BC with ankylosing spondylitis, rheumatoid arthritis, and plaque psoriasis from 2013 to 2020 to evaluate two policy interventions: (1) *new starts:* individuals initiating infliximab or etanercept required to start a biosimilar (implemented between 2/2016 and 7/2017) (2) *mandatory switching*: those already receiving infliximab or etanercept to switch to the biosimilar version to maintain coverage (implemented between 5/2019 and 11/2019) A segmented linear regression was used to model the level and trend change in biosimilar etanercept and infliximab utilization and spending before and after the two policy interventions. **Results** We identified 208,984 adult BC residents who qualified for public drug coverage and were eligible for analysis. After the *new start* policy, we found a small gradual increase in the proportion of biosimilar etanercept prescriptions of 0.65% (95%CI 0.44, 0.85) per month. The monthly trend of the proportion of total spending on biosimilar etanercept also increased (0.51, 95%CI 0.28, 0.73). After the *mandatory switching* policy, there was a sustained increase in the proportion of biosimilar etanercept and infliximab prescriptions of 76.98% (95%CI 75.56, 78.41) and 58.43% (95%CI 52.11, 64.75), respectively and a persistent increase in spending on biosimilar etanercept and infliximab of 78.22% (95%CI 76.65, 79.79) and 71.23% (95%CI 66.82, 75.65), respectively. **Conclusion** *New start* policies resulted in small, gradual increases in biosimilar utilization. A *mandatory switch* policy had a marked immediate and sustained impact on uptake. These findings may be particularly relevant to areas with more concentrated insurance systems where mandatory switching policies could lead to greater savings.

ICW7-3

The incidence of malignancy in RA patients with prior malignancy who receive biologic and targeted synthetic DMARDs treatment - FIRST registry-

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Conflict of interest: None

[Objective] To evaluate the incidence of malignancy in RA patients with prior malignancy who receive b/ts DMARDs treatment. [Methods] RA patients were enrolled from the FIRST registry, which is a multicenter prospective cohort study with longitudinal data on disease activity and treatment at each rheumatology visit for b/tsDMARDs treatment in RA. Patients were initiated b/ts DMARDs between Aug, 2005 and Jun, 2022. In the FIRST registry, screening for malignancy using high resolution CT has been implemented for all patients at baseline and patients who diagnosed with malignancy were not received b/tsDMARDs treatment. The primary endpoint was incidence ratio (IR) (new diagnosis of malignancy/100 patient-years) and standardized incidence ratio (SIR) for malignancies in RA patients with or without prior malignancy in the observation period. [Results] A total of 3107 RA patients treated with b/tsDMARDs. Of these, 309 patients had a prior malignancy. Total patient-years of exposure was 9838.8 patient-years in all RA patient group. 81 patients developed a new malignancy. The IR [100PY: 95%CI] were 0.82 [0.65-1.02] and the SIR [95%CI] were 0.94 [0.74-1.17]. We assessed for association with risk of malignancy by the b/tsDMARDs treatment using the Cox proportional hazards model, and older age and male were identified as risk factors. Patient with a prior malignancy was not identified. Total patient-years of exposure was 901.2 patient-years in RA patient with prior malignancy group. 4 patients developed a new malignancy and 5 had recurrence. The IR [100PY: 95%CI] were 0.99 [0.45-1.89] and the SIR [95%CI] were 0.79 [0.35-1.50]. After IPTW adjustment, we compared the IR between patients with and without a prior malignancy using the Kaplan-Meier method. There was no difference between the two groups. [Conclusions] There is no evidence that b/tsDMARDs treatment increase the risk of developing malignancy in RA patients with a prior malignancy.

ICW7-4

The efficacy of b/tsDMARDs in rheumatoid arthritis patients not taking methotrexate; a study in the NinJa (National Database of Rheumatic Diseases in Japan)

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Conflict of interest: None

Purpose: Methotrexate (MTX) plays a central role in the treatment of rheumatoid arthritis, but there are a certain number of patients who are not using MTX due to background or adverse events. To examine the effects of b/tsDMARDs in rheumatoid arthritis patients not taking MTX, we did analysis of the data of NinJa. Methods: Patients not taking MTX in both 2019 and 2020 were selected, and the ΔCDAI (CDAI in 2020 - CDAI in 2019) was determined, which was used as the objective variable. As explanatory variables, we included each b/tsDMARD that was not used in 2019 but used in 2020 (newly introduced b/tsDMARD) as binary variables, whether b/tsDMARD-naïve or not. In addition, background factors such as CDAI, sex, age, and disease duration in 2019 and the use of each b/ts/cs DMARD in 2019 were included as covariates for adjustment, and linear regression analysis was performed. Results: Of the 2902 patients analyzed, 79% were female, mean age was 68.9±13.0 years, mean disease duration was 15.0±11.9 years, and median CDAI in 2019 was 4.4 (1.7-9.0). For newly introduced b/tsDMARDs, coefficients were significantly small in TOF by -2.75 (p=0.009), ETN including biosimilars by -2.52 (p=0.011), and TCZ by -1.74 (p=0.015); other b/tsDMARDs showed no significant difference. For variables for adjustment, the coefficients of agents used in 2019 were 0.78 (p<0.001) for corticosteroids, 0.98 (p=0.015) for ETN, and 0.93 (p=0.001) for ABT, showing a significant difference. These agents could be interpreted as potentially reducing disease activity since their effects are regarded as potential CDAI reduction when introducing other b/tsDMARD. Conclusion: Real-world data allowed us to estimate the effect of b/tsDMARDs on patients not taking MTX. ETN, TOF and TCZ are expected to have a significant effect on reducing disease activity even in the absence of MTX. While ABT does not appear to have an immediate effect when introduced, it may contribute to a potential reduction in disease activity.

ICW7-5

The factors associated with trajectories of functional limitation in rheumatoid arthritis with b/tsDMARD: the KURAMA longitudinal cohort study incorporating a restricted cubic spline regression modeling approach

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Conflict of interest: Yes

[Objective] Although functional limitations measured with the Health Assessment Questionnaire (HAQ) can fluctuate considerably over time in RA, previous studies assumed a linear trend or measured at an earlier time. The study aims to identify predictors associated with trajectories of HAQ scores over a long-term period using nonlinear modeling. [Methods] KURAMA is a long-term RA cohort that has collected disease activity and HAQ at every visit. RA patients who started b/tsDMARD were included. Nonlinear restricted cubic spline regression with interaction terms (duration from b/tsDMARD start × each predictor) was performed. [Results] Among 865 patients with 28440 HAQ measurements and up to 11 years of follow-up, the overall mean HAQ score over time followed a J-shaped curve, with initial improvement, from the presumed effect of DMARDs,

followed by a gradual increase. HAQ score for low-dose glucocorticoid use (1-5 mg/day) was initially similar to that for no use (P=0.27) and significantly lower than for high-dose use (>5 mg/day) (P=0.002), but later increased more than for no use (P for interaction = 0.045). Although low-dose MTX use (1-8 mg/w) was significantly associated with lower HAQ compared with no use (P=0.004), HAQ for high-dose MTX use (9-16 mg/w) was similar to that for no use (P=0.34). Concomitant interstitial lung disease was associated with higher HAQ at baseline (P<0.001) and increased HAQ over time (P for interaction=0.02). Higher Clinical Disease Activity Index and more than 2 b/tsDMARDs use were significantly associated with higher HAQ, suggesting difficult-to-treat (D2T) RA had a more functional burden. [Conclusion] Short-term low-dose or no glucocorticoid use is recommended in terms of physical function. Although MTX is a key drug for preventing functional decline, high-dose MTX may cause paradoxical physical limitations from presumed burdens of adverse effects. Avoiding progression to D2T RA is also important from the viewpoint of functional limitations.

ICW8-1

A Meta-Analysis of Safety of Fostamatinib on Rheumatoid Arthritis: A Concern on Neutropenia and Infection

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Conflict of interest: None

[Objective] Fostamatinib, an oral spleen tyrosine kinase (SYK) inhibitor, has been studied in clinical trials of many autoimmune disorders. It has recently been approved by the US FDA for the treatment of patients with immune thrombocytopenic purpura (ITP) and has interestingly been applied to the treatment of rheumatoid arthritis (RA). However, the safety of this drug in RA is still unclear. Thus, in this study, we aimed to demonstrate the side effects of fostamatinib in RA using meta-analysis of randomized controlled trials (RCTs). [Methods] A systematic search of scientific online databases, and RCTs with a placebo were included. For the doses of fostamatinib, 100 mg BID based on the US FDA for ITP treatment was selected. All complications specified in the trials were pooled and determined using the risk ratio (RR) and a 95% confidence interval (95%CI) with Mantel-Haenszel method. Percentage of inconsistency index (I2) value of less than 25 was considered minimal heterogeneity. [Results] For systemic searching, enrolled 6 RCTs involved 904 fostamatinib-treated patients and 893 placebo-treated patients exhibited that patients who received fostamatinib had a significantly higher risk of developing neutropenia when compared to placebo (5 studies, RR = 3.13, 95%CI = 1.29-7.60, I2 = 0). At the same time, susceptibility to infection including upper respiratory infection (URI) and urinary tract infection (UTI) also increased in patients who received fostamatinib (5 studies, RR = 2.00, 95%CI = 1.15-3.48, I2 = 0). [Conclusions] Our study showed that the treatment of fostamatinib in RA patients exhibited a significant association with neutropenia and infection which may be rendered by a decrease in the peripheral white blood cells (WBC), which is a significant side effect that should be concerned. More data are needed to clarify the incidence of other adverse events and serious adverse reactions, especially with the large longitudinal studies.

ICW8-2

Higher albumin levels and tocilizumab treatment are associated with positive changes in bone mineral density in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] This retrospective cohort study aimed to evaluate the impact of disease-modifying antirheumatic drugs (DMARDs) and commonly performed blood tests on changes in bone mineral density (BMD) in patients with rheumatoid arthritis (RA). [Methods] The patients registered for RA at National Taiwan University Hospital according to either the 1987 or 2010 criteria were screened for eligibility. Patients received serial BMD tests measured by dual-energy X-ray absorptiometry from January 2010 to December 2019 were included. Patients aged <20 years, receiving dialysis or with active malignancy were excluded. The outcomes were interval changes of BMD (g/cm^2) at lumbar spine and/or femoral neck. The effects of DMARD therapies and blood parameters were analyzed using generalized estimating equation with adjustment for age, gender, body mass index, baseline BMD, cumulative doses of glucocorticoids (GCs), and anti-osteoporotic therapy (AOT). Statistical analysis was performed using software R. [Results] This study included 162 patients (87% female). A total of 297 intervals of BMD tests were available (173 at lumbar spine and 124 at femoral neck). The median (interquartile range) age was 62.6 (56.4-70.9) years, RA duration was 77.8 (31.2-102.3) months, and follow-up time was 46.9 (27.2-68.7) months. The treatments used included biologic and targeted synthetic DMARDs in 60 (37%) patients, AOT in 68 (42%) patients, GCs in 89 (54.9%) patients, and methotrexate in 99 (61.1%) patients. In the analysis of BMD at femoral neck, significant and positive effects were observed in tocilizumab treatment (estimated coefficient = 0.030, p = 0.033) and the levels of albumin (estimated coefficient =0.041, p = 0.001). On lumbar spine, no significant effect of DMARD therapies and common blood parameters was found. [Conclusions] The findings showed that higher albumin levels and tocilizumab treatment correlated with increased femoral neck BMD after adjusting risk factors and AOT.

ICW8-3

Pharmacokinetics, Pharmacodynamics, Bioavailability, and Immunogenicity of Obexelimab Following Subcutaneous Administration in Healthy Japanese and Non-Japanese Volunteers

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Conflict of interest: Yes

[Objective] Obexelimab is a novel bifunctional antibody that inhibits B-cells, CD19-expressing plasma cells, and plasmablast activity and is expected to provide clinical benefits across multiple autoimmune disorders. In previous Phase 2 studies, intravenous (IV) administration of obexelimab was well-tolerated, and preliminary efficacy was demonstrated in patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and immunoglobulin G4-related disease (IgG4-RD). The purpose of this study was to 1) evaluate the pharmacokinetics (PK), pharmacodynamics (PD), and immunogenicity of obexelimab following subcutaneous (SC) administration, and 2) compare PK/PD profiles between healthy Japanese and non-Japanese volunteers. [Methods] Fifty healthy volunteers (25 Japanese and 25 non-Japanese subjects) were enrolled in this open-label, parallel group, multiple-dose study. Subjects were randomized to 5 cohorts to receive 3 doses of obexelimab [Cohorts 1 to 5: 125 mg SC, 250 mg SC, 375 mg SC, and 250 mg IV every 2 weeks; 125 mg SC weekly, respectively]. Each cohort consisted of 10 subjects with 5 subjects from each population. Serial blood samples were obtained for determination of PK, immunogenicity, CD19 receptor occupancy (RO), and absolute B cell counts (ABC). [Results] All tested SC dosing regimens were well-tolerated. Dose-proportional PK was observed following SC doses with a bioavailability of ~60%. No statistically significant differences in PK were found between healthy Japanese and non-Japanese subjects. Anti-drug antibody (ADA) incidence was low (4 to 12%) and may have contributed to lower drug concentrations in one subject. Complete CD19 RO and a nadir of ~ 50% of ABC baseline levels were maintained during dosing period in both populations. [Conclusions] No ethnic differences in obexelimab PK/PD were observed in this study. SC formulation was well-tolerated to support further clinical development of obexelimab to treat B-cell mediated autoimmune diseases.

ICW8-4

Predictive factors of efficacy of first-line CTLA4-Ig in patients with rheumatoid arthritis (RA) and high disease activity - FIRST registry-

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Conflict of interest: None

[Objective] It remains unclear which first-line biological disease-modifying anti-rheumatic drugs (bDMARDs) are appropriate for which patients with RA. The aim of this study was to determine what factors are predictive of a highly effective CTLA4-Ig population in bio-naive RA patients based on a large RA cohort (FIRST registry). [Methods] This study enrolled RA patients (n=1351; TNF inhibitor [TNFi]: n=616, IL-6 receptor inhibitor [IL-6i]: n=399, CTLA-4Ig: n=336) who were administered the first bDMARDs between July 2013 and February 2022. The primary endpoint was clinical disease activity index (CDAI) remission rate at 24 weeks. [Results] The CDAI remission rates at Week 24 were TNFi: 36.0%, IL-6i: 28.3%, and CTLA4-Ig: 26.8%. Univariate and multivariate logistic regression analysis demonstrated that CDAI remission was associated with lower pain VAS and lower HAQ in the TNFi group, lower CDAI and higher CRP levels in the IL-6i group, and higher anti-CCP antibodies (ACPA) titers in the CTLA4-Ig group. ROC curve analysis yielded the cut-off value of ACPA, indicating the CDAI remission in the patients who received CTLA4-Ig as 39.3 U/ml. In patients with ACPA titers ≧39.3 U/ml, the CTLA4-Ig group (n=180) had higher CDAI remission at Week 24 compared to the non-CTLA4-Ig group (n=488) (CTLA4-Ig, 37.5% vs. non-CTLA4-Ig, 28.7%, p=0.028) after adjustment by propensity score-based inverse probability of treatment weighting. The CTLA4-Ig group that achieved CDAI remission (n=50) had a higher proportion of patients with lower ACPA titers at Week 24 than at baseline compared to the CTLA4-Ig group not achieved CDAI remission (n=130) (remission group, 77.2% vs. non-remission group, 37,8%, p, 0.001). [Conclusions] In RA patients who were administered CTLA4-Ig, high ACPA titer at baseline was associated with a good outcome. Furthermore, CDAI remission of CTLA4-Ig may be associated with reduction of ACPA titers, suggesting ACPA titers may be predicting factors for prognosis.

ICW8-5

Body mass index exhibits differential efficacy among biologic anti-TNF agents in rheumatoid arthritis - The ANSWER cohort study -

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Conflict of interest: None

[Objective] Previous reports have suggested that body composition is one of the baseline factors which indicate refractoriness to biologic anti-TNF (aTNF) agents. However, how higher BMI patients respond to each individual drug is unclear. To assess whether obesity affects clinical outcomes in rheumatoid arthritis (RA) patients treated by anti-TNF agents. [Methods] In the Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort, a real-world retrospective clinical database for rheumatic diseases, RA patients who were treated with anti-TNF agents were included consecutively and followed. Overweight was defined as a body mass index (BMI) >23, and patients were divided into overweight ("OW") and non-overweight ("non-OW"). The simplified disease activity index (SDAI) was compared after drug administration. In order to reduce biases, patients were stratified by the propensity score matching method. A missing follow-up visit value is replaced by last observation carried forward analysis. [Results] A total of 2116 cases before propensity score matching who met the inclusion criteria were analysed. SDAI at month 12 was significantly higher in OW patients with certolizumab pegol (median value, 10.1 in non-OW vs -7.8 in OW, p=0.018). Any other anti-TNF agents did not exhibit the significant difference in SDAI at month 12 between non-OW and OW. [Conclusions] Overweight patients of rheumatoid arthritis have better response when induced by certolizumab pegol, but not by other anti-TNF agents.

ICW8-6

Efficacy and safety of adalimumab with reduced versus maximum tolerated methotrexate dose in patients with rheumatoid arthritis (MIRACLE): a randomized, non-inferiority trial

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Conflict of interest: Yes

[Objective] Efficacy of biologics and methotrexate (MTX) combination therapy is well established; however, the optimal usage of MTX remains unclear. We aimed to clarify the efficacy and safety of adalimumab with reduced MTX dose in patients with rheumatoid arthritis (RA) showing an inadequate response to MTX. [Methods] The MIRACLE study was conducted across 24 hospitals in Asia. We recruited MTX-naive patients with RA with disease duration <2 years. MTX was initiated orally and increased to the maximum tolerated dose (MTD) by week 12. Patients who did not achieve remission based on the Simplified Disease Activity Index (SDAI) at week 24 were randomly assigned (1:1) to the continued MTD group or the reduced dose group (6-8 mg/week) and received adalimumab 40 mg biweekly. The primary outcome was non-inferiority of the reduced dose group for SDAI remission at week 48 to the MTD group with a pre-specified non-inferiority margin of -15% based on a two-sided 90% confidence interval (ClinicalTrials. gov: NCT03505008). [Results] Of 300 patients enrolled, 291 patients were included in the full analysis set. The mean SDAI at study enrollment was 26.5±12.4. At week 24 with the mean MTX dose of 12.6±2.9 mg/week, 36.1% achieved remission and continued MTX monotherapy. We randomized 134 patients; 68 patients in the MTD and 66 patients in the reduced dose group and started adalimumab. Remission rates at week 48 were 38.4% and 44.8%, respectively, with the adjusted risk difference being 6.4% (-7.0% to 19.8%), which met the non-inferiority margin of -15%. Other efficacy assessment including the health assessment questionnaire disability index <0.5 and Δmodified total

Sharp score ≦0.5 did not differ significantly. Adverse events after week 24 were more frequent in the MTD group (35.3% vs. 19.7% p=0.054). [Conclusions] The MIRACLE study highlights that the efficacy of adalimumab combined with reduced MTX dose was not inferior to that with the MTD, with a better safety profile.

ICW9-1

Serum Decoy Receptor 3 (TNFRSF6B) and Soluble TNFRSF1B in Rheumatoid Arthritis: Biomarkers of Disease Activity and Treatment Response to Methotrexate

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Conflict of interest: None

Objectives: To study the serum levels of decoy receptor 3 (DcR3; TNFRSF6B) and soluble TNFRSF1B (sTNFRSF1B) in rheumatoid arthritis (RA) at baseline and at 4 months as biomarkers of disease activity and treatment response to methotrexate. **Methods:** Methotrexate and steroids naïve RA patients who were treated with only methotrexate in escalating doses (maximum dose 25 mg/wk) over 4 months were enrolled in the study. Disease activity was assessed using DAS28CRP (3 variables) at baseline and at 16 weeks with a collection of blood samples for measuring the levels of TNFRSF6B and sTNFRSF1B using commercially available ELISA kits. Patients were classified as responders and non-responders at 16 weeks as per EULAR criteria and levels of both the markers were compared. Serum samples from 30 healthy controls (HC) were also used for comparison. Variables are expressed as median (range) and non-parametric tests were used. P-value <0.05 was considered significant. **Results:** At baseline (n=73; F:M=68:15; DAS28CRP=5.34 (3.95-7.65)), serum levels of TNFRSF6B and sTNFRSF1B were higher in patients as compared to HC (p<0.001). At baseline, both the markers showed a weak correlation (r=0.22; p=0.02) with each other but did not correlate with DAS28CRP. Levels of baseline TNFRSF6B were significantly higher in seropositive RA patients as compared to seronegative. At 4 months (n=73; DAS-28CRP=4.08 (1.42-7.03)), 49 patients were classified as responders and 24 as non-responders. There was no difference in the levels of baseline TNFRSF6B and sTNFRSF1B among responders and non-responders. However, levels of both markers decreased significantly at 4 months as compared to baseline values in responders (p<0.001 for both) but not in non-responders. **Conclusion:** Serum decoy receptor 3 (TNFRSF6B) and sTNFRSF1B levels are higher in patients with RA. Their levels decrease significantly with methotrexate therapy at 4 months in responders making them suitable markers of disease activity and treatment response.

ICW9-2

Activation of type I interferon pathway in serum of patients with anti-MDA5 positive dermatomyositis

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Conflict of interest: None

[Objective] Anti-melanoma differentiation-associated gene 5 (MDA5) antibody-positive dermatomyositis (DM) is typically characterized by amyopathic DM and rapidly progressive interstitial lung disease. It was reported that type I interferon (IFN) gene signature was upregulated in the peripheral blood mononuclear cells and the skin tissues from the anti-MDA5 DM patients. The elevated serum concentrations of IFN-α and ferritin were also reported in these patients. However, the role of type I IFN in anti-MDA5 DM has yet to be fully elucidated. We aimed to study the activity of IFN-α/β and IFN regulatory factor (IRF) in sera of patients with polymyositis (PM) and DM, and their association with the clinical features. [Methods] The reporter cell lines which secrete secreted embryonic alkaline phosphatase (SEAP) in response to IFN-α/β and those secrete luciferase and SEAP in response to activation of IFN-stimulated response elements and NF-κB, respectively, were incubated with sera of active PM/DM patients harboring anti-MDA5 antibodies (MDA5, $n = 22$) and anti-aminoacyl-tRNA synthetase (ARS) antibodies (ARS, $n = 23$), and healthy controls (HC, $n = 32$). The levels of SEAP and luciferase were measured and their correlation with clinical data were analyzed. [Results] The sera of MDA5 patients demonstrated significantly higher IFN-α/β and IRF activities than those of ARS patients and HC ($p < 0.001$), whereas no significant difference was detected in the NF-κB activities. The IFN-α/β and IRF activities induced by the MDA5 patients sera were correlated with the serum ferritin levels ($r = 0.53$ and 0.54, respectively), whereas they did not significantly correlate with the serum anti-MDA5 antibody titers, serum KL-6 levels, percent-predicted forced vital capacity, or percent-predicted diffusing capacity of the lung for carbon monoxide. [Conclusions] Activation of IFN-α/β and IRF in sera of active anti-MDA5 positive DM patients and their association with serum ferritin were suggested.

ICW9-3

Serum biomarker profile identifies two distinct clinical phenotypes in microscopic polyangiitis complicated by interstitial lung disease

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Conflict of interest: None

[Objective] To address the pathomechanism of microscopic polyangiitis (MPA) complicated by interstitial lung disease (ILD) using serum biomarker profile and pulmonary histopathology. [Methods] Forty-nine MPA patients [MPA-ILD (n = 32), MPA without ILD (n = 17)] were recruited into this study, and nineteen serum biomarkers were examined. Based on the biomarker profiles, principal component analysis (PCA) and cluster analysis were performed to classify patients with MPA-ILD into subgroups. Clinical characteristics and prognosis were assessed for each subgroup. Two lung biopsies were examined following hematoxylin-eosin staining and immunostaining. [Results] T-cell and macrophage polarization was skewed toward the Th 2 cells and M2 macrophages in MPA-ILD groups compared to MPA without ILD groups. The PCA allowed classification of the 19 biomarker profiles into three groups: (1) B cell- and neutrophil-related cytokines, vascular angiogenesis-related factors, extracellular matrix-producing factors, (2) Th1-driven cytokines, M1 macrophage-driven cytokines and Th2-driven cytokines, and (3) M2 macrophage -induced and -driven cytokines. The cluster analysis stratified the patients with MPA-ILD into clinically fibrotic dominant (CFD) and clinically inflammatory dominant (CID) groups. Severe infections were significantly higher in the CFD group than in the CID group. The 4-year severe infection-free survival rate was significantly lower in the CFD group (15.8%) than in the CID group (82.1%) (log-rank test, p=0.02). The initial serum levels of IL-4 was significantly higher in the CFD group than in the CID group, and strong IL-4 immunostaining was confined to these CCR4-positive Th2 cells in the interstitium of MPA-ILD lungs. [Conclusions] Classification of MPA-ILD based on serum biomarker profile would be useful in predicting the disease activity and the complication of severe infection in MPA-ILD. Activation of Th2 cells may plays a key role in the pathomechanism of MPA-ILD.

ICW9-4

Autoantibodies to the Survival of Motor Neuron (SMN) complex as a novel marker associated with 'typical' mixed connective tissue disease (MCTD)

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Conflict of interest: None

[Objective] Anti-U1 RNP antibodies (Abs) are essential for the MCTD diagnosis but not specific or not associated with disease activity. Anti-SMN complex Abs is known to be present with anti-U1RNP Abs, however, the significance is unclear. The aim of this study was to investigate

the clinical significance of anti-SMN complex Abs in patients with MCTD. [Methods] 158 consecutive cases with anti-U1 RNP Abs (newly diagnosed; MCTD n=67, SLE n=74, SSc n=17) were enrolled in this study. Serum anti-SMN complex Abs were screened by immunoprecipitation immunoprecipitation of ^{35}S-methioneine-labeled cell extracts. [Results] Anti-SMN complex Abs were detected in 35.8% (24/67) of MCTD patients. Namely, the sensitivity of anti-SMN complex Abs positivity was lower than anti-U1 RNP Abs which has 100% sensitivity. However, the Anti-SMN complex Abs positivity was significantly higher than SLE (8.1%) and SSc (11.8%), and thus, the positive predictive value of anti-SMN complex Abs was 75.0% (24/32) and was higher than that of anti-U1 RNP Abs (42.4%, 67/158). In MCTD patients, anti-SMN complex Abs positivity was associated with the prevalence of both pulmonary arterial hypertension (54.2% vs. 7.0%, p<0.001, Odds ratio: OR 15.7) and interstitial lung disease (87.5% vs. 44.2%, p<0.001, OR 8.8). In addition, nailfold microvascular abnormalities were more common in MCTD patients with anti-SMN complex Abs (71.4% vs. 25.6%, p<0.001). When MCTD patients were classified based on the combination of their clinical features of SLE, SSc, and IIM, the prevalence of anti-SMN complex Abs was the highest, detected in 76.5%, in a subset with clinical features of all 3 components: SLE, SSc, and IIM. Moreover, all three cases of death within 1 year of the treatment were positive for anti-SMN Abs (log-rank test, p=0.014). [Conclusions] Anti-SMN complex Abs are specific for MCTD and appear to be a new biomarker for poor prognosis and also associated with "typical MCTD" that has the feature of SLE, SSc, and IIM.

ICW9-5

Serum interleukin-1 receptor antagonist is a potential marker of disease activity in large vessel vasculitis

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Conflict of interest: Yes

[Objective] Twenty-one consecutive patients with active, treatment-naïve LVV (Takayasu arteritis, TAK, n=8 and giant cell arteritis, GCA, n=13) and 14 healthy controls (HC) were included in this study. We measured serum levels of IL-1β and IL-1Ra and examined their association with disease activity. Indian Takayasu's Arteritis Activity Score (ITAS) was used to measure disease activity. Remission was defined as complete resolution of clinical symptoms. Disease relapse was defined as the recurrence of clinical symptoms, resulting in the intensification of immunosuppressive therapy by attending physicians. [Methods] Twenty-one consecutive patients with active, treatment-naïve LVV (Takayasu arteritis, TAK, n=8 and giant cell arteritis, GCA, n=13) and 14 healthy controls (HC) were included in this study. We measured serum levels of IL-1β and IL-1Ra and examined their association with disease activity. Indian Takayasu's Arteritis Activity Score (ITAS) was used to measure disease activity. Remission was defined as complete resolution of clinical symptoms. Disease relapse was defined as the recurrence of clinical symptoms, resulting in the intensification of immunosuppressive therapy by attending physicians. [Results] Serum levels of IL-1Ra were significantly higher in TAK (465.3 pg/mL, p<0.01) and GCA (384.9 pg/mL, p<0.01) compared with HC (170.4 pg/mL). GCA but not TAK showed higher levels of serum IL-1β compared with HC (0.12 pg/mL vs 0.012 pg/mL, p<0.01). Serum levels of IL-1Ra positively correlated with ITAS scores in patients with TAK (rho=0.89, p<0.01) and with serum levels of C-reactive protein in patients with GCA (rho=0.65, p=0.019). Of note, serum IL-1Ra levels did not improve at one month after remission induction therapy in relapsed patients, whereas serum IL-1Ra levels were decreased in patients with non-relapsed patients. [Conclusions] Serum IL-1Ra levels reflect disease activity and may predict future disease relapse in patients with LVV.

ICW9-6

The novel autoantibody for beta-2-glycoprotein I complexed with HLA-DR is associated with arterial thrombosis in Japanese female patients with connective tissue diseases

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Conflict of interest: None

[Objective] Beta-2-glycoprotein I complexed with HLA-DR molecule (β2GPI/HLA-DR) was recently found to be a major target of antigen in antiphospholipid syndrome (APS). This study aims to analyze the frequencies and titers of anti-β2GPI/HLA-DR antibodies in patients with various connective tissue diseases, and associated clinical features with these antibodies. [Methods] Serum samples were collected from female outpatients of our center in 2020-2021. Clinical and laboratory data were retrieved from medical records and questionnaires. Anti-β2GPI/HLA-DR antibody was compared with the risk score reported as an adjusted global APS score (aGAPSS). The cutoff was calculated using receiver operating characteristic (ROC) analysis. Finally, we assessed the impact of anti-β2GPI/HLA-DR antibodies on arterial thrombosis in addition to the conventional risk model. [Results] Samples were collected from 704 patients, that include 260 SLE or MCTD. Sixty-six patients fulfilled the classification criteria for APS. Seventy-seven patients had one or more histories of arterial thrombosis, and 14 patients had a history of both arterial and venous thrombosis. The titers were significantly higher in patients with both arterial and venous thrombosis than those without thrombosis. In cases, with aGAPSS >10 or triple positive APS, the titers tended to be higher. The ROC showed the sensitivity, specificity, and area under the curve (AUC) for arterial thrombosis were 33.8%, 91.4%, and 0.60 with a cutoff value, of 172. By the multivariable analysis with multiple imputations, the odds ratio of anti-β2GPI/HLA-DR antibody ≧172 was 5.11 (p < 0.001). When adding the cutoff value to the conventional risk factors improved the AUC from 0.677 to 0.730. Determined net reclassification improvement and integrated discrimination improvement were statistically significant. [Conclusions] Anti-β2GPI/HLA-DR antibody is associated with arterial thrombosis in female patients with connective tissue diseases.

ICW10-1

Long term safety and effectiveness of belimumab therapy in patient with SLE: A single center retrospective analysis

Takehiro Nakai[1], Sho Fukui[1,2], Futoshi Iwata[1], Takahiro Asano[1], Hiroki Ozawa[1], Satoshi Kawaai[1], Yukihiko Ikeda[1], Haruyuki Yanaoka[1], Hiromichi Tamaki[1], Mitsumasa Kishimoto[1,3], Ken-ichi Yamaguchi[1], Masato Okada[1]
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Conflict of interest: None

[Objective] Many clinicians use belimumab as a maintenance therapy of SLE, but there is scarce data on belimumab safety/effectiveness profile in real world practice. Therefore, we conducted this single center retrospective cohort to analyze belimumab safety profile in our hospital. [Methods] Patient with SLE who was treated with belimumab at our institute were included in our study. We analyzed the drug retention rate, LLDAS achievement rate, flare free rate and severe infection rate. [Results] Of the 567 patients with SLE followed up in our hospital, 95 used belimumab and to 92 were included in the study. Drug retention rate of belimumab was around 90% at 52 weeks and over 80% at day 1000 after initiation of belimumab. Severe infection occurred in less than 10% at week 52 and around 20% of the patient at day 1000 after initiation of belimumab. Even though 26.1% of the patient with SLE flared at least once during the follow up period, more than 70% of the patient achieved LLDAS at 52 weeks and around 90% achieved LLDAS at day 1000 after initiation of belimumab therapy. In terms of glucocorticoid requirements belimumab administration significantly decreased glucocorticoid demands. (initiation day of belimumab: 8.88 [6.00, 15.00] mg/day, 26 weeks after initiation: 6.00 [3.94, 8.00] mg/day, 52 weeks after initiation: 5.00 [1.79, 7.00] mg/day, in the end of the study period; 3.00 [0.46, 6.06] mg/day.) [Conclusions] Belimumab has high drug retention rate. Even though some experience lupus flare in short term, most of the patient on belimumab achieved LLDAS during the follow up and glucocorticoid demand decreased. Therefore,

continuation of belimumab is recommended if it is not contraindicated.

ICW10-2

Two-year Outcome of Belimumab Therapy in Patients with Systemic Lupus Erythematosus

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Conflict of interest: None

[Objective] We investigated the 2-year outcomes of belimumab (BEL) additive on standard of care (SoC) in patients with SLE in the real-world setting. [Methods] Sixty-four SLE patients treated with BEL additive to SoC for 2 years (BEL+SoC) and 341 patients treated with SoC were recruited. Patient background was adjusted with propensity score matching; 11 items including age, sex, disease activity, glucocorticoid (GC) dose, 33 patients in each group remained for analysis. Disease activity was measured by SLE disease activity scale (SLEDAS). [Results] The median SLEDAS at 2 years was significantly decreased from baseline in BEL+SoC (2.08 to 1.12, p<0.001) but not in SoC (2.09 to 2.03, p=0.055). Low disease activity was achieved in significantly higher frequency with BEL+SoC compared to SoC, 29 (88.8%) and 17 (51.5%) patients respectively (p=0.023). However, no difference was observed in remission rate (72.7% in BEL+SoC and 51.5% in SoC, p=0.127). Median daily prednisolone (PSL) dose significantly decreased in both treatment group (BEL+SoC; 6.0 to 3.5 mg/day, p<0.001, SoC; 5.0 to 4.0 mg/day, p<0.001) without statistical difference (p=0.112). However, PSL dose was significantly reduced in BEL+SoC (-3.0 mg, median) compared to SoC (-1.0 mg) (p=0.004). Disease recurrence occurred in 5 (15.2%) patients in BEL+SoC and 4 (12.1%) patients in SoC (p=0.714). Recurrence tended to be seen later in the observation period in the BEL group (10 months or later) and earlier (1 month or later) in the Soc group. [Conclusions] Add-on treatment with BEL was effective to achieve low disease activity during PSL tapering which would lead to a larger difference in total organ damage in the longer term. However, recurrence was observed in both groups indicating the need to investigate particular PSL tapering strategies for each individual patient.

ICW10-3

Effect of Belimumab on Patient-Reported Outcomes in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] Demonstrate the effect of belimumab (BEL) on quality of life (QOL) in systemic lupus erythematosus (SLE) patients measured by patient-reported outcomes (PROs). [Methods] SLE patients treated with BEL in addition to standard of care (SoC) (BEL+SoC) and those treated only with SoC were recruited. PROs were collected by Lupus Impact Tracer (LIT) in 23 patients in each group matched for disease activity and LIT score at baseline. Changes in LIT score, SLE disease activity index (SLEDAI), and physician's global assessment (PGA) after 6 months were compared with baseline. [Results] LIT score was significantly decreased in BEL+SoC from 26.3 [0.0-72.5] [median range] to 12.5 [0.0-70.0], p=0.041), while SoC showed no change (27.5 [5.0-67.5] to 27.5 [2.5-75.0], p=0.415). Question component regarding the daily life activity was significantly decreased in BEL+SoC (1.0 [0.0-4.0] to 0.0 [0.0-3.0], p=0.045) whereas question regarding depressive mood was significantly decreased only in SoC (0.0 [0.0-4.0] to 0.0 [0.0-3.0], p=0.012). SLEDAI was significantly decreased in patients with BEL+SoC (2.0 [0.0-12.0] to 2.0 [0.0-5.0], p=0.024), but was consistent in SoC (2.0 [0.0-6.0] to 2.0 [0.0-6.0], p=0.750). Besides, PGA was significantly decreased in BEL+SoC (0.46 [0.0-2.4] to 0.06 [0.0-0.80], p<0.001). There was no correlation between changes in LIT score and PGA (r=0.304, p=0.159) or SLEDAI (r=-0.015, p=0.947) in BEL+SoC. Also, similar results were obtained in patients with SoC (LIT score vs PGA; r=0.056, p=0.802: LIT score vs SLEDAI; r=-0.276, p=0.203). [Conclusions] Treatment with BEL in addition to SoC improved PROs based on LIT scores, especially on the daily life activity component. On the other hand, the depressive mood component only improved in SoC indicating less expectation with BEL for this item. Our results indicate BEL as a useful tool not only for previously known glucocorticoid tapering effect but also for improving QOL leading to treat to target approach.

ICW10-4

Efficacy and safety of belimumab in patients with active lupus nephritis in real-life settings: LOOPS registry

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Conflict of interest: None

[Objective] Although the BLISS-LN trial showed the efficacy of belimumab (BEL) in induction therapy for patients with active lupus nephritis (LN), its efficacy is unknown in clinical practice. This study aimed to reveal the efficacy and safety of BEL in induction therapy for patients with active LN in real world settings. [Methods] This study included systemic lupus erythematosus patients who had biopsy-proven ISN/RPS class III or IV LN with or without coexisting class V and had standard induction therapy (Standard-of-care (SoC); glucocorticoid (GC) and either mycophenolate mofetil or cyclophosphamide). The efficacy of BEL combined with SoC (BEL+SoC group, patients in whom BEL was administrated within six months after the start of standard induction therapy, n=24) was compared with SoC (SoC group, n=21). The primary endpoint was the complete renal response (CRR) at one year. [Results] No significant difference was observed in baseline patient background between the two groups. During a one-year observation period, three patients discontinued BEL (continuation rate: 87.5%). There was no significant difference in CRR at one year between the two groups (SoC vs. BEL+SoC = 40.0% vs. 50.0%, p = 0.71). GC dose at one year (PSL equivalent, mg/day) was significantly lower in the BEL+SoC group (SoC vs. BEL+SoC = 5.0 [5.0-7.5]) vs. 5.0 [3.0-5.0] (median [IQR]), p = 0.04). There were no significant differences in SELENA-SLEDAI, BILAG index, anti-dsDNA antibody titer, and complement CH50, however the BEL+SoC group showed higher rate of LLDAS achievements (SoC vs. BEL+SoC = 25.0% vs. 68.2%, p = 0.02) and DORIS remission (SoC vs. BEL+SoC =15.0% vs. 54.5%, p = 0.02). The incidence of adverse events (SoC vs. BEL+SoC = 42.9% vs. 41.7%, p = 0.76) was not significantly different between the two groups. [Conclusions] Adding BEL to SoC in active LN patients may control disease activity without increasing adverse events and achieve an early reduction in GC, LLDAS, and remission.

ICW10-5

Safety and Efficacy of Anifrolumab for Systemic Lupus Erythematosus (SLE) in Clinical from LOOPS registry

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Conflict of interest: None

[Objective] Selecting patients with systemic lupus erythematosus (SLE) suitable for anifrolumab treatment in clinical practice remains challenging. This study analyzed the safety and efficacy of anifrolumab under real clinical conditions, focusing on SLE patients with minor flares, and to identify the patients suitable for receiving anifrolumab. [Methods] This

study enrolled 20 SLE patients with a minor flare (an increase of 1 or more within the range of SELENA-SLEDAI less than 10 without progression of kidney, nerve, or other vital organ involvement despite receiving standard treatment) and those treated with anifrolumab. The primary endpoint was the change in SLEDAI at 12 weeks after introducing anifrolumab. Secondary endpoints were the retention rate, improvement rate per organ disorder, time to improvement, adverse events, and change in GC dose. [Results] Anifrolumab was introduced to control minor flare disease activity due to exacerbation of arthritis (15/20 patients), skin lesions (12/20 patients), and hematopenia (6/20 patients) in SLE patients. The retention rate of anifrolumab was 100% over 12 weeks. SELENA-SLEDAI scores improved significantly ($p<0.001$) from 5.3±2.0 to 2.3±2.1 after anifrolumab introduction. The time to the symptomatic improvement of arthritis, skin lesions, and hematopenia was 9.5±3.2, 7.4±4.2, and 6.7±4.6 weeks, respectively, after introducing anifrolumab. The rate of SLEDAI score improvement in patients who developed arthritis, skin lesion, and hematopenia were 66.7%, 67.7%, and 50.0%, respectively. The physician global assessment (0-3) improved significantly from 1.4±0.7 to 0.6±0.5 ($p<0.001$). GC dose tended to decrease from 4 weeks, from 8.9±5.7 to 6.0±2.7 mg/day (prednisolone equivalent) ($p=0.10$). There were no cases of relapse and CTCAE grade 2 or severe adverse events. [Conclusion] Anifrolumab might be effective in SLE patients with minor flares and in clinical practice. The drug showed a GC-sparing effect.

ICW10-6

Relationship between the effect of belimumab on immunophenotype and the discontinuation of glucocorticoids in patients with SLE in the maintenance phase: LOOPS registry, FLOW study

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Conflict of interest: None

Objectives: The effects of belimumab (BLM) on the peripheral blood immunophenotype in the patients with systemic lupus erythematosus (SLE) are unknown. Patients with SLE in the maintenance phase were analyzed to determine the relationship between immunophenotypes and BLM efficacy. **Methods**: Patients with SLE (n=110) in the maintenance phase (SELENA-SLEDAI < 10, glucocorticoid [GC] dose ≦ 0.2 mg/kg/day) were assessed. Based on the standard human immune cell subset classification protocol by NIH/FOCIS, peripheral immunophenotypes were analyzed in the SLE patients and matched healthy controls (n=76), and were compared. They were also compared between the baseline and after 6 months for two maintenance phase groups: (1) standard of care (SoC) using hydroxychloroquine or mycophenolate mofetil (SoC group: n=46); and (2) SoC with BLM (BLM+SoC group, n=64). **Results**: The proportion of naïve-CD4 T-, -CD8 T-, and -B cells was lower, and that of the memory CD4 T-, memory CD8 T-, class-switched memory B-, and IgD-CD27-B cells, and plasmocytes was higher in the SLE patients than in controls. The relapse rate ($p=0.04$) was significantly lower in the BLM+SoC group than in the SoC group. Compared with the SoC group, the GC dose after one year was significantly lower ($p<0.01$) was significantly higher in the BLM+SoC group. In the BLM+SoC group, 31.3% (20/64) of patients discontinued GC, significantly more than the SoC group ($p=0.01$). The proportion of activated Tfh cells ($p=0.02$), IgD-CD27-B cells ($p<0.01$), and plasmocytes ($p=0.04$) was significantly decreased six months after BLM introduction. In the BEL+SoC group, 18 (28.1%) who discontinued GC had no relapse for one year and showed a significantly lower proportion of $IgD^{-}CD27^{-}$B cells six months after BLM introduction ($p=0.04$). **Conclusion**: A reduction in $IgD^{-}CD27^{-}$B cells due to BLM may help to control disease activity and enable the reduction/discontinuation of GC in SLE patients in the maintenance phase.

ICW11-1

Nonbacterial endocarditis and ischemic stroke as the initial manifestation of SLE with antiphospholipid syndrome

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Conflict of interest: None

Introduction Systemic Lupus erythematosus (SLE) is a multisystem autoimmune inflammatory disorder and stroke is a well known occurrence of the disease. However stroke as the initial manifestation is rare. Non bacterial endocarditis is a well known yet a rare manifestation of SLE and can cause embolic stroke. **Case presentation** A 39 year old previously healthy Sri Lankan female presented with sudden onset right upper limb and facial weakness. Apart from a recent increase in hair loss she did not have any other clinical manifestations of SLE. Clinical examination revealed right upper limb weakness and right sided upper motor neuron facial nerve weakness. MRI brain revealed bilateral centrum semiovale ischemia and CT cerebral angiogram showed complete occlusion of left internal carotid artery possibly by a thrombus. ESR was 92 mm/hour with a normal CRP. She developed pancytopenia following admission. Transthoracic 2D echocardiogram revealed a vegetation attached to the atrial surface of the posterior mitral valve leaflet suggestive of non bacterial endocarditis. Serial blood cultures were negative. Autoimmune workup revealed positive ANA and DsDNA antibodies. Lupus anticoagulant test was positive with positive anti cardiolipin antibody. A diagnosis of SLE with antiphospholipid syndrome (APLS) complicated with non bacterial endocarditis and ischemic stroke was made. She was treated with high dose glucocorticoids and anticoagulation. Aspirin, Hydroxychloroquine and Mycophenolate Mofetil were added to her treatment regime. Her condition improved and she remained well with mild residual weakness of the right upper limb at subsequent clinic visits. **Conclusion** This case highlights the importance of early recognition and timely management of underlying connective tissue diseases in young stroke patients even in the absence of preceding clinical features of such a disease. Stroke in this patient could have resulted from thrombosis due to APLS or embolization from cardiac vegetations.

ICW11-2

Clinical Characteristics of Adverse Pregnancy Outcome Patients with APL-Positive in Chinese Cohort

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Conflict of interest: None

[Objective] To compare clinical, laboratory, adverse pregnancy outcomes (APOs), and live birth rate in women with persistently positive antiphospholipid antibodies (aPLs) in China. [Methods] Women with persistent aPLs (LA, aCL, anti-β2GPI) positive were recruited for the prospective study from Peking Union Medical College Hospital. Demographic, clinical and pregnancy data were recorded at the baseline. Student's T-test was used to compare values following normal distribution. The Chi-square test and Fisher's exact test were used to compare categorical variables. [Results] Between 2009 and 2021 we enrolled 612 pregnant women, of whom 209 had APOs with persistent aPLs-positive. A total of 474 pregnancies occurred in our center. The live birth rate before enrollment was 17.29% (69/399), compared with 74.67% (56/75) after enrollment. 31.58% (n=66) had isolated early miscarriages, similar to the percentage of isolated middle and later period APO (n=92, 44.02%). β2GPI was more common in patients with isolated early miscarriage. Late APOs occured more frequently in women who did not receive LDA/LMWH. Among the isolated early miscarriage group, over half of the patients had once miscarriage (n=42), only 8 patients had three consecutive miscarriages. In the late APO group, most patients can be diagnosed with APS (n=84, 91.3%). In our cohort we found that fetal loss was the most common type of APO (n=182,

40.1%), followed by pregnancy-induced hypertension, with 19 times preeclampsia and 10 times eclampsia. There was no difference in the proportion of preterm births before or after 34 weeks. [Conclusions] In this study, a significant increase in the live birth rate was shown after aPLs were identified. Late-period miscarriage was the most frequent poor outcome. Patients with early miscarriages, however, only 18.2% of them may diagnose APS, should also be treated if patients suffered two consecutive miscarriages to obtain a better pregnancy outcome.

ICW11-3

Clinical features and risk factors of first thrombosis in obstetric antiphospholipid syndrome

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Conflict of interest: None

[Objective] The long term thrombosis, risk factors and treatment of obstetric antiphospholipid syndrome (OAPS) patients are limited. The aim of this study was to investigate the clinical features and risk factors for first thrombosis in isolated OAPS patients. [Methods] Clinical and laboratory data of all patients with primary OAPS were collected from the electronic medical record system. All patients fulfilled the 2006 revised criteria for APS. Patients with thrombosis before diagnosis were excluded. The first thrombotic event that occurred after diagnosis in the enrolled patients was followed up. Risk factors independently associated with first thrombosis in isolated OAPS were identified by logistic regression. [Results] A total of 186 isolated OAPS patients were included in the study. During a mean follow-up of 5.4 years, 11 patients developed thrombotic events, giving a 6 years cumulative thrombotic incidence of 6.7%. Of these, six were arterial thrombosis, including five stroke and one myocardial infraction. Five were venous thrombosis, including three deep vein thrombosis and two pulmonary embolism. The disease duration (OR = 1.155, 95% CI: 1.054-1.265, p = 0.002), low complement 4 (OR = 5.522, 95% CI: 1.131-26.954, p = 0.035) and the use of glucocorticoids (OR = 38.020, 95% CI: 4.325-334.200, p = 0.001) were risk factors for OAPS patients of first thrombosis, while use of hydroxychloroquine (HCQ) may decrease the risk of thrombosis. [Conclusions] OAPS patients are at an increased risk of long-term thrombosis. The disease duration, low complement 4 and use of glucocorticoids were risk factors for first thrombosis in OAPS patients, while the use of HCQ may decrease the risk of thrombosis.

ICW11-4

Immune Cell Profiling in Antiphospholipid Syndrome Reveals High Expression of CD11c+Tbet+ B Cell in Obstetric Patients

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Conflict of interest: None

[Objective] Primary antiphospholipid syndrome (PAPS) is an autoimmune disorder characterized by the presence of pathogenic autoantibodies. The key immune cell subsets change in PAPS patients remains unclear. To achieve a single-cell perspective of APS immunopathogenesis, we leveraged the high-dimensionality of mass cytometry (CyTOF) to assess peripheral blood mononuclear cell (PBMC) profiles in different clinical phenotypes of APS. [Methods] We employed CyTOF with 42 markers panel (including, T/B/NK/Monocyte) in PBMCs from 35 PAPS patients, 5 antiphospholipid antibodies (aPLs) carriers, and 10 healthy controls. All PAPS patients fulfilled the 2006 Sydney criteria. CyTOF data was analyzed by FlowJo and the R package. The dimensional reduction with tSNE (t-distributed Stochastic Neighbor Embedding) was performed to identify unique cell populations in PAPS patients. Comparisons between groups were performed by Mann-Whitney U test and One-way ANOVA. [Results] Mapping a comprehensive immunological profile of PBMCs, we observed a direct correlation of the increased frequency of **$CD11c^{+}Tbet^{+}$ B cells** in obstetric APS patients (OAPS) compared to HC (**OAPS *vs.* HC, p = 0.0063**). Notably, this population of B cells exhibited the differentiation characteristics of double negative B cells, with significantly lower expression of IgD, CD21, CD27 and CD38. The $CD11c^{+}Tbet^{+}$B cells are involved in the extrafollicular pathway, which can generate long-term autoreactive antibody-secreting cells and plasma cells in a T-cell-independent manner. In addition, $CD11c^{+}Tbet^{+}$B cells from OAPS patients showed enhanced expression of the checkpoint molecules CD86 and PD1. This suggests that the extrafollicular pathway may be associated with abnormal immunomodulation. [Conclusions] Collectively, these findings identified the increased $CD11c^{+}Tbet^{+}$ B cells as a marker of OAPS patients. Moreover, the overactivated extrafollicular response is involved in sustained auto-antibody production in APS patients.

ICW11-5

Metabolomics analysis identifies biomarkers for APS and suggests potential new pathway for APS pathogenesis

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Conflict of interest: None

Objective: The goal of this study is to utilize high-throughput metabolomics screening to identify new biomarkers and dysregulated pathways in primary APS patients. **Methods:** Fasting serum samples were collected from 20 primary APS patients and 17 healthy controls. High-throughput metabolomics screening of 247 small molecule metabolites were performed via gas chromatography coupled mass spectrometry. Multiple variate analysis, principal components analysis (PCA), partial least squares discriminant analysis (PLS-DA), and pathway analysis were completed. SYTOX Green NETosis assay was performed utilizing freshly prepared healthy donor neutrophils with various stimulants including PMA, PMA+ DPI, normal human IgG, antiphospholipid antibodies (aPL), sphingosine-1 phosphate (S1P), and aPL plus various concentration of S1P. **Result:** 50 circulating small molecule metabolites were significantly different between primary APS patients and healthy controls. PLS-DA modeling was performed and demonstrated a clear separation between primary APS patients and healthy controls. 15 metabolic biomarkers that made the biggest contribution to the differentiation of primary APS patients and the healthy controls assessed by variable importance on projection score were identified. Pathway analysis revealed that sphingosine metabolism was the most enriched pathway among primary APS patients. To further elucidate the role of sphingosine metabolism in APS, we examined the effect of S1P, the product of sphingosine metabolism, on aPL mediated NETosis. aPL mediated NETosis was significantly potentiated by S1P in a concentration dependent manner. S1P did not trigger NETosis by itself. **Conclusion**: This study comprehensively profiled the serum metabolites of primary APS patients and identified metabolic biomarkers that have the potential to be used as a diagnostic tool for differentiating APS from healthy controls. The study also revealed a potential significant role of S1P/S1PR axis in APS pathogenesis.

ICW12-1

Patient Background and Goal Attainment Rates in the Three Arrows Study (Hiroshima Area Multicenter T2T Early Stage Rheumatoid Arthritis Registry Study) (Interim Report 3)

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Conflict of interest: None

[Objective] To understand the characteristics and disease activity of untreated early-stage rheumatoid arthritis patients in the Hiroshima area and to verify the response to treatment with the T2T strategy. [Methods]

The study was conducted from June 2018 to March 2022. We collected medical information on newly diagnosed untreated rheumatoid arthritis patients at the time of diagnosis (week 0), after 24 weeks, and after 52 weeks at our hospital and at the collaborating institutions. Treatment was determined by agreement between the patients and their physicians according to the T2T strategy. [Results] A total of 204 patients were enrolled, with age at diagnosis [mean±SD] 64.6±14.3 years old, 132 (65%) female, 149 (73%) positive for rheumatoid factor, 138 (68%) positive for anti-CCP antibody, Steinbrocker Stage (I/II/III/IV=112/78/7/4), Class (1/2/3/4=53/108/41/0), and 29 patients dropped out of the study. 122 (60%) had a history of any kind, and 138 (68%) had complications. At each observation point (0/24/52 weeks), MTX use was 174 (85%)/163 (80%)/127 (62%), respectively, and MTX dose was 6.9±1.2/10.3±3.7/10.2±3.4 mg. Oral PSL use was 41 (20%)/27 (13%)/23 (11%), oral PSL dose was 8.2±6.6/4.0±4.5/2.3±1.2 mg, and analgesic use was 117 (57%)/66 (32%)/43 (21%). In addition, 69 (34%) patients used csDMARDs other than MTX and 45 (22%) used biologics or JAK inhibitors during the entire period (3 patients changed b/tsDMARDs once and 1 patient twice). SDAI improved from 21.8±13.1 at diagnosis to 7.1±6.5 at 24 weeks and 5.1±5.2 at 52 weeks. Forty-six percent achieved SDAI remission, and 86% improved to below low disease activity. [Conclusions] A domestic cohort study reported DAS28-ESR remission in 55.9% and low disease activity or less in 76.4% (IORRA, 2018). Disease activity at 52 weeks in this study was generally consistent, indicating the validity of this observational study.

ICW12-2

Associated factors with frailty in patients with rheumatoid arthritis ~T-FLAG study using 2022 data~

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Conflict of interest: None

[Objective] Early diagnosis of frailty, a pre-stage of nursing care, is important in treating rheumatoid arthritis (RA). This study aimed to examine factors associated with frailty in RA patients. [Methods] 656 RA patients, who visited outpatients (three hospitals) from June to September 2022, were included in this study. Frailty was evaluated using the Japanese Cardiovascular Health study criteria (J-CHS). Patients were classified into frailty and non-frailty groups (robust and pre-frailty groups), and their backgrounds were compared with an univariate analysis. Subsequently, factors associated with frailty were examined via multiple logistic regression analysis. Next, only patients with interstitial pneumonia (IP) (102 cases) were extracted, classified into the frailty group and the non-frailty group, and the use of antirheumatic drugs (methotrexate, steroids, molecular-targeted drugs) was examined. [Results] The frailty group (152 cases) was older than the non-frailty group (504 cases) (66.8 vs. 73.6 years, p <0.001) and had worse disease activity (DAS28-ESR: 2.7 vs. 3.7, p <0.001) as well as a higher rate of IP (12.7% vs. 25%, p <0.001). The adjusted odds ratio (95% confidence interval) associated with frailty was age 1.04 (1.01-1.06, p <0.001), disease duration 1.03 (1.00-1.05, p <0.034), IP 1.74 (1.01-2.98), p =0.044) and DAS28-ESR 1.85 (1.55-2.21, p <0.001). Among patients with IP, the frailty group (64 cases) had a lower rate of use of molecular-targeted drugs than the non-frailty group (38 cases) (45.3% vs. 23.7%, p=0.035). [Conclusions] Our study showed that not only DAS28-ESR but a history of interstitial pneumonia was a factor associated with frailty in RA patients. Treatment enhancement was required even for RA patients with IP in order to improve their frailty. We should use molecular-targeted drugs more often since many medicines are available for patients with IP.

ICW12-3

A study of improvement from Frailty in rheumatoid arthritis from the T-FLAG study

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Conflict of interest: None

[Objective] Frailty is a concept that describes a state of vulnerability and includes the reversibility of return to a healthy state. Rheumatoid arthritis (RA) causes physical dysfunction and contributes to frailty, but with appropriate intervention, improvement from frailty can be expected. The purpose of this study was to investigate factors associated with improvement from frailty in RA patients. [Methods] Of 458 RA patients (T-FLAG Study) who completed a questionnaire on frailty including the Kihon Checklist (KCL), 321 patients who were frailty/pre-frailty at baseline were included. After 2 years, patients who had improved from frailty to pre-frailty/robust or pre-frailty to robust were included in the improvement group, and the other patients were included in the non-improvement group. Multivariate analysis was used to examine factors associated with improvement at 2 years. The cutoff values of the factors related to improvement were calculated by ROC analysis. [Results] There were 83 patients (25.9%) in the improvement group. There were significant differences in age at baseline (63 vs. 68 years), DAS28-CRP (1.89 vs. 2.36), HAQ-DI (0.19 vs. 0.65), and KCL score (7.0 vs. 8.7) in the improvement group vs. the non-improvement group. There was no significant difference in disease duration (10 vs. 12 years) and BMI (21.8 vs. 22.3 years). Multivariate analysis revealed that age (OR: 0.97, 95% CI: 0.95-0.99) and HAQ-DI (OR: 0.20, 95% CI: 0.09-0.46) were independent factors associated with improvement. The age and HAQ-DI cutoff values related to improvement were 72 years (sensitivity 73.5%, specificity 44.1%) and 0.25 points (sensitivity 78.3%, specificity 58.9%). [Conclusion] Age and HAQ-DI were found to be indices for improvement in RA patients. Since frailty has multifaceted factors, if the HAQ-DI, which is a physical function assessment, is low, even if the patient is frailty, it may be possible to improve with appropriate intervention.

ICW12-4

Does frailty reflect methotrexate discontinuation due to adverse events in rheumatoid arthritis patients? -T-FLAG study-

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Conflict of interest: None

[Objective] Methotrexate (MTX) is an anchor drug in the treatment of rheumatoid arthritis (RA). On the other hand, frailty is defined as the intermediate condition between being healthy and having a disability, which may lead to negative healthy outcomes and, thus adverse events of RA drugs are expected to increase. This study aimed to investigate relationship between frailty and MTX discontinuation due to adverse events in RA patients. [Methods] Of 538 RA patients (T-FLAG study) who visited us between June and August 2020, 323 used MTX. After 2 years of follow-up, we investigated final follow-up date and adverse events leading to MTX discontinuation. Frailty was defined as a score of 8 or more on the Kihon Checklist (KCL). Cox proportional hazards regression analysis (adjusted for age and sex) was performed to determine factors associated with MTX discontinuation due to adverse events. [Results] Of 323 patients (251 women, 77.7%), 24 RA patients (7.4%) discontinued MTX due to adverse events during the 2-year period. Age was 64.5±13.9/68.5±11.7 years (those with MTX continuation/discontinuation, p=0.17), disease duration was 11.7±10.1/9.4±8.7 years (p=0.28), CDAI was 5.6±7.3/6.2±6.0 (p=0.70), KCL was 5.9±4.1/9.0±4.9 points (p<0.05), and the proportion of frailty was 31.8/58.3% (p<0.05). MTX discontinuation due to adverse events was significantly associated with frailty (hazard ratio 2.82, 95%

confidence interval 1.24-6.39). Adverse events were liver dysfunction in 6 patients (25.0%), pneumonia in 5 patients (20.8%), and renal dysfunction in 3 patients (12.5%). [Conclusions] RA patients with frailty are more likely to use MTX since it was reported that frailty was significantly associated with higher disease activity of RA. Our finding suggest that frailty was the significant factor of MTX discontinuation due to adverse events. Therefore, the occurrence of MTX adverse events should be carefully monitored when using MTX in RA patients with frailty.

ICW12-5

Risk Factors for Progressing to Difficult-to-Treat Rheumatoid Arthritis (D2T RA) in Young and Elderly Patients with RA from FIRST Registry

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Conflict of interest: None

(Objective) Elderly-rheumatoid arthritis (RA) patients are increasing, therefore treatment strategies considering their life-stage are needed. In addition, it worth to estimate the risk of difficult-to-treat (D2T) RA progression and treat the patients at D2T RA-preconditions intensively. The study aimed to describe the characteristics of young and elderly RA patients who would progress to D2T RA. **(Methods)** Data were collected from FIRST registry (N=4,530). RA patients who were administrated 1st b/tsDMARDs after August 2013 were included and divided into the young group (<65 years) and the elderly group (≧65 years). The primary endpoint was the progression rate of D2T RA according to the EULAR definition for both groups. The secondary endpoints were the correlation between the patient background at the administration of 1st b/tsDMARDs and the progression to D2T RA. The difference of the mechanism of action of 1st b/tsDMARDs with regard to progression to D2T RA was also analyzed. **(Results)** A total of 1,133 patients were extracted, and 76/576 cases (13.2%) of the young group and 79/557 cases (14.2%) of the elderly group progressed to D2T RA after 27.5 months (p=0.66). In young group, high BMI (OR: 1.07 [1.01-1.13]) and high CDAI (OR: 1.03 [1.00-1.05]) at the administration of 1st b/tsDMARDs correlated with the D2TRA progression, whereas none of the elderly patient-background correlated with the D2T RA progression. On the other hand, the mechanism of action of 1st b/tsDMARDs correlated with D2T RA progression in both the young and older groups; the patients who was administrated IL-6 receptor inhibitors as the 1st b/tsDMARDs less progressed to D2T RA (IL-6Ri vs. TNFi/CTLA4-Ig/JAKi HR: young group; 0.47 [0.24-0.94], elderly group; 0.51 [0.27-0.96]). **(Conclusions)** Young and elderly RA patients similarly progressed to D2T RA. Our data suggests that the mechanism of action of 1st b/tsDMARDs impact on the progression: therefore, their meticulous agent selection is needed.

ICW13-1

Granulomatosis with polyangiitis presenting as isolated multiple renal tumor-like masses: a case report and systematic literature review

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Conflict of interest: None

[Objective] Granulomatosis with polyangiitis (GPA) is a systemic autoimmune disorder characterized by granulomatous inflammation and small-to-medium vessels necrotizing vasculitis. Mass lesions, also described as tumor-like masses, are uncommon manifestations. [Methods] Starting from our case, a complete literature review was conducted using searching engine in PubMed and as mesh terms, granulomatosis with polyangiitis, Wegener's granulomatosis, renal mass lesions, renal tumor-like masses. We focused on clinical features, treatment strategy and outcomes. [Results] A 49-year-old female was admitted to our Unit because of persistent high fever, generalized weakness and arthomyalgias lasting for 2 months. Blood tests showed elevated CRP (147 mg/L), ESR (116 mmh) and low hemoglobin (104 g/L), normal renal function test and negative infectious disease investigations. PET and contrast CT scan showed bilateral multiple rounded renal lesions (SUVmax 20). The presence of ANCA-PR3 (42.3 KU/L) positivity and renal biopsy (necrotizing granuloma) confirmed the GPA diagnosis. She was treated with high-doses glucocorticoids and rituximab (1000 mgx2). A progressive improvement was observed. The follow-up CT scan confirmed the almost complete regression of the lesions. Eight patients with GPA renal masses were reported in the literature. They were mainly women, with a median age of 46 [27-65] years. Renal masses were observed at disease onset and ANCA positivity was found in 87.5% of the cases. A clinical improvement was obtained with a combination of glucocorticoids and cyclophosphamide or rituximab. [Conclusions] GPA presenting as isolated multiple renal masses is extremely rare. Early diagnosis and prompt initiation of immunosuppressive therapy can prevent disease progression and irreversible damage.

ICW13-2

Ankylosing spondylitis Coexisting with Liver fluke infection: a case report and review of the literature

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Conflict of interest: None

[Objective] Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory arthritis. One of the most popular theories presume that the onset of AS in susceptible individuals may be caused by infections, and that infections have the potential to modulate and attenuate immune responses. Numerous studies have investigated AS-related infections, including bacterial, viral, fungal, and microorganisms. However, there is rarely reported in AS coexisting with liver fluke infection. This study aimed to investigate the association between infections and disease activity of AS, and review the literature. [Methods] We described the diagnosis and treatment of a case suffering from AS and liver flukes. A 27-year-old male who had a history of AS for 10 years, and inflammatory low back pain is the main manifestation. Ten years ago, the patient was in stable condition after treatment with biological agents. However, 10 days before admission, the patient experienced a recurrence of lumbosacral pain. An MRI scan showed bone marrow edema in the left sacroiliac joint, while laboratory indicators indicate that erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were increased. Rheumatologists consider disease activity, during hospitalization, liver fluke eggs were detected in the stool by routine examination. Taking a history, the patient had an irregular diet and had eaten sashimi a month ago. Considering the patient combined with a liver fluke infection, we prescribed praziquantel. [Results] After the treatment, no parasite eggs were found in the stool routine. Interestingly, the lumbosacral pain was significantly relieved, and relevant inflammatory indicators also returned to normal. [Conclusions] Liver fluke infection may lead to the disease activity of AS, so it is necessary to pay attention to the diet habits of patients with AS. Before using biological agents, routine fecal eggs should be screened to improve the effectiveness of treatment and obtain better prognosis.

ICW13-3

IgA Vasculitis as an Initial Presentation of HIV in a Young Filipino Male: A Case Report

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Conflict of interest: None

Background: Vasculitis is uncommonly associated with Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome (HIV/AIDS) with an estimated incidence of <1%. **Case Summary:** We report

the case of a young Filipino male who was admitted for acute onset of purpuric rash, joint pains, and severe abdominal pains. Exploratory laparotomy was performed due to suspected intussusception on imaging but only edematous and erythematous bowels were identified intraoperatively. High dose steroids were empirically started for suspected IgA vasculitis as patient developed hematochezia postoperatively. However, rashes progressed in spite of initial therapy and nephritis was documented with a urine protein: creatinine ratio of 6.07 g/g. Anti-Neutrophil Cytoplasmic Antibody (ANCA), Hepatitis B and C serology, and Syphilis Rapid Plasma Reagent (RPR) tests were all negative, but his HIV antibody test was positive and CD4 count measured at 87 cells/mm3. Patient was eventually assessed to have HIV associated vasculitis with nephritis. **Outcome:** He was started on Highly Active Antiretroviral Treatment (HAART) which gradually resolved his rashes, while steroids were gradually tapered. **Discussion:** This case exemplifies vasculitis as a presentation of HIV/AIDS, and that it can be an initial manifestation of the infection.

ICW14-1

Comparing injecting local anesthesia in the overlying skin to not giving it prior to Intraarticular Injection of glucocorticoid - A Randomized Controlled trial

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Conflict of interest: None

[Objective] Compare procedural pain in intra-articular injection between using local anesthesia to overlying skin or not. [Methods] Open label randomized controlled trial included patients with rheumatoid arthritis or spondyloarthritis undergoing intra-articular injections (of glucocorticoid) to paired medium-large joints. First the left joint was injected followed by right joint after a gap of 10-minutes. Randomization by software whether local anesthesia (5 ml of 2% Lignocaine using a 23G needle) would be given to the left or right joint. Primary endpoint was immediate procedural pain felt by the patient using the 'Numerical Rating Scale and Faces Pain Scale-Revised. Secondary endpoints were 1-hour pain assessment, patient preference and complications. Paired t-test and Wilcoxon Signed Ranked test was used (paired data). Trial number CTRI/2021/07/034777 [Results] Included 42 patients undergoing paired joint injections; joints were knee (21 patients), wrists (14), ankles (5) and elbows (2). Most were middle aged with mean age (±SD) 44.6 ± 14 years, 71% being females having rheumatoid arthritis (37) and spondyloarthritis (5 patients). There was a significantly lower immediate procedural pain in the joint over which the skin was given local anaesthesia compared to that not given it (4.7 (1.7), 5.6 (1.6), p<0.01, difference -1.1, 95% CI -1.5 to -0.7) (Figure 1). This was also reduced pain in the that joint at 1-hour post procedure (3.3 (1.4), 4.0 (1.6), p<0.01). Majority of patients (78.6%) preferred the procedure with local anaesthesia (Figure 2). There was no difference in complications of hypopigmentation or purpura nor in residual pain prick-site at 1-month. [Conclusions] Local anaesthesia of the overlying skin led to a definite but modest reduction in pain felt by the patient during intraarticular injection.

ICW14-2

Automatic evaluation of atlantoaxial subluxation in rheumatoid arthritis by a deep learning model

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Conflict of interest: None

[Objective] The purpose of this work is to develop an artificial intelligence using deep learning model, assessing atlantoaxial subluxation in rheumatoid arthritis (RA), which can often be ambiguous in clinical practice. [Methods] We collected 683 X-ray images of the cervical spine of the 307 patients with RA. Among these images, 566 were used for training the deep learning model, 38 were used for validating the model during the training process, and remaining 79 were used for testing the performance of the trained model. The model consisted of two steps. At the first step, a neural network including a convolutional neural network identified the location of atlantoaxial joint. At the second step, another neural network output the atlantodental interval (ADI) and space available for the spinal cord (SAC). Finally, these output values were compared with those by clinicians to evaluate the performance of the model. [Results] Among the 79 cervical images for testing the performance, the trained model identified the atlantoaxial joint in all cases. The values of ADI and SAC were positively correlated among the model, and two clinicians. The sensitivity of atlantoaxial subluxation diagnosis with ADI by the model was 0.78 and the specificity was 0.75. [Conclusions] We present the development of an artificial intelligence model for the evaluation of cervical lesions of patients with RA. The completed model correctly detected cervical spine lesions and was demonstrably shown to be useful for quantitative evaluation.

ICW14-3

Effect of denosumab on bone destruction in rheumatoid arthritis in clinical practice: A prospective cohort study

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Conflict of interest: None

[Objective] Although denosumab (DNS) has been shown to inhibit bone destruction in rheumatoid arthritis (RA) in clinical trials, data in daily practice are scarce. There is also concern about a decrease in bone mineral density (BMD) after DNS discontinuation. Here we examined the efficacy of DNS in daily practice and investigated the effect of DNS on the differentiation of peripheral blood monocytes (PBM) into osteoclasts (OCL). [Methods] We performed a prospective observational study of DNS-naïve RA patients with osteoporosis or progressive bone erosion. We divided the patients into two groups, DNS-treated (DT) and DNS-naïve (DN) groups and collected clinical data longitudinally. We also isolated PBM and differentiated them into OCL, and compared cell counts between the two groups. [Results] Of the 39 participants, 13 belonged to the DT group and 22 to the DN group. At enrollment, there were no differences in disease duration, disease activity, or DMARD usage between the groups. The DT group had higher rate of glucocorticoid use (33.3% vs 0%, p = 0.014) and lower BMD at the femoral neck (T-score: -2.5 ± 0.7 vs -1.7 ± 0.8, p = 0.011) than the DN group. The DT group showed significant decrease of serum BAP and TRACP-5b levels at 3 months compared to the DN group (-6.0 ± 3.1 vs 0.8 ± 3.7, p < 0.001, and -257.4 ± 121.2 vs -21.8 ± 85.3, p < 0.001, respectively). There was no difference in modified total sharp score at 12 months between the two groups (0.95 ± 1.29 vs 0.57 ± 0.94, p = 0.34), but lumbar spine BMD was significantly improved in the DT group than in the DN group (0.37 ± 0.25 vs 0.12 ± 0.23, p = 0.01). The PBM ability to differentiate into OCL was higher in the DT group than in the DN group (p = 0.007). [Conclusions] The effect of DNS on improving bone metabolic markers and BMD was observed, not on suppressing bone destruction in daily practice. The effect of DNS on the OCL differentiation suggests that DNS discontinuation may be a risk for worsening osteoporosis.

ICW14-4

Building AI model that predicts change of bone mineral density from plain hand X-ray in RA patients using KURAMA cohort

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is known as a risk factor for osteoporosis. However, few patients with osteoporotic fractures measured bone mineral density (BMD) before fracture. Thus, there is still a demand for developing a simple screening method. The previous study showed that BMD correlates with the second metacarpal cortical index (2MCI). This study aims to test the efficacy of 2MCI for predicting the transition of BMD using artificial intelligence (AI). [Method] Patients who received a set of tests including DXA and bilateral hand X-rays multiple times with a minimal interval of two years between the first and last tests were included. 2MCI was defined as the ratio between the thickness of the cortex and the width of the bone of the second metacarpal. We examined the correlation between changes in 2MCI and BMD of the hip and the forearm. Then, we built a AI model that predicts BMD of the target year using the base year's BMD and change of 2MCI. [Result] Among the RA patients enrolled in KURAMA cohort, 302 patients met the criteria. The mean age was 62.6 years. Baseline cross-sectional analysis showed a significant correlation between 2MCI and BMD of the hip and forearm ($p<0.01$), and ROC analysis with a cut off 70% T-score showed an AUC of 0.79 in the hip and 0.91 in the forearm. A longitudinal study showed a significant correlation between change in BMD and change in 2MCI ($p<0.01$). For testing AI models, we used Pycaret for unbiased comparison and found that Bayesian Ridge showed the best accuracy for predicting the target year's BMD of hip and forearm using base year's BMD and change of 2MCI (R^2=0.907 for forearm and 0.889 for hip). [Conclusion] Establishing a simple and efficient method for osteoporosis screening is a social issue in an aging society. This study showed that 2MCI significantly correlates not only with BMD at a single time point but also with changes in BMD. Also we built AI model for BMD prediction using 2MCI and clinical parameter.

ICW14-5

A machine learning model that predicts RA progression from undifferentiated arthritis -KURAMA and ANSWER cohort study-

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Conflict of interest: Yes

[Objective] Early diagnosis and treatment of rheumatoid arthritis (RA) improve clinical outcomes. Undifferentiated arthritis (UA) is arthritis that does not fit a specific diagnosis. Half of the UA undergo spontaneous remission, while 30% of cases develop RA. Therefore, in UA, identifying patients at high risk for developing RA and providing close monitoring is required. Machine learning, including deep learning, which is comparable to and in some cases surpasses the performance of human experts, is broadening its application in medicine. This study aims to build a machine-learning model that predicts the development of UA to RA. [Methods] For model training, a total of 322 UA patients in KURAMA cohort were analyzed. For variables to train models, we chose 24 clinical features, which are easy to obtain in daily clinical practice. The target variable was the final diagnosis. We built models using Random forest (RF), XGBoost (XGB), Logistic regression (LR), and Deep neural network (DNN) and compared their performances. For model validation, we used data of 88 UA cases in ANSWER cohort. [Results] We trained models using 24 clinical parameters at the first clinical visit, performed 10-fold cross-validation, and evaluated model performance by averaging accuracy and AUC. The performance of the models was 73.5%, 74.2%, 74.5%, and 85.1% in precision and 0.760, 0.734, 0.748, and 0.895 in AUC for RF, XGB, LR, and DNN, respectively. DNN showed the highest performance. We then applied the DNN model to external validation data from ANSWER cohort and found that the prediction accuracy was 80.0%. [Conclusions] Using parameters available in clinical practice, we developed a DNN model that effectively predicted RA development in internal and external UA datasets. Applying a machine learning approach might enable identifying patients at high risk of RA progression and improve the clinical management of UA patients.

ICW15-1

Comparison of Two Doses of Leucovorin in Severe Low-dose Methotrexate toxicity - A Randomized Controlled Trial

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Conflict of interest: None

[Objective] The antidote for low-dose methotrexate toxicity (due to inadvertent overdose like daily dosing) is leucovorin, but its optimum dose is unclear; thus, we compared two different doses of leucovorin, usual (15 mg) or high-dose (25 mg), given intravenously every 6 hours. [Methods] Open-label RCT included patients with severe low-dose (≦50 mg/week) methotrexate toxicity defined as WBC ≦2 x 10^9/L or platelet ≦50 x 10^9/L and randomized them to receive either usual (15 mg) or high-dose (25 mg) intravenous leucovorin given every 6 hours. Primary outcome was mortality at 30 days and secondary outcomes were hematological recovery and mucositis recovery. Trial Registration CTRI/2019/09/021152. [Results] 38 patients were included in this study, 19 patients each were randomized to receive either usual or high dose leucovorin. The most common cause of methotrexate toxicity was erroneous dosing (taken daily or alternate day instead of weekly) (68%), followed by renal failure (37%). The median white blood and platelet count were 0.8 x 10^9/L and 23.5 x 10^9/L. Number (%) of deaths over 30-days was 8 (42) and 9 (47) in usual and high-dose leucovorin groups (Odds ratio 1.2, 95% Confidence interval 0.3 to 4.5, p=0.74). On Kaplan-Meier, there was no significant difference in survival between the groups (hazard ratio 1.1, 95% CI 0.4 to 2.9, p=0.84). On multivariable cox-regression, serum albumin was the only predictor of survival (hazard ratio 0.3, 95% CI 0.1 to 0.9, p=0.02). There was no significant difference in hematological recovery (7, 6 days, p=0.9, hazard ratio 1.0, 95% CI 0.4-2.7) or mucositis recovery between the 15 and 25 mg groups (5, 4 days, p=0.59, hazard ratio 1.5 (95% CI 0.6-3.7). [Conclusions] There was no significant difference in survival or time-to hematological recovery between the two doses of leucovorin. Severe low-dose methotrexate toxicity carried a significant mortality.

ICW15-2

Can We Predict Response to Methotrexate in Rheumatoid Arthritis: Results from a Multicentre, Randomized Controlled Trial on Methotrexate Escalation in RA

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Conflict of interest: None

Objectives: Methotrexate (MTX) is the gold standard, first-line therapy for Rheumatoid Arthritis (RA) globally, but 30-40% of patients fail to respond to it. Prediction of treatment response is an important facet of personalized medicine in RA. We sought to identify demographic and clinico-laboratory predictors of MTX response in RA, which have not yet been reliably identified. **Methods:** Patients with active RA (SJC≧2 and TJC≧4) aged 18-55 years, not on DMARDs (except HCQ and low-dose prednisolone) who had been enrolled in the multicentre, parallel-group RCT comparing two different MTX escalation strategies in RA (MEIRA), were included. All these patients received MTX monotherapy started at 15 mg per week and escalated to 25 mg per week by 4-8 weeks. MTX response was defined as EULAR good or moderate response (based on DAS28-3v) at 16 weeks. Stepwise, multivariable logistic regression was done using key demographic (age, gender, BMI, comorbidities), clinical (disease duration, DAS28 and its components, HAQ), and laboratory parameters (RF, anti-CCP, MTX-polyglutamates, IL-6, MMP-3, ESR, CRP) as independent variables to identify predictors of MTX response. Two-tailed p-value <0.05 was considered statistically significant (Trial Reg: CTRI/2018/12/016549). **Results**: A total of 178 patients [84% females, mean age 40 (9) years, mean DAS28-CRP=5.4 (1.1)] were included; 113 (63.5%) were categorized as MTX responders at 16 weeks. Age (OR 0.95, p=0.01), BMI (OR 1.12, p=0.006), and RF (OR=0.34, p=0.045) were found to be independent predictors of MTX response on multivariate analysis. On sensitivity analysis with DAS28ESR-based EULAR response, age (OR=0.945, p=0.003) and RF (OR=0.42, p=0.059) were replicated as independent predictors of MTX response, in addition to pre-treatment swollen joint count (OR=0.94, p=0.05). **Conclusion:** Younger age, RF negativity, higher BMI, and lower pre-treatment swollen joint count are potential predictors of MTX response in RA.

ICW15-3

Time trend of RF seropositivity in Japanese patients with rheumatoid arthritis between 2000 and 2021: data from the IORRA cohort

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Conflict of interest: Yes

[Objective] The incidence of rheumatoid factor (RF)-positive RA has been reported to be decreasing (Kaipiainen-Seppanen O, *et al.* J Rheumatol. 2006.). Patients' age, a decrease in smoking, and an increase in obesity might be associated with the change in RF positivity (Myasoedova E, *et al*. Ann Rheum Dis. 2020.), however, these need to be further investigated in other registries and races. We aimed to investigate the time trend of RF seropositivity in Japanese RA patients using data from the Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort. [Methods] Among patients enrolled in the IORRA cohort between 2000 and 2021, data of patients with disease duration of <3 years at enrolment and those who measured serum RF levels were included in this study. The time period was divided into 2000-2010 and 2011-2021. The effect of the time period on RF seropositivity was analyzed using multivariable analysis after adjusting for age, sex, smoking, body mass index (BMI), and disease activity. [Results] Of 6,365 patients enrolled, 5,088 (81.2%) patients were female, the median age was 54.9 (interquartile range: 43.9-64.5), and 4,585 (73.1%) were RF-positive. The proportion of RF-positive patients was 74.9% in 2000-2010, which significantly decreased to 70.0% in 2011-2021 (p<0.0001). The proportion of the current smoker (17.8% vs. 9.8%) and BMI (21.1 vs. 20.1) also decreased over time. After adjusting for the confounding factors, the time period (2011-2021) was associated with being RF-negative in this model (odds ratio: 1.24, 95% confidence interval: 1.08-1.43, p=0.003). [Conclusions] The proportion of RF-positive RA patients with disease duration <3 years has decreased in the IORRA cohort, and thus the serological status of patients with RA may have been changing in the clinical setting over time.

ICW15-4

Establishment of an Optimal Treatment Strategy from the Perspective of the Continuation Rate of Biologic/Targeted Synthetic Disease-Modifying Antirheumatic Drugs in Elderly Patients with Rheumatoid Arthritis: From the FIRST registry

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Conflict of interest: None

Objectives: Japan is a super-aging society, and establishment of treatment strategies for elderly patients with rheumatoid arthritis (RA) is an urgent issue. This study analyzed the long-term continuation rate (CR) of biologic/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) in elderly RA patients. **Methods:** Subjects were RA patients (n=2292) in whom b/tsDMARDs were introduced. The CRs of b/tsDMARDs for three years were analyzed in non-elderly patients (≦64 years; n=1149), semi-elderly patients (65-74 years; n=679), and elderly patients (≧75 years; n=464). COX proportional hazard model was used to analyze the effect of b/tsDMARDs on CR. **Results:** CRs of all b/tsDMARDs did not differ among three age groups. In semi-elderly patients, the CRs of TNF inhibitors (TNFi, n=252), IL-6 receptor inhibitors (IL-6Ri, n=169), CTLA4-Ig (n=180), and JAK inhibitors (JAKi, n=78) were 56%, 68%, 61%, and 67%, respectively. After adjustment for age, sex, disease activity, and number of previously used b/tsDMARDs, the use of IL-6Ri (HR 0.64, 95% confidence interval [CI] 0.45-0.90) and JAKi (HR 0.53, 95% CI 0.33-0.85) contributed to an increase in CR. The CR in elderly patients was TNFi (n=128): IL-6Ri (n=118): CTLA4-Ig (n=182): JAKi (n=36)= 49:69:70:69 (%). When similarly adjusted, the use of CTLA4-Ig contributed to an increase in CR (HR 0.65, 95%CI 0.45-0.92), and JAKi contributed to an increase in CR in patients who did not respond to ≧2 b/tsDMARDs. In semi-elderly patients, IL-6i (OR 0.30, 95%CI 0.18-0.52) and JAKi (OR 0.44, 95%CI 0.211-0.92) showed less discontinuation due to no response and contributed to an increase in CR. However, in elderly patients, CTLA4-Ig showed a lower rate of discontinuation due to adverse events (OR 0.45, 95%CI 0.23-0.87) and contributed to an increase in CR. **Conclusion:** The efficacy and safety of b/tsDMARDs differ by age in elderly RA patients, suggesting the possibility of selecting a drug suitable for patients in each age group.

ICW15-5

Vascular effect of treat to target in early rheumatoid arthritis patients - a 5-year prospective study

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Conflict of interest: None

[Objective] Whether treating to target over time is associated with long-term vascular outcomes in early rheumatoid arthritis (ERA) remained unclear. [Methods] This was a 5-year prospective study in patients with ERA. Consecutive ERA patients without overt cardiovascular disease were recruited, Patients received tight-control treatment in the first year, followed by standard-of-care management subsequently. Subclinical atherosclerosis was assessed using high-resolution carotid ultrasound (US) at

baseline and year 5. The primary outcome was subclinical atherosclerosis progression (AP+), defined as incident plaque or an increased region harboring plaques, and/or maximum carotid intima-media thickness (max cIMT) progressed to over 0.9 mm at year 5. Cumulative averages of the area measured cumulative disease activity under the curve for disease activity 28-erythrocyte sedimentation rate (ca-DAS28-ESR) over a period of 5 years. Persistent LDA was defined as ca-DAS28-ESR ≦3.2. [Results] One-hundred and four ERA patients (age: 52±11 years, 81 (78%) female) who completed five years of follow-up were included in this analysis. There was a marked improvement in disease activity after five years of treatment (DAS-ESR at baseline: 5.8±0.9 vs. 3.2±1.2 at year 5, $p<0.001$). Fifty (47%) patients achieved persistent LDA. Forty-two patients (40.4%) had AP+. Patients in the AP+ group were older, had higher Framingham risk scores (FRS), and had higher exposure to anti-hypertension drugs at baseline. The use of medication throughout the study period was similar across the two groups. Moderate and high disease activity was an independent predictor with AP+ (OR=3.19, 95% CI: 1.11-9.22, $p=0.032$) after adjustment for A*nti-CCP positive* and Framingham risk score at baseline. [Conclusions] Achieving persistent LDA was an independent predictor of subclinical atherosclerosis in ERA. Effective long-term suppression of disease activity is required to minimize cardiovascular risk.

ICW16-1

Pain in idiopathic inflammatory myopathies, other systemic autoimmune rheumatic diseases, and healthy controls: A report from the COVAD study

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Conflict of interest: None

[Objective] To compare pain intensity among patients with idiopathic inflammatory myopathies (IIMs), patients with other systemic autoimmune rheumatic diseases (AIRDs), and healthy controls (HCs). [Methods] Data were collected from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) study, an international cross-sectional online survey, from December 2020 to August 2021. Pain experienced in the preceding week was assessed using a 0-10 visual analogue scale (VAS). To assess pain in IIMs subtypes and a possible impact of demographics, disease activity, general health status and physical function on pain scores a negative binomial regression analysis was performed. [Results] Responses from 6,988 participants (15.1% with IIMs, 27.9% with other AIRDs and 57.0% HCs) were included in the analysis. The median pain VAS in patients with IIMs, other AIRDs, and HC were 2.0 (IQR 1.0-5.0), 3.0 (IQR 1.0-6.0), and 1.0 (IQR 0-2.0), respectively ($p<0.001$). Regression analysis adjusted for sex, age, and ethnicity revealed that overlap myositis and antisynthetase syndrome had the highest pain VAS (4.0, 95%CI 3.5-4.5, and 3.6, 95%CI 3.1-4.1, respectively). An additional association between pain and poor functional status was observed in all groups. Female sex was associated with higher pain scores in almost all scenarios. Increasing age was associated with higher pain VAS scores in some scenarios of disease activity, and Asian and Hispanic ethnicities had reduced pain scores in some functional status scenarios. [Conclusions] Patients with IIMs reported higher pain levels than HCs, but less than patients with other AIRDs. Pain is a disabling manifestation of IIM and is associated with a poor functional status.

ICW16-2

Trade-off between the use of glucocorticoids and immunosuppressants: Reduced rate of disease flares in Japanese patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] The outcomes for patients systemic lupus erythematosus (SLE) have considerably improved in recent years. The current concept of the "treat-to-target" strategy has been applied to SLE. Consequently, in our department, a trade-off between immunosuppressants and glucocorticoids (GCs) has been aggressively attempted in recent years to prevent the cumulative organ damage associated with GC use. We therefore retrospectively examined whether or not disease control in Japanese patients with SLE had improved in the past 20 years. We also studied the possible associations with disease flare and the altered balance between the use of GCs and immunosuppressants. [Methods] We enrolled Japanese patients with SLE who visited our medical center during 2013-2017 (Group A, 75 patients) and compared them with patients encountered during 1999-2003 (Group B, 69 patients; not overlapping with Group A). Disease flare was defined as new BILAG 2004 A or B scores in at least one system. [Results] Lupus nephritis and neuropsychiatric manifestations were less frequently observed in Group A than B ($p=0.042$ and $p=0.045$, respectively). Although the initial GCs dosage was similar between the groups, the inclusion rate of immunosuppressants in the initial SLE treatment was significantly higher in Group A than B (56% vs. 6% in Group B, $p<0.001$). The median number of SLE flares per person-year was significantly lower in Group A than B (0.01 vs. 0.3, respectively, $p<0.001$), and a propensity score-matched analysis indicated the association of SLE flare with the non-use of immunosuppressants in the initial treatment ($p=0.012$). At the time of disease flare, the dose-increment of GCs was smaller in Group A than B (PSL conversion: median 5 vs. 14 mg/day, respectively, $p=0.005$), and the continuation of the same dose of GCs was observed in 38% in Group A, while it was very rare (2%) in Group B. [Conclusions] The recent aggressive use of immunosuppressants in Japan resulted in a reduction in the rate of SLE flare.

ICW16-3

Machine learning-based diagnosis of systemic immune-mediated diseases by immunophenotyping data

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Conflict of interest: Yes

[Objective] Systemic immune-mediated diseases are occasionally

challenging to diagnose and comprehend their pathogenesis. Although immunophenotyping is helpful in understanding the pathology and stratifying patients in each rheumatic disease, the usefulness of cross-disease immunophenotyping data remains elusive. We constructed a machine learning method for diagnosing diseases and clarifying the important cells to differentiate them. [Methods] Immunophenotyping of 235 patients with systemic immune-mediated diseases, including 78 systemic lupus erythematosus (SLE), 22 mixed connective tissue disease (MCTD), 48 idiopathic inflammatory myopathy (IIM), 48 systemic sclerosis (SSc), 20 rheumatoid arthritis (RA), and 19 large vessel vasculitis (LVV) were undertaken. We collected the clinical data and analyzed a total of 29 types of immune cells from peripheral blood mononuclear cells using flow cytometry. We performed random forest with the immunophenotyping data and k-means clustering analysis. [Results] The random forest method was applied to classify systemic immune-mediated diseases, and overall accuracy rate reached 70.0% (95% CI: 46.0-88.0%). The sensitivities and the specificities to distinguish SLE, IIM, and SSc from other diseases were 78.3%/80.9%, 98.2%/71.4%, and 78.6%/66.1%, respectively. The top 15 important subsets were applied to conduct k-means clustering and found 3 clusters. Cluster 1 was IIM and SLE dominant and enriched by CD4+ T cells; cluster was SLE dominant and enriched by plasmablasts and double-negative B cells; cluster 3 was SSc dominant and enriched by myeloid dendritic cells and non-classical monocytes. [Conclusions] The systemic immune-mediated diseases were classified by the random forest using the immune cell proportions data. This study also revealed important immune cells to differentiate the diseases. Our data may corroborate the understanding of the pathogenesis and future stratification of systemic immune-mediated based on immunophenotyping.

ICW16-4

Comparisons of systemic lupus erythematosus disease activity score (SLE-DAS) and systemic lupus erythematosus activity index 2000 (SLEDAI-2K) and validation of definitions to classify disease activity based on the SLE-DAS with reference to patient-reported outcomes: the Kyoto Lupus Cohort study

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Conflict of interest: Yes

[Objectives] Although the systemic lupus erythematosus disease activity score (SLE-DAS) and its definitions to classify disease activity have been recently developed to overcome the drawbacks of the SLE disease activity index 2000 (SLEDAI-2K), performance of the SLE-DAS for patient-reported outcomes (PROs) has not been examined. We aimed to compare the SLE-DAS with the SLEDAI-2K and validate definitions of low disease activity state (LDA), clinical remission, and categories of disease activity based on SLE-DAS in terms of PROs. [Methods] We assessed generic quality of life (QOL) using Medical Outcome Survey 36-Item Short-Form Health Survey (SF-36), disease-specific QOL with Lupus Patient Reported Outcome tool (LupusPRO), burden of symptoms using SLE Symptom Checklist (SSC), and patient's global assessment (PtGA) in addition to physician's global assessment (PhGA). [Results] Of the 335 patients with SLE, a strong correlation between SLE-DAS and SLEDAI-2K was found (Spearman's $\rho = 0.71$; $P < 0.001$). After adjusting for age, sex, disease duration, dose of corticosteroid, use of hydroxychloroquine and immunosuppressant, and coexistence of other connective tissue diseases, both SLE-DAS and SLEDAI-2K were significantly and inversely associated with LupusPRO, SSC, and PhGA. The magnitudes of the mean absolute error, root mean square error, Akaike information criterion, and Bayesian information criterion were comparable between SLE-DAS and SLEDAI-2K. SLE-DAS LDA, a Boolean and an index-based remission, and categories of disease activity (remission, mild and moderate/severe activity) were significantly associated with health-related QOL of LupusPRO, SSC, and PhGA, not SF-36 or PtGA. [Conclusion] No clear differences were identified in the use of SLE-DAS over SLEDAI-2K in assessing PROs in patients with SLE. The definitions to classify disease activity based on the SLE-DAS were validated against several PROs. Both SLE-DAS and SLEDAI-2K are effective tools regarding PROs.

ICW16-5

Does shared decision-making affect the quality of life in SLE patients?: the TRUMP2-SLE study

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Conflict of interest: None

[Objective] Shared decision-making (SDM) has been recognized to be important for SLE treatment. However, evidence of the impact of SDM on the quality of life (QoL) in SLE patients is lacking. Here we examined the effect of SDM on QoL through a multicenter observational study. [Methods] This is a cross-sectional study of SLE patients attending five facilities in Japan from June 2020 to August 2021. We collected data including SDM-Q-9, an SDM scale, and LupusPRO, a scale of disease-specific QoL for SLE. We compared the association between SDM and health-related quality of life (HRQOL) and non-health-related quality of life (non-HRQOL) included in LupusPRO using the general linear models. Furthermore, we conducted multivariate analyses of the association between each domain of LupusPRO and SDM-Q-9, using gender, age, SELENA-SLE Disease Activity Index, disease duration, immunosuppressants, hydroxychloroquine, marriage, academic background, and income as independent variables. Analysis was performed after extracting patient data with SDM-Q-9 and target LupusPRO domains that were not missing, and missing values of independent variables were imputed by multiple imputation. [Results] A total of 519 patients (87.7% female, age 47.4±14.9 years) were included. The median SDM-Q-9, HRQoL, and non-HRQoL were 76 [IQR 62-89], 86 [74-94], and 49 [39-59], respectively. Better SDM was associated with greater non-HRQoL score converted to 100 points (per 10 pt increase, 2.2 pts, 95%CI 0.14-0.30). In each domain, for every 10-point increase in SDM, the domains for cognition, physical health, emotional health, and satisfaction with care increased by 1.8, 1.1, 1.5, and 8.0 in 100-point equivalents (95%CI, 0.05-0.31, 0.004-0.22, 0.02-0.29, 0.65-0.95, respectively), suggesting that SDM contribute to good physical and mental health, and satisfaction with physician. [Conclusions] A better SDM may lead to a better QoL in SLE patients.

ICW16-7

PROMIS Global Health And Quality Of Life Among Idiopathic Inflammatory Myositis And Autoimmune Rheumatic Diseases: Data From Covid-19 Vaccination In Autoimmune Diseases (COVAD) Study

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Conflict of interest: None

Objective: We aimed to determine the global health and quality of life in idiopathic inflammatory myositis (IIM) patients and compare them with autoimmune rheumatic diseases (AIRDs), non-rheumatic autoimmune diseases (nrAIDs) and healthy controls (HC). **Methods:** Covid-19 vaccination in autoimmune diseases (CoVAD) survey 2, an international e-survey (109 countries, 157 collaborators) conducted in Jan-May 2022, collected data on PROMIS10a_global physical (PGP), mental health (PGM), fatigue VAS, pain VAS, PROMIS_Fatigue 4a score (F4a), PROMIS_short form10 (SF10a), among IIM patients, AIRDs and HCs. **Results:** Among the 10502 complete respondents, IIM were 1582 (15.0%), AIRDs were 4700 (44.7%), nrAIDs were 545 (5.1%). IIM patients were older aged 59.1 (14.4) years [71.6% females, and 82.7% Caucasians]. Dermatomyositis (DM) (31.0%) and inclusion body myositis (IBM) (24.9%) formed the major subsets. IIM patients had higher comorbidities ($p<0.001$) and AID multimorbidity ($p<0.001$) compared to the others. IIM patients had lower PGP (12.1±2.5), lower PGM (12.8±3.4), higher F4a (11.2±4.1), lower SF10a (33.4±10.8), and higher pain VAS (3.2±0.9) scores compared to AIRDs, nrAIDs and HCs (all $p<0.001$) indicating overall poorer physical/mental health, and higher fatigue, pain scores. Active IIM had lower PGM, higher pain VAS, F4a compared to inactive IIM. In linear regression, PGP positively correlated with high HDI (estimate: 2.627, ref: low_HDI), active/improving disease (0.845), and negatively by age (-0.012), male gender (-0.366), IBM (-1.487), and worsening disease (-0.609). Similarly, PGM positively correlated by inactive (0.886), stable disease (0.566) and negatively by pre-existing mental health disorders (-2.147), AID multimorbidity (-0.414), medium HDI (-4.421, ref: low_HDI) and active/worsening disease (-0.718) (all $p<0.05$). **Conclusions:** IIM patients had poorer physical health, mental health and higher pain, fatigue scores compared to AIRDs, HCs, more so among active disease.

ICW17-1

Risk of infection in patients with systemic lupus erythematosus is different between male and female

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Conflict of interest: None

[Objective] Although gender difference in disease characteristics of systemic lupus erythematosus (SLE) has been reported, there have been few reports on the gender difference in the risk of infection of patients with SLE. In this study, we compared the risks of infection in patients with SLE between males and females and attempted to find the characteristic features of the risk factors in each group. [Methods] We checked the medical records of patients with SLE treated at our hospital for more than 6 months. We examined risk factors for infection requiring hospitalization and compared them between males and females. [Results] Among 313 patients with SLE, 47 (15.0%) were admitted to our hospital for the treatment of infection. Infection occurred more frequently in males than in females (33.3% vs 12.0%, $p<0.01$, odds ratio (OR) 3.59, 95% confidence interval (CI): 1.65~7.60). In multivariable analysis, the risk factors for infection in males were the complication of other connective tissue diseases ($p=0.018$, OR 21.48, 95%CI: 1.70~250.57) and low complement ($p=0.018$, OR 94.03, 95%CI: 2.18~4063.07), whereas the risk factors in females were duration of disease ($p=0.010$, OR 1.05, 95%CI: 1.01~1.09), use of prednisolone more than 7.5 mg/day ($p<0.01$, OR 5.66, 95%CI: 2.13~15.04) and complication of interstitial pneumonia ($p<0.01$, OR 6.15, 95%CI: 1.62~23.28). [Conclusions] Infection occurred more frequently in males than in females among the patients with SLE. Concerning the risk for infection in patients with SLE, treatment could have a greater effect on females and disease activity could have a greater effect on males.

ICW17-2

Biologics not associated with mortality of Pneumocystis jirovecii pneumonia in patients with rheumatoid arthritis; Results from Registry to provide new evidence and insights for the management of pneumocystis pneumonia in non-HIV-infected patients (RE-VISION-PCP)

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Conflict of interest: None

[Objective] To compare the outcomes of Pneumocystis jirovecii pneumonia (PCP) between patients with rheumatoid arthritis (RA) treated or not treated with biologics. [Methods] In this registry, we compared the clinical characteristics and outcomes of PCP in consectuive patients with RA treated or not treated with biologics and also analyzed the outcomes after adjusting for confounders using overlap weight methods. Patients with Human Immunodeficiency Virus, organ transplant, and malignancy were excluded. [Results] Eight one-patients were enrolled in this study, including the biologics group (n = 39) and the non-biologics group (n = 42). No patients received Janus Kinase inhibitors. Five patients died and 11 patients developed respiratory failure during hospitalization. At the diagnosis of PCP, biologics group was significantly higher lymphocyte count, total protein, albumin, and C reactive protein than non-biologics group, but respiratory status was no significantly differences between the groups. The 30-day and 180-day survival rate in the biologics group was 97.4% and 90.5%, respectively, and those in the non-biologics group was 97.3% and 89.7%, respectively. Although intubation with mechanical ventilation rate in both groups was similar, non-invasive positive-pressure ventilation or High-flow-nasal-canula rate in the biologics group was significantly lower than that of non-biologics group (P = 0.01). Kaplan-Meier survival curves for death showed that there were no significantly differences between biologics and non-biologics group. After adjusting using overlap weighting, the 30-day and 180-day survival rate was also no significantly differences between the groups. [Conclusions] In patients with RA who developed PCP, biologics was not associated with mortality of PCP.

ICW17-3

Prevalence, Determinants and Patterns of Infections in a Cohort of Patients with Systemic Lupus Erythematosus in Sri Lanka

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Conflict of interest: None

[Objective] Infections in systemic lupus erythematosus (SLE) patients can lead to serious consequences. We aimed to describe prevalence, types and patterns of infections and their association with disease flares and immunosuppressive drugs. Although recent studies from South Asian region report a significant burden of this problem, it had never been studied in Sri Lankan setting before. [Methods] A retrospective analysis of records of

SLE patients who attend University Rheumatology Clinic at National Hospital of Sri Lanka was conducted. Patients who were 14 years or more, fulfilling ACR criteria for SLE diagnosis were included. [Results] Out of 74 participants, 65 (87.8%) were females. Mean age of participants was 36.6 (±13.1) years. Dominant organs of involvement in majority were kidney (n=38,51.4%) and skin (n=10,13.5%). Thirty-eight (51.4%) patients has had at least one infection while 28 (37.8%) has had infections within first 5 years from diagnosis. There were 70 episodes of infections in total and 15 (20.3%) patients had more than one episode of infection. Main systems/ organs affected by infections were respiratory tract (n=23,32.9%), genitourinary tract (n=22,31.4%) and skin (n=13,18.6%). A specific pathogen was identified only in 43 (61.4%) of these infections and out of these tuberculosis (n=8,11.4%) was the causative agent in the majority followed by fungi (n=5,7%). Fifty-nine (84.3%) of these infections required in-patient care while 32 (45.7%) necessitated the use of intravenous antibiotics. Disease flares were seen within 3 months from onset of infection in 18 (25.7%) infection episodes. At the time of infection, 57 (81.4%) were on prednisolone while 37 (52.9%) and 25 (35.7%) were on hydroxychloroquine and azathioprine respectively. [Conclusions] Infection prevalence in this cohort of SLE patients was comparable with that of other developing countries. Respiratory system was the commonest system involved while tuberculosis was the commonest identifiable causative agent.

ICW17-4

Quantitative computed tomography analysis predicts progression to severe illness of pneumocystis pneumonia in patients with connective tissue disease

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Conflict of interest: None

[Objective] Pneumocystis pneumonia (PCP) is a serious infectious disease that can occur in patients with connective tissue disease (CTD). PCP typically presents with ground grass opacity (GGO) and consolidation on computed tomography (CT) imaging, while it remains unclear whether CT findings can predict disease prognosis. We aimed to clarify the relationship between lung imaging and prognosis in PCP patients with CTD by using quantitative CT (qCT). [Methods] This was a single-center retrospective study at Hokkaido University Hospital. Abnormal lung volumes (ALV, %) at the time of PCP diagnosis were automatically calculated by an artificial intelligence-based qCT analysis. GGO and consolidation were defined with a threshold CT value of -300 HU (GGO ≦ -300, consolidation > -300). Intubation, intensive care unit (ICU) admission, and death were defined as critical events (CEs). The association between ALV, laboratory data, and CEs was analyzed by logistic regression analysis and survival analysis. [Results] A total of 28 patients were enrolled, and CEs occurred in 5 patients (17.9%, 5 intubation or ICU admission, 2 death). Consolidation volumes were significantly larger in the CEs group than in the non-CEs group (8.0% vs 1.5%, p=0.005), while GGO volumes were not significantly different (55.1% vs 47.3%, p=0.95). Serum β-D-glucan (p=0.41), KL-6 (p=0.98), and LDH (p=0.08) levels did not show significant differences between the two groups. Logistic regression analysis showed consolidation volumes were associated with the occurrence of CEs (odds ratio=1.29 (1% increments), p=0.028). The hazard ratio for developing CEs was 3.55 (95%CI: 0.59-21.2) for consolidation volume ≧ 2% and 13.05 (95%CI: 2.16-79.1) for ≧ 5%. Mortal events occurred only in cases with consolidation volume ≧ 5%. [Conclusions] In PCP patients with CTD, consolidation volume, but not GGO, was significantly associated with the occurrence of CEs. In particular, consolidation volume ≧ 5% may predict poor prognosis.

ICW17-5

Risk assessment of CT screening in rheumatoid arthritis patients with pulmonary non-tuberculous mycobacterial infection and its contribution to retention of molecular targeted therapy from FIRST registry

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Conflict of interest: None

[Objective] The frequency and characteristics of pulmonary NTM disease (PNTM) in patients with rheumatoid arthritis (RA) requiring induction of biologic and targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD) remain unknown. In this study, we used CT to accurately diagnose PNTM complicated with RA before induction of b/tsDMARD and investigated its frequency and clinical characteristics. [Methods] The study included 4648 RA patients who underwent chest CT imaging before the introduction of b/tsDMARD. The primary endpoint was the frequency of PNTM in RA patients who underwent chest CT. Secondary endpoints included clinical characteristics of patients with PNTM, the retention rate of b/tsDMARD up to 24 months, RA disease activity, and the rate of PNTM relapse. [Results] The CT screening before introducing b/tsDMARD identified 107 patients suspected of PNTM, 33 of whom had PNTM based on positive culture test. The prevalence of PNTM was calculated to be 721/100,000, nearly six times higher than that of the general population in Japan. Out of the 33 cases, 28 showed no symptoms, 14 showed no abnormal findings on plain chest radiographs, and abnormal findings were demonstrated only on CT. In terms of clinical characteristics, PNTM was prevalent among males, older individuals, and those with lower BMI, higher CRP, higher RF/ACPA antibody positivity, and a higher rate of use of b/tsDMARD. In 28 of 33 patients, b/tsDMARD was introduced in combination with antimicrobial agents once the infectious lesions were under control. There was no significant difference in b/tsDMARD retention rate (53.9% vs 63.2%, p=0.38) and CDAI (7.6 (IQR 4.14-15.8) vs. 5.7 (IQR 1.60-13.3), p=0.15) at 24 months between the PNTM and non-PNTM groups. There were no cases of recurrent PNTM. [Conclusion] CT imaging before introducing b/tsDMARD enabled the diagnosis of PNTM, which was asymptomatic and undetectable on plain radiographs.

ICW17-6

Safety and efficacy of the adjuvanted recombinant zoster vaccine in patients with rheumatic disease: a prospective cohort study (Zoster-J)

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Conflict of interest: None

Objective: We investigated prospectively the safety and efficacy of the adjuvanted recombinant zoster vaccine (RZV) in patients with rheumatic disease taking immunosuppressive therapy. Methods: Patients aged≧50 were included. The primary endpoint was safety. Adverse reactions collected for 30 days after each two doses and disease flare compared with and without vaccine. Disease flare was defined as new/switching or increased dose of treatments during 6 months. The secondary endpoint was incidence of herpes zoster (HZ). Vaccine efficacy against HZ was evaluated after completing two doses. Selection bias was adjusted by propensity score-based inverse probability of treatment weighting (IPTW). Results: 124 patients were evaluated either vaccinated (n=74) or unvaccinated (n=50). The variables of age, history of HZ, glucocorticoids and methotrexate usage were balanced between groups. The use of Janus kinase inhibitors was significantly higher (68.9% vs 48.0%, p=0.02) and biologics was significantly lower (24.3% vs 52.0%, p<0.01) in vaccinated group than in unvaccinated group. In 49 patients vaccinated, local adverse reactions occurred in 45/49 (91.8%): pain (85.7%), redness (63.3%) and swelling (71.4%) in median 4 days. Systemic adverse reactions occurred in 35/49 (71.4%): myalgia (61.2%), fatigue (59.2%) and fever (42.9%) in median 2 days. Disease flare of rheumatic disease were reported by 3/61 (4.9%) in vaccinated group and 2/40 (5.0%) in unvaccinated group. During a mean follow-up period of 0.8 years, HZ occurred in 4 vaccinated patients (among them, 2 patients were reported before getting the 2nd vaccine) and in 3 unvaccinated patients. The Hazard ratio (HR) was 0.56 (95%CI, 0.09-3.37; p=0.53) before IPTW adjustment and 0.48 (95%CI, 0.08-2.90; p=0.43)

after IPTW adjustment. Conclusions: Our study did not identify any safety concerns of RZV in patients with rheumatic disease. However, larger and longer observation are required to confirm its efficacy in this population.

ICW18-1

Osteosarcopenia as a predictor of ADL capability in RA patients undergoing rehabilitation - report from convalescence rehabilitation wards

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Conflict of interest: None

[Objective] Prevention of sarcopenia, osteoporosis, osteosarcopenia (OS) and frailty is an urgent issue in order to prevent the need for long-term care and extend healthy life expectancy in anticipation of the era of 100-year lifespan. In patients with rheumatoid arthritis (RA), synthetic glucocorticoids are associated with a 2.6-fold decrease in bone density over 2 years compared to patients without it. OS is said to be a combination of osteoporosis and sarcopenia. According to a report from the ROAD study, people who currently have OS have extremely higher risk of migration to frailty than those with sarcopenia alone or osteoporosis alone. OS has been reported to have a high risk of falls and fractures, while others has reported a small impact. The actual state of OS, including its prevalence, is thus not well unknown. The purpose of this study was to characterize the physique, physical function, and nutritional status of OS in RA patients in convalescent wards and outpatient settings. [Methods] This retrospective study included consecutive RA patients admitted to convalescent rehabilitation wards. To determine which patients had sarcopenia, we used the European Working Group on Sarcopenia in Older People criteria. [Results] In total 58 participants (40 women) were included in this study. (mean age 77.9±8.1 years) In patients with RA, ASR-ESR, HAQ-DI, locomotive degree ≧2, and non-use of MTX were significant predictors of frailty. Participants with OS showed lower FIM-M at discharge than those without this condition (median 72 vs 85, P<0.001). Factors of OS were Low body weight, severe wrist deformity, history of steroid use, and no history of biologics use. [Conclusions] OS appears to be a predictor of how well RA patients can engage in activities of daily living after rehabilitation. The use of biologics in patients with RA to achieve clinical remission and reduce steroid use may improve OS and metabolic abnormalities and significantly improve ADL in RA patients.

ICW18-2

Prediabetes and sulphonylureas increased the risk of major cardiovascular events in patients with inflammatory arthritis: a population based cohort study

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Conflict of interest: None

[Objective] To evaluate the effect of prediabetes and oral hypoglycemic agents on risk of major cardiovascular events (MACE) in patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA). [Methods] This was a population-based retrospective cohort study. Patient identification and data retrieval were conducted using a big-data platform (The Hospital Authority Data Collaboration Lab) in Hong Kong. Patients with the diagnoses of RA or PsA according to the ICD9-CM were recruited from 2006 to 2015 and followed up until end of 2018. Time-dependent Cox proportional hazards regression models were used to analyze the association between the fasting glucose level and use of oral hypoglycemic agents with MACE. [Results] A total of 13,905 patients (12,233 RA and 1,672 PsA) were included. 934 patients (7.0%) developed first MACE after a total of 119,571 patient-years of follow-up. After adjusting for medications, inflammation and other cardiovascular (CV) risk factors, diabetes mellitus (DM) was a independent predictor of MACE. In the subgroup analysis of patients not on any DM medications, the time-varying fasting glucose level of prediabetic state (5.6-6.9 mmol/L) was found to be independently associated with higher risk of MACE (HR 2.43, 95%CI 1.97-2.99). On ther other hand, in patients already on DM treatments, MACE risks were similar between patients with fasting glucose level <5.6 mmol/L and 5.6-6.9 mmol/L. In addition, metformin was found to be protective against MACE after adjusting for covariates (HR 0.73, 95%CI 0.54-1.00); while sulfonylurea was associated with 55% higher risk of developing MACE (HR 1.55, 95%CI 1.14-2.09). [Conclusions] In a large cohort of patients with RA and PsA, prediabetic state and sulphonylureas use were found to be associated with increased risk of MACE. To optimize CV outcomes in inflammatory arthritis patients, close diabetic monitoring with earlier treatments taking into consideration their differential effects on CV risk is recommended.

ICW18-3

Predictors of long-term prognosis in rheumatoid arthritis-related interstitial lung disease

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Conflict of interest: Yes

[Objective] The aim of the study was to identify specific clinical and serum protein biomarkers that are associated with longitudinal outcome of RA-associated interstitial lung disease. [Methods] 60 RA patients with clinical and serological profiles were assessed by HRCT and pulmonary function tests, PFTs, at baseline Year 0 and 5 years post enrollment Year 5. Progression versus non-progression was defined based on changes in Quantitative Modified HRCT scores and PFTs over time. Specific serum protein biomarkers were assessed in serum samples at baseline and Year 5 by Multiplex enzyme-linked immunosorbent assays. [Results] At Year 5, 32% of patients demonstrated progressive RA-ILD, 35% were stable, and 33% improved. Baseline age and rheumatoid factor RF were significantly different between RA-ILD outcomes of progression vs. no-progression, *p less than* 0.05. Changes in levels of CXCL11/I-TAC and MMP13 over 5 years also distinguished pulmonary outcomes, *p less than* 0.05. A final binary logistic regression model revealed that baseline age and changes in serum MMP13 as well as CXCL11/I-TAC were associated with RA-ILD progression at Year 5, *p less than* 0.01, with an AUC of 0.7772. [Conclusions] Collectively, these analyses demonstrated that baseline clinical variables age, and RF, and shifts in levels of selected serum proteins CXCL11/I-TAC and MMP13 were strongly linked to RA-ILD outcome over time.

ICW18-4

A Foe or a Friend? The Dose-Dependent Effect of Systemic Steroid on Cardiovascular Outcome in Rheumatoid Arthritis Patients: a population-based cohort study

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Conflict of interest: None

Objectives: We aimed to study the effect of systemic steroid treatment on rheumatoid arthritis (RA) patients' risk of major adverse cardiovascular events (MACE). By controlling inflammation, steroid may counteract accelerated atherosclerosis, thus we also explored ***whether there existed a CV-neutral dose and duration*** of steroid. Methods: RA patients from 2006-2015, without MACE at baseline, were recruited from a citywide database, and followed till the end of 2018. The primary outcome was the first occurrence of a MACE. Demographics, traditional CV risk factors, data of inflammatory markers and treatment, particularly prednisolone dose and duration, were collected for cox regssion analysis to look for predictors of MACE. Results: Among 12,233 RA patients with 105,826 patient-years of follow-up, 860 (7%) of them developed MACE, with the crude incidence rate 8.13 per 1000-person-years. Systemic steroid was prescribed in 34% of all patients at baseline. Steroid use, together with high levels of inflammatory markers, increased the risk of MACE with a significant adjusted hazard ratio (HR) of 1.7. However, when looking at different steroid doses and durations, daily prednisolone dose of **up to 5 mg,** when used for longer than 3 months, **was NOT found to significantly increase the incidence of MACE** (adjusted HR 0.83, p = 0.3), compared with no steroid. On the other hand, daily dose above 5 mg significantly increased the risk of MACE (adjusted HR 2.02, p < 0.001), regardless of the duration of use. In Kaplan-Miere analysis, the MACE-free survival curve of the group re-

ceiving maximum prednisolone dose of 1-5 mg/day overlapped with the group receiving no steroid. The MACE-free survival of the group receiving steroid for longer than 6 months was also significantly poorer than the groups on shorter duration of steroid. Conclusions: In general steroid increased the risk of MACE in RA patients. However, at daily dose of prednisolone up to 5 mg, it did not increase, if not reduce, the risk of MACE.

ICW18-5

Incidence and risk factors of major cardiovascular events in rheumatoid arthritis and psoriatic arthritis: a population-based cohort study

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Conflict of interest: None

[Objective] To evaluate the incidence and risk factors of major adverse cardiovascular events (MACE) in patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA). [Methods] A population-based retrospective cohort of RA and PsA patients was identified in a citywide database. All patients recruited from Jan 2006 to Dec 2015 were followed until the end of 2018. The outcome was the occurrence of a first MACE. Covariates of interest included traditional cardiovascular (CV) risk factors, inflammatory markers and pharmacotherapies. Time-dependent cox proportional hazard models were used to identify the independent predictors of MACE. [Results] A total of 13,905 patients (12,233 RA and 1,672 PsA) were recruited. After a total of 119,571 patient-years of follow-up, 934 (7.0%) patients developed a first MACE. The adjusted incidence was similar between RA and PsA (incidence rate ratio 0.96, 95%CI 0.75-1.22, p=0.767). After adjusting for traditional CV risk factors, the time-varying erythrocyte sedimentation rate and C-reactive protein levels, and the use of glucocorticoids were independently associated with higher risk of MACE in both the RA and PsA cohorts. In RA, the use of methotrexate, non-selective non-steroidal anti-inflammatory drugs (NSAIDs), and cyclo-oxygenase-2 inhibitors were associated with fewer MACE. The use of biologic disease modifying anti-rheumatic drugs was not associated with MACE in both RA and PsA. [Conclusions] The incidence of MACE was similar in patients with RA and PsA. Systemic inflammation and glucocorticoid use independently increased the risk of MACE in inflammatory arthritis, while methotrexate and NSAIDs use were protective against the development of MACE in RA.

ICW19-1

A comparison of elderly-onset SLE with adult-onset SLE - A nested case-control study of a Singapore cohort

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Conflict of interest: None

Introduction: Elderly-onset systemic lupus erythematosus (SLE) is classically associated with less cutaneous manifestations but more insidious onset; however, there is conflicting literature regarding the outcomes of elderly-onset SLE (EoSLE) as compared to adult-onset SLE (AoSLE). Objective: To compare clinical manifestations, disease activity and outcomes in EoSLE and AoSLE patients in a Singapore cohort. Methods: This is a nested case-control study of EoSLE (50 years and older) and AoSLE (between 18 and 49 years of age) patients from a prospective study cohort conducted in Tan Tock Seng Hospital from 2002 to 2017. Clinical manifestations, disease activity, therapy, end-organ damage and comorbidities at the baseline visit (V0) and the last follow-up study visit (VL) were compared, and the results statistically analysed. Results: 65 EoSLE and 125 AoSLE patients with sufficient information were matched. The prevalence of mucocutaneous features such as malar rash (p<0.001) and oral or nasal ulcers (p=0.002) was significantly higher in the AoSLE group. EoSLE patients had more cardiovascular manifestations (p<0.001) and constitutional symptoms such as weight loss (p=0.009) and fatigue (0=0.001). Accrued organ damage measured by SLICC/ACR index was significantly higher (p<0.001) in EoSLE patients. EoSLE patients had a higher comorbidity burden of hypertension, hyperlipidaemia and osteoporosis (p<0.001 for all). A significantly higher proportion of EoSLE patients received cardiovascular medications and bisphosphonates. More AoSLE patients received antimalarials (p=0.035) and immunosuppressants (p=0.022). Conclusion: We demonstrated differences in presentation and accumulated organ damage between the EoSLE and AoSLE groups. EoSLE patients had similar disease activity, but significantly more comorbidity burden and accumulated organ damage compared to AoSLE. Our observations are in concordance with our other population cohorts.

ICW19-2

Predictive factors for renal outcome during remission induction treatment period in lupus nephritis

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Conflict of interest: None

[Objective] This study aimed to identify predictive factors for renal outcome during remission induction treatment period in lupus nephritis (LN). [Methods] This retrospective single-center observational study comprised 85 patients with LN from 2006 to 2020. Baseline was defined as the day of the initiation of remission induction therapy. Clinical and laboratory data were collected at 0, 2,4, 8, 12, and 52 weeks from the baseline. We defined complete renal remission (CRR) as urine protein creatinine (Cr) ratio (UP) <0.5 g/gCr and an estimated glomerular filtration rate that was no worse than 10% below the preflare value or ≧ 90 ml/min/1.73 m^2 at 52 weeks. [Results] A total of 85 patients were enrolled. Among them, 72 (88%) patients were female and the mean age was 38 years old. Renal biopsy was performed in 76 cases, and 67 (78.8%) patients were diagnosed as having Class III or IV. Nine patients were diagnosed as LN based on significant proteinuria and/or urine sedimentation in the absence of renal biopsy. At 52 weeks, 48 (56.5%) patients achieved CRR. Serum Cr and UP at baseline were not significantly different between CRR and non-CRR groups. The rate of decrease (%) in serum Cr of the CRR group at each period from baseline was significantly higher, and UP at 12 weeks was significantly decreased in the CRR group. Multivariate logistic regression analysis showed that the rate of decrease in serum Cr from baseline to 12 weeks (odds ratio=1.02 (1% increments), p=0.01), UP at 12 weeks (odds ratio=0.71, p=0.02) were identified as independent predictive factors for CRR. Based on ROC curve, UP≦0.8 g/gCr at 12 weeks was considered the best cutoff to predict CRR. [Conclusions] The decrease of serum Cr and UP≦0.8 g/gCr at 12 weeks were independent predictors of CRR. Further intensive treatment would improve the renal outcome in the patients with those predictors.

ICW19-3

Increased mortality in patients with neuropsychiatric lupus: A retrospective cohort study

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Conflict of interest: None

[Objective] Patients with systemic lupus erythematosus (SLE) have a higher risk of neuropsychiatric lupus, which could be fatal. The aim of this study was to identify the prognostic factors for mortality in patients with neuropsychiatric lupus. [Methods] Patients with SLE treated at Chang Gung Memorial Hospital were included in this observational cohort study. This study conducted univariate and multivariate COX regression, as well as Kaplan-Meier survival curve analysis, to investigate mortality risk in SLE patients. [Results] The average age at admission was 40.78 ± 15.92 years. A total of 110 (16.0%) of the 689 SLE patients had neuropsychiatric involvement. Patients with neuropsychiatric lupus shorter follow-up, higher disease activities, and higher incidence rates of comorbidities than patients without neuropsychiatric involvement. Cox regression adjusted analysis indicated that neuropsychiatric lupus (hazard ratio = 2.059, 95% CI = 1.283, 3.302, p = 0.003), old age at admission (HR = 1.052, 95% CI = 1.040, 1.063, p < 0.001), high SLEDAI score (HR = 1.051, 95% CI = 1.013, 1.091, p < 0.001), and end-stage kidney disease (ESKD) (HR = 2.560, 95% CI =

1.648, 3.978, $p < 0.001$) were all linked to increased mortality. Moreover, the Kaplan-Meier survival curve analysis revealed that patients with neuropsychiatric had a higher mortality rate (log-rank test, $p < 0.001$). [Conclusions] A high proportion of SLE patients have manifestations of neuropsychiatric lupus. Moreover, SLEpatients with initial presentation of neuropsychiatric lupus have a greater risk of mortality. Therefore, these patients need prompt diagnosis and treatment.

ICW19-4

Health related quality of life (HRQoL) and its influencing factors in patients with Systemic Lupus Erythematosus attending the Rheumatology clinic at National Hospital of Sri Lanka

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Conflict of interest: None

Objective The aim of this study was to assess the health-related quality of life (HRQoL) and its influencing factors in patients with SLE attending the Rheumatology clinic at National Hospital of Sri Lanka. **Methods** A cross sectional study was conducted and patients who had been diagnosed with SLE according to 2012 EULAR/ACR criteria with a disease duration of more than six months were recruited. The study instrument consisted of a self-administered SF 36 questionnaire and an interviewer administered questionnaire consisting of three parts; SLEDAI 2k 30-day score, SLICC damage index and sociodemographic data. Descriptive statistics, Pearson Correlation- Coefficient test and Student T Test were used for data analysis. **Results** A total of 60 participants were selected which had a female predominance (98.3%), a mean age of 36.15yrs (+/- 12.96) with the mean disease duration being 6.01 yrs. Majority had low disease activity (76.7%) with a mean SLEDAI score of 5.08 and mean SLICC damage index of 1.4. Out of the eight domains of SF36 health related quality of life (range 0-100; higher scores indicate better function), the lowest value was in the general health domain (mean 45.36), while the highest was in social well-being domain (74.01). The physical health component summary (56.59) was lower than that of the mental health component summery (65.69). Patients with low disease activity scored significantly lower values ($p< 0.05$) for all eight domains and the two summary components, compared to patients with active disease. Physical and mental summary components had a correlation with age (r= -0.48, -0.40), ESR (r= -0.38, -0.39) as well. **Conclusions** The disease has a negative impact on the quality of life of patients with SLE and a high disease activity causes a significant reduction in all aspects of HRQoL. Thus, actively assessing the quality of life in SLE patients, specially those who have above risk factors and managing accordingly will help to improve the overall patient outcome.

ICW19-5

Hydroxychloroquine dose and continuation rate in systemic lupus erythematosus

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) is an essential drug in the treatment of systemic lupus erythematosus (SLE). Although the efficacy of HCQ has been established in studies with a dose of 6.5 mg per ideal body weight, it has been recommended to administer at a dose of 5 mg or less per actual body weight to reduce the risk of retinopathy. This study aimed to clarify the effect of HCQ dose on its continuation rate in Japanese patients. [Methods] This retrospective single-center observational study enrolled patients with SLE on HCQ. Patients were followed up from the initiation of HCQ until the discontinuation or the last visit. First, the risk factors for the discontinuation of HCQ were evaluated by Cox regression analysis. Second, patients were classified into two groups with a threshold of 5 mg per actual body weight (low-dose group and high-dose group), and continuation rates were compared. Finally, to evaluate the efficacy of HCQ, clinical information was assessed on the day of initiation and after one year between low-dose and high-dose groups in patients without additional immunosuppressive drugs. [Results] A total of 231 patients were enrolled, and 48 (20.8%) discontinued HCQ after a median of 2 (IQR 1-41) months. The one-year continuation rate was 80.1%. In a multivariate Cox regression analysis, dose per actual body weight was identified as an independent risk factor for discontinuation (HR=1.29 [1.02-1.62], $p<0.05$). The low-dose HCQ group had a significantly higher continuation rate than the high-dose group (one-year continuation rate; 83.2% vs. 72.8%, respectively, $p<0.05$). The levels of complement, anti-dsDNA antibodies, and glucocorticoid dose significantly decreased one year after initiation of the HCQ in both low-dose and high-dose groups ($p<0.05$). [Conclusions] In Japanese patients, generally with a lower body mass index than Western patients, HCQ at 5 mg or less per actual body weight may provide greater continuation to high-dose therapy.

ICW19-6

High chronicity index of the modified NIH (National Institute of Health) scoring system of lupus nephritis is associated with increased risk of end-stage kidney disease: a retrospective single-center study

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Conflict of interest: None

[Objective] Revision of ISN/RPS (International Society of Nephrology/ Renal Pathology Society) classification was suggested by a working group of for lupus nephritis classification, and modified NIH (National Institutes of Health) activity and chronicity scoring system was recommended to evaluate active and chronic lesions of lupus nephritis in all classes. It is still unclear whether this modified NIH scoring system is useful to estimate prognosis of lupus nephritis patients. [Methods] We conducted a retrospective cohort study in Japanese subjects with biopsy-proven LN, between 1977 and 2022. Pathologic lesions were evaluated based on ISN/RPS 2003 classifications and the modified NIH scoring system. Patients were grouped by activity index (low, 0-5; moderate, 6-11; high, 12-24), and chronicity index (low, 0-2; moderate, 3-5; high, 6-12). The primary outcome was a composite of end-stage kidney disease (ESKD) or all-cause death. [Results] Seventy subjects with a median age of 31 years were included. Median follow-up period was 11.3 years. For the activity index, multivariable analysis adjusted by age and serum creatinine did not show any significant relationship for the primary outcome. For the chronicity index, multivariable analysis, adjusted by age and serum creatinine revealed that moderate (HR 6.18, 95% CI 1.15 to 33.3; $p = 0.034$) and high chronicity indices (HR 20.33, 95% CI 1.14 to 360.50; $p = 0.04$) were significant risk factors for the primary outcome. Among the components, global sclerosis was a significant risk factor for the primary outcome. [Conclusions] Moderate and high chronicity indices were associated with an increased ESKD and death risk for LN. This modified NIH activity and chronicity scoring system may help physicians predict long-term prognosis for patients with lupus nephritis.

ICW20-1

Investigation of poor prognostic factors in patients with asymptomatic dermatomyositis

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Conflict of interest: None

[Objective] To predict factor related to mortality and poor functional prognosis in clinically amyopathic dermatomyositis (CADM) patients. [Methods] CADM patients diagnosed and treated with remission induction therapy in our institute from 2013 to 2021 were enrolled. Death due to respiratory failure or initiation of home oxygen therapy (HOT) were defined as end-stage lung disease (ELD). Clinical information at diagnosis associated with ELD were analyzed retrospectively by logistic regression analysis. [Results] We enrolled 31 CADM patients with 24 females (77%). Median age [interquartile range] 57 [47, 67] years, anti-MDA5 antibody

(Ab) positive in 25 patients (81%) and anti-ARS Ab positive in 4 patients (13%). Among the 27 patients (87%) with interstitial lung disease (ILD), rapidly progressive (RP) ILD was observed in 17 patients (55%) and, 8 patients (26%) had a smoking history. Serum KL-6 and ferritin at diagnosis were 768.65 ± 523.90 (mean ± SD) U/ml and 490.65 ± 609.41 ng/ml, respectively. ELD was observed in 10 patients with 8 patients with death due to respiratory failure and 2 patients initiated HOT. All patients with ELD were females, anti-MDA5 Ab positive and had RP-ILD. Analysis to predict ELD revealed baseline age, anti-MDA5 Ab titer and serum albumin level as significant predicting factors (OR 1198;95% CI 0.04-0.21, p=0.01, OR 50;95% CI 0.0002-0.001, p=0.01 and OR 0.027;95% CI -3.28- -0.32, p=0.03). Cut-off value of each predicting factor was 61 years old, 3100 U/ml, and 3.1 mg/dl. Possession of more than 2 of these factors increases the likelihood of ELD by 75% or more. [Conclusions] Our results demonstrated that age, high anti-MDA5 Ab titer and low serum albumin level at diagnosis as poor prognosis in CADM. Moreover, accumulation of related factors increases the incidence of ELD.

ICW20-2

Characterization of circulating microvesicles in patients with idiopathic inflammatory myopathies reveals relationship with IIM phenotype and treatment response

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Conflict of interest: None

[Objective] Few biomarkers are currently available for monitoring of idiopathic inflammatory myopathies (IIM). Microscopic extracellular vesicles (mEVs) are small lipid-bilayer particles involved in modulation of immune response. We aim to investigate correlates between plasma mEVs and clinical and laboratory features of IIM. [Methods] Adult IIM patients and age-/sex-matched healthy controls (HD) were included. mEVs were isolated through size exclusion chromatography and ultra-filtration. Particles morphology, concentration and surface marker characterization were assessed via transmission electron microscopy, nanoparticle tracking analysis and imaging flow cytometry respectively. Data were cross-sectionally analyzed; parametric Student-t test and one-way ANOVA with Bonferroni correction was used. [Results] We included 45 IIM patients and 45 HD. The specific IIM diagnosis was identified. 39 (86.7%) patients were receiving glucocorticoids and/or immunosuppressants at the time of blood sampling. Immunophenotyping revealed a significantly increased proportion of CD19+ mEVs, indicating a likely B cell origin. IIM patients displayed significantly increased mEV concentrations compared to HD (mean± SD [mEVs/mL], $1.95x10^{10}$±$1.47x10^{10}$ vs. $1.45x10^{10}$±$7.82x10^{9}$, p=0.025). mEVs concentrations were significantly higher in treatment-naïve patients and decreased upon treatment. Patients with IIM onset less than 6 months displayed higher circulating levels of mEVs ($3.20x10^{10}$±$2.42x10^{10}$ vs. $1.80x10^{10}$±$1.80x10^{10}$, p=0.042), as did seropositive patients against seronegative ($2.09x10^{10}$±$1.63x10^{10}$ vs. $1.49x10^{10}$±$0.43x10^{10}$, p=0.063). Cancer associated myositis patients displayed the highest levels of circulating mEVs. [Conclusions] Circulating, B cell-derived mEVs are significantly increased in IIM, especially in recent-onset, seropositive, treatment-naïve disease. Our findings reinforce the potential role of mEVs as biomarkers for early diagnosis, treatment response and disease monitoring in IIM.

ICW20-3

Impact of remission induction therapy on long-term outcomes of anti-MDA5-positive dermatomyositis with interstitial lung disease: Comprehensive analysis of long-term follow-up of a multicenter clinical trial and a single-center retrospective cohort

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) accompanied by anti-melanoma differentiation-associated gene 5 (MDA5)-positive dermatomyositis (DM) often progresses rapidly and takes poor prognostic outcomes. Recently, we reported the efficacy of combination therapy with high-dose glucocorticoid (GC), calcineurin inhibitor (CNI) and intravenous cyclophosphamide (IVCY) in the multicenter clinical trial (UMIN000014344). However, there is no evidence of their management during remission maintenance phase. In this study, we evaluated their long-term outcomes and the effect of induction therapy on remission maintenance. [Methods] All the participants in our previous trial were observed for more than 5 years and analyzed. Moreover, we retrospectively enrolled another consecutive 73 anti-MDA5-positive adult DM-ILD patients in our institute from 2001 to 2022 and combined them with the trial participants for further analysis. 68 patients in total had achieved remission and survived more than 6 months. According to the induction treatment, we classified the patients into 2 groups, Group T (n=56); triple combination therapy (GC, CNI and IVCY) and Group C (n=12); mono/dual-therapy (GC with or without CNI). We compared the recurrence-free rate and drug-withdrawal rates of immunosuppressive agents after treatment initiation. [Results] The overall survival and the recurrence-free survival at 5 years were 100% for the participants in the previous trial. The 5-year cumulative withdrawal rates of CNI and GC were 70% and 53%, respectively. In the comprehensive analysis, the recurrence-free rates of Group T were significantly higher than Group C (90% vs. 56%, p=0.021). In addition, drug-withdrawal rates of CNI and GC at 10 years in Group T was significantly higher than in Group C (79% vs. 0%, 43% vs. 0%, respectively, p<0.05). [Conclusions] Triple combination therapy at induction phase can reduce the risk of recurrence and facilitate drug-withdrawal in anti-MDA5-positive DM-ILD.

ICW20-4

Autoimmune multimorbidity and fatigue in women with idiopathic inflammatory myopathies: results from the international COVAD patient-reported e-survey

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Conflict of interest: Yes

Objective: Little has been reported about the potential effect of gender on clinical outcomes in patients with idiopathic inflammatory myopathies (IIMs). We aimed to investigate gender differences in treatments, disease activity, and patient-reported outcomes (PROs) of IIM patients utilizing data obtained in the COVID-19 vaccination in autoimmune disease (COVAD) study, an international self-reported e-survey assessing the safety of COVID-19 vaccination in patients with autoimmune diseases (AIDs). **Methods:** The survey data regarding demographics, corticosteroid or immunomodulatory agent use, disease activity, and PROs including fatigue and pain VAS, PROMIS Short Form - Physical Function 10a was extracted from the COVAD database and compared between women and men. Factors affecting disease activity and each PRO were determined by multivariable analysis. **Results:** 1197 responses from IIM patients obtained between April and August 2021 were analysed. 845 (70.6%) were women. Women were younger, and more likely to suffer from autoimmune multimorbidity, defined as three or more AID diagnoses for each patient (94/845 [11.1%] *vs* 11/352 [3.1%], P0.0001). In patients with IIMs other than inclusion body myositis, disease activity and corticosteroid use were comparable in both genders, whereas immunomodulatory agent use was different, with more hydroxychloroquine use in women (131/717 [18.3%] *vs* 11/159 [6.9%], Bonferroni P = 0.0082). The median fatigue VAS was significantly higher in women (5 [IQR 3-7] *vs* 4 [IQR 2-6], P = 0.036), while the other PROs were comparable. The multivariable analysis revealed women, residence in high-income countries, overlap myositis, and autoimmune multimorbidity as independent factors for higher fatigue VAS. **Conclusion:** Women with IIMs frequently suffer from autoimmune multimorbidity and experience increased fatigue compared to men, calling for greater attention and further research on targeted treatment approaches.

ICW20-5

High fatigue scores in patients with idiopathic inflammatory myopathies: a multigroup comparative study from the COVAD e-survey

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Conflict of interest: None

Introduction: A diagnosis of idiopathic inflammatory myopathies (IIMs) confers a risk of disability and poor quality of life, potentially contributed by multiple factors including fatigue, though fatigue is not systematically reported in these individuals. Methods: We compared visual analog scale (VAS) scores (0-10 cm) for fatigue (VAS-F) in patients with IIMs, non-IIM systemic autoimmune diseases (SAIDs) and healthy controls (HCs) using data from the international patient self-reported COVID-19 Vaccination in Autoimmune Diseases (COVAD) e-survey, from December 2020 to August 2021. Determinants of fatigue were analyzed in regression models. Results: 6,988 respondents (mean age 43.8 years, 72% female; 55% White) were included in the analysis. The overall VAS-F score was 3 (IQR 1-6). Patients with IIMs had similar fatigue scores (5, IQR 3-7) to non-IIM SAIDs [5 (IQR 2-7)], but higher compared to HCs (2, IQR 1-5; $P<0.001$), regardless of disease activity. In adjusted analysis, higher VAS-F scores were seen in females (Reference Female; coefficient -0.17; 95%CI: -0.21to-13; $P<0.001$) and Caucasians (Reference Caucasians; coefficient -0.22; 95%CI: -0.30 to -0.14; $P<0.001$ for Asians and coefficient -0.08; 95%CI: -0.13 to 0.30; $P=0.003$ for Hispanics) in our cohort. Conclusions: A diagnosis of IIMs confers an equal risk of fatigue as other SAIDs, with females and Caucasians at a greater risk. This is an aspect of disease that is underreported and not at the forefront of patient care.

ICW20-6

The novel autoantibodies against transcription factor SP4 play an important role for reducing cancer risk in Polymyositis/Dermatomyositis patients

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Conflict of interest: None

[Objective] The strong association between Polymyositis/Dermatomyositis (PM/DM) and malignancy had been well reported. The decision of treatment and prognosis are affected by complications, thus careful screening for malignancy at the diagnosis of PM/DM is essential. Recently, authors reported a new autoantibody (Ab) against transcription factor Sp4 (anti-SP4) which specific to PM/DM. However, whole clinical feature of anti-SP4 Ab in PM/DM is still unclear. Thus, we investigated the role of anti-SP4 Ab for screening of malignancy in PM/DM patients. [Methods] Adult Japanese IIM patients (N=185) who were treated at Tokai University hospital from 2012 to 2022 and healthy controls (N=15) were enrolled. Anti-ARS, SRP Ab were screened by RNA-immunoprecipitation and anti-MDA5, Mi-2, HMGCR, Ku and TIF-1 Ab were detected by immunoprecipitation with [35S] methionine-labeled HeLa cells. Anti-SP4 was detected by immunoprecipitation and confirmed using Immunoprecipitation using [35S]-labelled in vitro transcription/ translated (IVTT) method. Anti-SP4 Ab titers were measured using an enzyme-linked immune absorption assay. Clinical data was retrospectively collected. [Results] 58% with anti-synthetase, 19% anti-MDA5, 15% anti-TIF, 4% anti-SRP, 2% anti-Mi-2, 1% anti-HMGCR and Ku, and 2% negative for any known Abs. Anti-Sp4 Ab was most often detected in 19% in anti-TIF, and 9% with anti-ARS, 3% with anti-MDA5 Ab and 0.3% in negative for MSAs, respectively. Interestingly, only 1 patient had cancer history and among anti-TIF1γ-positive DM patients, none except 1 of patients with coexisting anti-Sp4 had cancer, while 73% of those without anti-SP4 had ($p<0.05$). [Conclusions] In our investigation, anti-SP4 Ab were often co-detected with MSAs, especially with anti-TIF1 Ab. Detection of anti-SP4 Ab indicated significant reduction of the risk of malignancy. Screening for anti-SP4 Ab is strongly recommended for PM/DM patients.

ICW21-1

Clinical Profile of Gout Patients Admitted During the COVID-19 Pandemic: A Cross-Sectional Analytical Study

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Conflict of interest: None

Background Gout impacts the course of hospitalized patients - certain clinical profiles and factors contribute to the development of in-hospital flares and increase the duration of hospital stay. This study reviews the most common admitting diagnosis of gout patients and explores predictors for in-hospital flare. **Methods:** This cross-sectional analytical study evaluated all patients with gout who were admitted to East Avenue Medical Center from March 2020 to December 2021. Medical records were reviewed for demographic data, admitting diagnoses (including COVID-19 status), co-morbid conditions, and occurrence of in-hospital flares. Mortality, length of hospital stay, and predictors of in-hospital flares were also determined from the chart review. **Results:** 85 adult patients with gout were admitted during the observation period. Upper gastrointestinal bleeding was the most common admitting diagnosis in 38.82% of gout patients while cardiovascular disease was the most frequent co-morbid condition in the cohort. 64.7% of included patients experienced an in-hospital flare. Placing the patient on non per orem (NPO) was the most common predictor for a flare. Patients diagnosed with gout prior to admission and those with tophi were less likely to experience a flare. There was no difference in mortality rates between patients who had an in-hospital flare and those who did not. **Conclusion:** Gastrointestinal disease was the most common admitting diagnosis for gout patients admitted during the COVID-19 pandemic. Majority of admitted gout patients will have an in-hospital flare, which was related to states of dehydration or volume loss - emphasizing the need to monitor for these predisposing factors.

ICW21-2

Clinical profile and blood uric acid levels of gout patients admitted at St Lukes Medical Center on year 2021

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Conflict of interest: Yes

[Objective] The aim of this study is to determine the co morbidities and Blood Uric acid level of inpatients with Gout arthritis admitted in St Lukes Medical Center Global city and Quezon City on year 2021. [Methods] A retrospective audit was undertaken on inpatients in which gout was coded as a primary or secondary diagnosis in St Lukes Medical Center Global City and Quezon City on Year 2021. Co morbidities and level of uric acid were recorded. Chart review were performed to get a more detailed information on the co morbidities and Level of uric acid of patients who were referred to Rheumatology service. [Results]: Of 61 inpatients with gout referred to rheumatology service on year 2021, 41 are known Hypertensive 17 patients are known diabetic, 13 patients are known case of chronic gout. 10 patients are known ckd. Among inpatients referred to rheumatology, 11 patient have hyperuricemia. 35 patients have normal blood uric acid during attack, 15 inpatients have no requested uric acid during attacks. [Conclusions] We have identified co morbidities of inpatients referred to rheumatology service during acute attacks. By addressing and treat co morbidities of these patients might prevent acute gout attack. Urate lowering therapy maybe inadequate for patients with known gout. Optimization of ULT maybe needed for prevent flares.

ICW21-3

The association between serum uric acid level s and handgrip strength in Korean population: nationwide study

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Conflict of interest: None

[Objective] Serum uric acid levels and handgrip strength were each associated with various diseases, including cardiovascular and musculoskeletal diseases. We investigate the association of serum uric acid level with handgrip strength in Korean population. [Methods] Data from 2016 to 2019 were collected from the Korea National Health and Nutrition Examination Survey. A total of 22,900 eligible participants were included (10,214 men and 12,686 women). Handgrip strength was defined maximal absolute handgrip strength from both hands divided by body mass index. Serum uric acid levels were divided into tertiles based on their distribution: ≦5.2, 5.3-6.2, and ≧6.3 mg/dL in men and ≦3.9, 4.0-4.6, and ≧4.7 mg/dL in women. As confounding factor, age, body mass index, smoking status, alcohol consumption, physical activity, hypertension, diabetes mellitus, cardiovascular diseases, arthritis and household income level were sequentially adjusted. We used multiple linear regression analysis and calculated 95% confidence intervals (CIs). P value <0.05 was considered statistically significant. [Results] Mean serum uric acid level was 5.91±1.33 mg/dL in men and 4.45±1.03 mg/dL in women. After adjusting confounding factors, the coefficients β (95% CI) for respectively was 1.627 (95% CI 0.937-2.317) in men and 0.693 (95% CI 0.605-0.701) in women respectively. [Conclusions] Serum uric acid level is significant associated with handgrip strength in Korean population. Especially in men, the higher the serum uric acid level, the stronger the handgrip strength.

ICW21-4

Quality of life in patients with gout on xantine oxidase inhibitors therapy

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Conflict of interest: None

Objectives: to evaluate the dynamics of the QoL in pts, taking ULD, who have achieved and have not achieved the target sUA level. **Methods**: 98 pts with gout were included in the prospective study. The follow-up period was 24 months, allopurinol or febuxostat at doses sufficient to achieve the target sUA level (<360 μmol/l) were used. The maximum daily dose of allopurinol - 900 mg, febuxostat - 120 mg. Pts who did not achieve the target sUA level continued taking ULD at the maximum dosages. The values of the Qol in dynamics were calculated using the SF-36v2 questionnaire. The assessment of the QoL was carried out separately in pts who achieved and did not achieve the target level of sUA. **Results**: 69 of 98 (70%) pts achieved the target sUA level, wherein allopurinol was taken by 46 pts, febuxostat - 34 pts. Pts who achieved the target level of sUA after 6 mo. of ULD usage, demonstrated a significant improvement in the physical health (PH), including physical functioning (PF), role limitations due to physical functioning (RP), general health (GH), as well as vitality (VT) ($p<0.05$ for all). After 12 and 24 mo. improvement was achieved in RH, GH and PF ($p<0.01$), RP, bodily pain intensity (BP) and VT ($p<0.05$). General mental health (MH), role-emotional functioning (RE) and social functioning (SF) were unchanged throughout the study. Pts who did not achieve the target sUA level after 6 and 12 mo. significantly improved: PF, RP ($p<0.05$ for all). After 24 months, for all QoL parameters, the values did not differ from the initial ones. **Conclusion**: The QoL in gout pts who achieved target sUA level continues to improve during the first year of ULD intake. Even if the target sUA level is not achieved, the QoL of patients with gout treated with ULD remains stable for at least 2 years of therapy. This predetermines the need to use maximum daily doses of ULD, even if the target serum UA level is not achieved.

ICW22-1

Identifying Risk Factors associated with the Development of Cardiovascular Events in an Asian cohort of Systemic Erythematosus Lupus patients

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Conflict of interest: None

Objective: To determine the risk factors associated with the development of cardiovascular events (CVE) in a cohort of Systemic Lupus Erythematosus (SLE) patient of Asian ethnicity in Singapore. **Method**: We analysed patients in the prospective Tan Tock Seng Hospital (TTSH) SLE cohort during the period 2002 to 2017. Patients without prior CVE at baseline visit (V_0) who subsequently developed CVE during the follow-up

were identified from this registry. Clinical information on traditional, SLE-associated, and treatment-associated risk factors were collected at baseline and at follow up. Predictors associated with development of CVE were analyzed using Chi-squared test and student's t test. **Results**: Out of 1000 patients recruited, 132 were excluded due to prior CVE before V_0 and/ or withdrew consent. Of the remaining 868 patients, 42 (4.8%) developed a CVE (16 angina/ acute myocardial infarction/ ischemic heart disease, 17 cerebrovascular accidents, 11 arterial thrombosis/peripheral vascular disease) after a median (Interquartile range IQR) time of 6.18 (2.70 - 9.13) years. Of those who developed CVE, the median (IQR) age of SLE diagnosis was 34.75 (25.89 - 44.95) years and median (IQR) SLE duration was 10.66 (4.31 - 15.45) years before CVE onset. The risk factors for development of CVE ($p<0.05$) include onset of SLE at an older age, longer disease duration, longer exposure to corticosteroids, less usage of hydroxychloroquine, presence of hypertension, hyperlipidemia, antiphospholipid syndrome and lower creatinine clearance at time of enrolment into the study. **Conclusion**: Besides traditional risk factors, age, disease duration and corticosteroid use are predictors of CVE in this prospective study. The use of hydroxychloroquine appear to be protective.

ICW22-2

Risk factors for cardiac involvement in idiopathic inflammatory myopathies

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Conflict of interest: None

[Objective] The aim of this study is to investigate the clinical characteristics and risk factors for cardiac involvement in idiopathic inflammatory myopathies (IIMs). [Methods] We retrospectively reviewed patients with IIMs who visited Keio University Hospital from 2002 to 2022. We divided patients into two groups according to the presence of symptomatic cardiac involvement and compared their clinical characteristics. We defined symptomatic cardiac involvement as the presence of chest pain, palpitation, leg edema, or respiratory distress with abnormal findings of cardiac examinations. [Results] We included 146 patients with IIMs. The mean age at disease onset was 55 years old, and 71.9% were female. Thirty-eight patients were polymyositis (26.2%), dermatomyositis in 92 (63.3%), immune-mediated necrotizing myopathy in 8 (5.5%), and anti-aminoacyl tRNA synthetase antibody syndrome in 7 (4.8%). Among them, 52 patients (35.6%) had abnormal findings on electrocardiography, echocardiography, and/or cardiac MRI, and 17 (11.6%) were diagnosed with symptomatic cardiac involvement. Multivariable analysis identified Raynaud's phenomenon (odds ratio [OR] 8.20, 95% confidence interval [CI] 2.10-32.02, p=0.003) and elevated neutrophil/lymphocyte ratio (OR 7.63, 95% CI 1.96-29.75, p=0.003) as independent risk for symptomatic cardiac involvement. There were no significant differences between the two groups in the positivity and types of autoantibodies, IIMs subtypes, presence of skin rash, malignancy, interstitial lung disease, history of cyclophosphamide use, and levels of CK, aldolase, CK-MB, troponin T, and CRP. During the observation period of 20 years, one patient died of cardiac involvement. [Conclusions] It is important to carefully examine cardiac involvement, especially in patients with Raynaud's phenomenon and elevated neutrophil/lymphocyte ratio.

ICW22-4

Safety and effectiveness of tacrolimus during pregnancy in patient with systemic lupus erythematosus: retrospective study in two Japanese tertiary referral centers

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Conflict of interest: None

[Objective] Tacrolimus (Tac) is widely used in the care of systemic lupus erythematosus (SLE), and it is compatible to use during pregnancy. However, its use is sometimes related to the endothelial damage. In terms of the pregnancy care, endothelial dysfunction causes adverse pregnancy outcomes (APO) including hypertensive disorders of pregnancy (HDP), pre-eclampsia, thus Tac use during pregnancy has a possibility to raise the frequency of APOs. Since there are limited data on Tac use during pregnancy, we conducted this study. [Methods] Patient with SLE who was followed up at two Japanese tertiary referral centers were included in our study. We divided the patients into two groups according to the use of Tac during pregnancy and analyzed the occurrence of HDP, pre-eclampsia and PROMISSE APO. [Results] A total of 123 pregnancies were included in the study and 28 pregnancies were treated with Tac. There were no difference in the BMI, age at conception, history of hypertension/ HDP. In regard to the organ manifestation, lupus nephritis (LN) and LN class III/IV were more common in pregnancies on Tac. (Tac vs not on Tac: LN: 53.6% vs 16.8%, p<0.001, LN class III/IV: 21.4% vs 5.3%, p=0.02) In addition, patients on Tac are more likely to be on immunosuppressant except Tac. (82.1% vs 36.8%, p<0.01) Though, pregnant on Tac tended to suffer from HDP, preeclampsia, no statistical differences were noted, (HDP: 25.0% vs 13.7%, p=0.16, preeclampsia: 10.7% vs 5.3%, p=0.16) and occurrence of PROMISSE APO did not differ between the two groups. (26.9% vs 23.3%, p=0.80) We reconfirmed this data by analyzing with logistic regression model which showed no difference between the two groups in each APOs (HDP: OR 2.1, 95% CI 0.75-5.9, p=0.16, preeclampsia: OR 2.16 95% CI 0.48-5.9 p=0.31, PROMISSE APO: OR 1.2, 95% CI 0.45-3.2 p=0.71) [Conclusions] Tac use during pregnancy did not show any significant increase in the HDP, preeclampsia, and PROMISSE APO so its use during pregnancy is acceptable.

ICW22-5

Risk Factors for Mortality in Patients with Rheumatoid Arthritis-associated Interstitial Lung Disease: A Single-center Prospective Cohort Study

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Conflict of interest: None

[Objective] To determine risk factors for mortality in patients with rheumatoid arthritis (RA) associated interstitial lung disease (ILD) in Korea [Methods] Data were extracted from a single-center prospective cohort for RA patients with ILD established in May 2017 in an academic referral hospital in Korea. Patients with RA-ILD enrolled between May 2017 and March 2022 were selected, and RA patients without ILD enrolled during the same period were selected as comparators. Mortality rate was calculated and causes of each death were investigated. We used Firth's Poisson regression model to identify risk factors for mortality in RA patients. [Results] A total of 610 patients were included: 198 RA-ILD patients and 402 RA-nonILD patients. There were nine deceased cases in the RA-ILD group during 370.7 person-years (PYs), and mortality rate was 24.3/ 1,000PYs. There was no deceased case in the RA-nonILD group during 1187.0 PYs. The most common cause of death was infection (5 cases), followed by lung cancer (3 cases). Only one patient was deceased due to aggravation of ILD. After adjusting for confounding factors, old age (incidence rate ratio [IRR] 1.09, 95% confidence interval [CI] 1.01-1.19), high RA activity (IRR 1.89, CI 1.15-3.11) and baseline forced vital capacity (FVC) <80% of predicted (IRR 4.16, CI 1.00-17.27) were identified as risk factors for mortality in RA-ILD patients. Computed tomography pattern was not associated with mortality risk in this study. [Conclusions] Patients with RA-ILD were at increased risk of mortality compared with RA-nonILD patients. The main cause of death was infection, and identified risk factors for mortality were age, disease activity of RA and baseline FVC in patients with RA-ILD.

ICW22-6

Pregnancy Outcomes Associated with Biologic Agent Exposure in Patients with Immune-mediated Inflammatory Diseases

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Conflict of interest: None

[Objective] This study aimed to analyze pregnancy outcomes based on biologic agents use in women with Immune-mediated Inflammatory Diseases (IMIDs) using the nationwide population-based database. [Methods] The study used the Korean National Health Insurance Service claims database to identify women of childbearing age with IMIDs (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, juvenile idiopathic arthritis, Crohn's disease, and ulcerative colitis) who had pregnancy-related codes between January 2010 and December 2019. We analyzed live births and adverse pregnancy outcoms based on the previous use of biologics. We also stratified the patients according to duration of biologic agent exposure before pregnancy and the use of biologics during pregnancy to analyze the pregnancy outcomes by subgroups. [Results] We identified 4,787 IMIDs patients with pregnancy events. Among them, 1,034 (21.6%) used biologics before pregnancy. Live birth rate was not different between the biologics group and biologics never-user group (75.0% vs. 75.2%). Multivariate analyses also showed that biologics use was associated with higher risk of intrauterine growth retardation (odds ratio [OR] 1.780), cesarean section (OR 1.183) and lower risk of gestational diabetes mellitus (OR 0.776) compared with biologics never-user. Biologics use during pregnancy was associated with higher risk of preterm delivery (OR 1.859), preeclampsia/eclampsia (OR 1.762), intrauterine growth retardation (OR 3.487), and cesarean section (OR 1.877), and lower risk of fetal loss (OR 0.274) compared with biologics never-user. [Conclusions] There was no difference in live birth rate between the biologics group and biologics never-user group. However, biologics use during pregnancy were associated with a risk of adverse pregnancy outcomes. IMID patients with biologics during pregnancy need to be carefully observed for adverse pregnancy outcomes.

ICW23-1

Evaluation of changes in antiphospholipid antibody titers following vaccination with COVID-19 mRNA in patients with antiphospholipid syndrome

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Conflict of interest: None

[Objective] The aim of this study is to evaluate the change of antiphospholipid antibodies (aPL) titers and the potential risk of thrombosis following SARS-CoV-2 mRNA vaccination in patients with antiphospholipid syndrome (APS). [Methods] This study comprised patients with primary APS (PAPS), APS associated with systemic lupus erythematosus (SLE/APS), SLE with positive aPL (SLE/aPL+), and SLE without aPL (SLE/aPL-). All enrolled patients received the second doses of SARS-CoV-2 mRNA vaccine. Serum anti-cardiolipin antibodies (aCL IgG, IgM) and anti-b_2GPI antibodies (ab$_2$GPI IgG, IgM) were detected by chemiluminescent immunoassay (CLIA, cut-off: > 20.0 U/mL), and anti-phosphatidylserine/prothrombin complex antibodies (aPS/PT IgG, IgM) were tested using an in-house enzyme-linked immunosorbent assay (ELISA, cut-off: >1.2 U/mL for aPS/PT IgG and >5.2 U/mL for aPS/PT IgM). aPL was evaluated before the first dose and four weeks after the second dose and "aPL positive" was defined according to the classification criteria. "Notable increase" of aPL titers was defined either more than 50% or newly positive after vaccination. Anti-SARS-CoV-2 spike protein antibody (S-IgG) (cut-off: >20 BAU/mL) was also tested. We observed patients for three months for the development of thrombosis after the second vaccination. [Results] A total of 118 patients were enrolled with 79 aPL-positive (19 PAPS, 25 SLE/APS, 35 SLE/aPL+) and 39 aPL-negative (SLE/aPL-). S-IgG was positive in 91 (77.1%) patients after vaccination. The rate of "notable increase" of aPS/PT IgG in aPL positive (13.9%) was significantly higher than that in aPL negative (2.6%) (p=0.047). No differences were observed in the titers of the other aPL. No acute thrombotic events were detected during the observation period. [Conclusions] aPS/PT IgG elevated after SARS-CoV-2 mRNA vaccination in some aPL positive patients, suggesting the importance of paying attention to the thrombosis after vaccination in aPS/PT positive patients.

ICW23-2

COVID-19 Vaccine Safety during Pregnancy and Breastfeeding in Women with Idiopathic Inflammatory Myopathies: Results from the COVAD Study

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Conflict of interest: None

Objectives: Patients with idiopathic inflammatory myopathies (IIM) are at high-risk for pregnancy adverse events (AE) and disease flares (DF) during and after pregnancy. We aimed at describing COVID19 vaccination (V) safety in pregnant/breastfeeding IIM from the ongoing multicentre 2nd COVID-19 Vaccination in Autoimmune Diseases (COVAD) study. **Methods:** We analysed the long-term (>7 days) V-related AEs, post-vaccination DF, COVID-19 infections, in 6 fully vaccinated pregnant/breastfeeding IIM. **Results:** Among complete responses from 9201 patients (pts), 6787 (73.8%) were women; 70 (1.1%) and 99 (1.5%) were pregnant and breastfeeding at the time of V, respectively. Of these, 6 women with IIM [age 28-38 yrs] were vaccinated during pregnancy (5/6) or breastfeeding (1/6). Half of them were of African descent and had associated comorbidities. Two of three patients with active disease experienced major V-AE, though reassuringly none were hospitalised. None of the pts with inactive disease reported any major AE. Notably, all women reporting major V-AE had

prior COVID-19. Four women reported a post-V DF [median 0.5 (0-36.25) days post 2nd dose]. All DF occurred in women with recent COVID-19 infection [171 (106-221) days, none requiring advanced treatments or intensive care], and half of these had active disease at the time of V. **Conclusions:** Among pregnant/lactating women with IIM, those with active disease were at a higher risk of major V-AE. All pts with major AE had prior COVID-19 and high antibody titres. It may be worthwhile checking antibody titres before administering boosters; individual risk profiling may be guided by the intensity of immunosuppression. Post-V DF were noted in most patients, though it is unclear whether these were related to vaccination, prior COVID-19, a pre-existent DF, or attributable to immune-hormonal changes of pregnancy. It then seems that benefits of V likely outweigh harms, given the added benefit of passive immunization to the fetus.

ICW23-3

COVID-19 Vaccine Safety during Pregnancy and Breastfeeding in Women with Autoimmune Rheumatic Diseases: Results from the COVAD Study

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Conflict of interest: None

[Objective] Persisting COVID-19 vaccine (V) hesitancy among pregnant (P) and breastfeeding (B) women with autoimmune rheumatic diseases (AIRD) can be attributed to the fear of adverse events (AEs) and disease flares (DF). We aimed at describing V safety in these vulnerable populations from the ongoing multicentre 2nd COVID-19 Vaccination in Autoimmune Diseases (COVAD) study. [Methods] Among complete responses from 9201 patients (pts), 6787 (73.8%) were women. Subgroups were identified upon diagnosis of AIRD vs healthy controls (HC) and the P/B status at the time of at least one dose of V. We analysed the long-term (>7 days) V-related AEs (minor and major), DF, and related treatment modifications. [Results] The mean age was 47 years (IQR 35-58); 47.5% were Caucasian. Among AIRD pts, 55.4% had at least 1 comorbidity. Six groups were identified: non-P, non-B AIRD pts (A, n=4862) or HC (D, n=1749); P AIRD pts (B, n=40); P HC (E, n=31); B AIRD pts (C, n= 52) or B HC (F, n=53). V rate (at least 1 dose received) was (group A-F): 97.8, 100, 96.2, 97.8, 96.8, 92.5%. One or more minor AEs were reported by 25.9, 40, 24, 19.8, 20.4%, while one or more major AEs by 4.6, 17.5, 2, 4.5, 3.3, 6.1%, and hospitalization by 1.1, 5 0, 1.2, 0, 2%. Groups B and C were compared with disease/age-matched control pts from A (n=2315) for the occurrence of DF after V. Change in the status of AIRD after V was judged as: i) Unchanged in 72.5, 78, 80%; ii) Improved in 10, 2, 2%; iii) Worsened in 17.5, 20, 18%. Treatment modifications due to worsening AIRD were reported by 27.5, 24, 21% of pts who had declared that their disease worsened after V. Particularly, started or increased steroids were reported by 25, 10, 16.7%, while switched/added new immunosuppressants by 10, 16, 7.6%. [Conclusions] P-B AIRD pts displayed good adherence to V. P AIRD pts experienced more AEs as compared to control pts and HC, but not more DF after V.

ICW23-4

Safety and tolerance of vaccines against SARS-CoV-2 infection in systemic lupus erythematosus: results from the COVAD study

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Conflict of interest: None

Objective: To determine COVID-19 vaccine-related adverse events (AEs) in the seven-day post-vaccination period in patients with systemic lupus erythematosus (SLE) versus autoimmune rheumatic diseases (AIRDs), non-rheumatic autoimmune diseases (nrAIDs), and healthy controls (HC). **Methods:** Data were captured through the COVID-19 Vaccination in Autoimmune Diseases (COVAD) questionnaire (March-December 2021). Multivariable regression models accounted for age, gender, ethnicity, vaccine type, and background treatment. **Results:** Among 9462 complete respondents, 583 (6.2%) were SLE patients (mean age: 40.1 years; 94.5% females; 40.5% Asian; 42.9% Pfizer-recipients). Minor AEs were reported by 83.0% of SLE patients, major by 2.6%. Pfizer-recipients

reported higher frequencies of overall AEs (OR: 2.2; 95% CI: 1.1-4.2; p=0.016) and injection site pain (2.9; 1.6-5.0; p<0.001) than recipients of other vaccines, Oxford/AstraZeneca-recipients more body ache, fever, chills (OR: 2.5-3.0), Moderna-recipients more body ache, fever, chills, and rashes (OR: 2.6-4.3). Hospitalisation frequencies were similar across vaccine types. AE frequencies were similar across treatment groups, albeit less frequent chills in antimalarial users versus non-users (0.5; 0.3-0.9; p=0.042). AE and hospitalisation frequencies were similar between patients with active and inactive SLE, and between SLE patients and comparators, albeit more frequent rashes in SLE versus HC (1.2; 1.0-1.5; p=0.038), less frequent chills in SLE versus AIRDs (0.6; 0.4-0.8; p=0.005) and nrAIDs (0.5; 0.3-0.8; p=0.003), and less frequent fatigue in SLE versus nrAIDs (0.6; 0.4-0.9; p=0.020). **Conclusion:** Despite discrepancies across COVID-19 vaccines regarding few minor AEs, they were overall well-tolerated by SLE patients irrespective of disease activity and background therapies.

ICW24-1

Prevalence and characteristics of Breakthrough Infection in Idiopathic Inflammatory Myositis After Third And Fourth Dose Of COVID-19 Vaccination: Results From COVAD Study

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Conflict of interest: None

Objective: To study the characteristics of breakthrough COVID-19 infections (BI) in completely vaccinated patients of idiopathic inflammatory myositis (IIM) and compare them with autoimmune inflammatory rheumatic diseases (AIRDs), non-rheumatic autoimmune diseases (nrAIDs), and healthy controls (HC). Methods: COVAD is a multinational, self-reported online survey conducted in 106 countries. Data was collected on vaccination, infection, treatment of COVID-19. BI was defined as any COVID-19 infection after at least 3 vaccine doses. Results: Of 7099 participants, 1604 (22.6%) were IIM aged 61.0 (49.0-70.0) years with 71.5% females. A total of 1101 (45.2%) had BI (136 IIM patients) once and 168 (7.5%) had BI (16 IIM patients) twice. COVID-19 infection following 2, 3, 4 vaccine doses had reduced (38.1%, 11.1%, 11.1% respectively) among IIM patients. IIM patients with BI were older, had higher comorbidities, AID multimorbidity compared to other groups. First BI was lower among IIM (n=136, 11.0%) compared to AIRDs [n=525, 16.3%; OR: 0.6 (0.5-0.7); p<0.001] and nrAIDs [n=60, 16.2%; OR: 0.6 (0.4-0.8); p=0.007] and similar to HC (n=289, 12.6%). IIM patients had frequent cough (OR: 7.8; 95%CI: 1.5-40.6; p=0.014) and longer resolution time (12.5 vs 7.0 days, p<0.001). First BI symptoms were similar in IIM and other AIRDs but had higher need for advanced treatment [OR: 1.9 (1.03-3.6); p=0.039]. Recipients of Sputnik [OR: 27.5 (1.5-488.5); p=0.024], Moderna [OR: 9.67 (1.1-84.5); p=0.04] and AstraZeneca [OR: 9.68 (1.19-78.4); p=0.033] vaccines had higher odds of first BI. Second BI was less in IIM patients [n=16, 1.2%; OR: 0.2 (0.1-0.5); p<0.001] compared to AIRDs (n=77, 2.4%), nrAIDs (n=16, 4.3%) and HC (n=59, 2.5%) with similar symptoms and severity. BI among IIM subsets, those with/without AID multimorbidity were similar. Conclusions: COVID-19 vaccination has decreased the frequency of BI. The symptoms and severity of BI in IIM were similar to other AIRDs, HCs except for the need for more frequent advanced medical treatment for COVID-19.

ICW24-2

Flares following COVID-19 Vaccination in patients with Idiopathic Inflammatory myopathies: Combined analysis from the COVAD studies

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Conflict of interest: None

Objective Flares following COVID-19 vaccination are an emerging concern among patients with idiopathic inflammatory myositis (IIMs), though the risk factors for these are poorly understood. We studied the prevalence, characteristics, and risk factors of COVID-19 vaccine related flares in patients with IIMs and other AIRDs. **Methods** We extracted data from the two COVID-19 vaccination in autoimmune diseases (COVAD) patient-self reporting e-surveys, circulated from March 2021-Feb 2022 and Feb-June 2022 respectively, capturing respondent demographics, comorbidities, AIRD details, COVID-19 infection history, and vaccination details. Flares of IIMs were defined as a. patient self-reported, b. immunosuppression (IS) denoted, c. clinical sign directed (new erythematous rash, or worsening myositis or arthritis), d. MCID worsening of PROMISPF10a score between the patients who had taken both the surveys. Predictors of

flares were analyzed in regression models. **Results** Of X total respondents 1278 patients with IIM (age 63 years, 70.3% female, 80.8% Caucasians), and Y AIRDs were included in the analysis. Flares of IIM were seen in 123/1278 (9.6%), 163/1278 (12.7%), 112/1278 (8.7%), and 16/96 (19.6%) by definitions a-d respectively with median time to flare being 71.5 (10.7-235) days, similar to AIRDs. Muscle weakness (69.1%), and fatigue (56.9%) were the most common symptoms of flare. Patients on rituximab (OR: 0.3; 95%CI: 0.1-0.7, p=0.009) and on azathioprine (OR: 0.3; 95%CI: 0.1-0.8, p=0.016), and those with active IIMs (OR: 0.3; 95%CI: 0.1-0.7, p=0.009) were at a comparatively lower risk of self-reported flares, while female gender and certain comorbidities predisposed patients with IIMs to flares requiring changes in immunosuppressive therapy. **Conclusions** A diagnosis of myositis confers an equal risk of post COVID-19 vaccine flares as other AIRDs, with certain individuals at higher risk who may be stratified for close monitoring accordingly. Formal definition of flares in IIM is needed.

ICW24-3

Comparison of SARS-CoV-2 vaccine response in patients with rheumatic musculoskeletal disease; mRNA-1273 induces higher Immunogenicity than BNT162b2

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Conflict of interest: None

[Objective] To compare the humoral and cellular immunogenicity and safety profiles of the SARS-CoV-2 mRNA vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) in patients with rheumatic musculoskeletal disease (RMD). [Methods] Previously uninfected patients with RMD and healthy individuals were recruited for the study. The patients received either the BNT162b2 or mRNA-1273, whereas the healthy controls received BNT162b2. Blood samples were obtained 3 weeks after the second vaccine dose for measurement of the SARS-CoV-2 neutralizing antibody titer and evaluation of the T-cell immune response to SARS-CoV-2 antigens using an interferon-gamma (IFN-γ) release assay. Adverse reactions were assessed using questionnaires. [Results] A total of 860 patients with RMD on immunosuppressants (704 and 156 received BNT162b2 and mRNA-1273, respectively) and 621 healthy controls were enrolled. The post-vaccination neutralizing antibody titers and seroconversion rates were significantly higher in the control individuals and mRNA-1273-vaccinated patients than in the BNT162b2-vaccinated patients. Age, glucocorticoid and immunosuppressant use (including methotrexate, mycophenolate, and rituximab) were associated with weak humoral responses. T-cell reactions against SARS-CoV-2 were also higher in and mRNA-1273-vaccinated patients. The proportions of reactogenicity, including fever and general fatigue, were significantly higher in mRNA-1273-vaccinated patients, while there was no significant difference in the frequency of post-vaccination RMD flares between the mRNA-1273- and BNT162b2-vaccinated patients (5.2% vs 3.7%, p=0.41). [Conclusions] We demonstrated mRNA-1273 elicited higher humoral and cellular immunogenicity than BNT162b2 did in patients with RMD. Although systemic reactogenicity occurred more frequently in the mRNA-1273-vaccinated patients, the proportions of RMD relapse were similar between the two patient groups.

ICW24-4

Delayed COVID-19 vaccine adverse events: Results from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) study

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Conflict of interest: None

[Objective] This study aims to analyze the delayed adverse events (ADEs) of COVID-19 vaccination among patients with idiopathic inflammatory myopathies (IIMs) and other systemic autoimmune and inflammatory disorders (SAIDs). [Methods] The COVAD study group launched a web-based self-reporting study, including patients from 106 countries. From Feb to June 2022, we collected demographics, IIM/SAID details, COVID-19 infection, and vaccination outcomes. Delayed ADEs (>7 days since vaccination) were classified into 4 main categories: injection site pain/soreness, minor ADEs, major ADEs, and hospitalization. The responses were analyzed utilizing descriptive statistics and multivariable regression. [Results] From 15,165 respondents, 8759 [median age 46 (35-58) years, 74.4% females, 45.4% Caucasians] met the inclusion criteria and were included in the analysis. IIMs were present at 1390 (15.9%) of those, 50.6% had other SAIDs, and 33.5% were healthy controls (HCs). 16.3% of IIMs patients reported minor ADEs, 10.2% faced major ADEs, and 2.9% required hospitalization. IIMs patients had a lower risk of minor ADEs than those with other SAIDs, though a higher risk of rashes compared to HCs [OR 4.0 (2.2-7.0), p<0.001]. In the IIMs subgroup, patients with active disease, overlap myositis, and ChadOx1 nCOV-19 (Oxford/AstraZeneca) recipients were at a higher risk of ADEs, while those with inclusion body myositis, and BNT162b2 (Pfizer) vaccine recipients were comparatively protected. Individuals with co-existing IIMs and SAIDs were at a higher risk of minor [OR 5.2 (3.3-8.2), p<0.001] and major ADEs [OR 2.1 (1.2-3.8), p<0.05] compared to those without comorbidity. [Conclusions] The vaccination outcomes in terms of ADEs were less likely in the IIM group in comparison to SAIDs individuals and comparable with HCs. Delayed ADEs were more commonly associated with overlap myositis and IIM with SAIDs comorbidity. The most favorable vaccine for respondents with IIMs was BNT162b2 (Pfizer).

ICW24-5

Flares in Autoimmune Rheumatic Disorders following COVID-19 vaccination - a Cross-Sectional Study based on COVAD-1 and COVAD-2 Surveys

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Conflict of interest: None

Objective: Flare in patients with autoimmune rheumatic disorders (AIRDs) following COVID-19 vaccination is a major concern leading to vaccine hesitancy. We aimed to assess the incidence, predictors and patterns of flares following vaccination in AIRD patients using the data from the 2nd COVID-19 vaccination in autoimmune diseases (COVAD) survey. **Methods:** The COVAD2 survey (157 collaborators; 106 countries) captured demographics, comorbidities, COVID-19 history, and vaccination details among AIRDs. Flares following vaccination were defined as patient-reported (a), increased immunosuppression (b), clinical exacerbations (c) and worsening of PROMIS scores (d). **Results:** Out of the 9202 complete responses, the incidence of flares in 3453 AIRDs patients was 11.3%, 14.8%, 9.5%, and 26.7% by definitions a-d respectively. Arthritis (61.6%) and fatigue (58.8%) were the most common symptoms. Self-reported flares were associated with higher comorbidities (p=0.013), mental health disorders (MHD) (p<0.001), and autoimmune disorder multimorbidity (AIDm) (p<0.001). In regression analysis, the presence of AIDm (OR=1.4; 95%CI: 1.1-1.7; p=0.003), MHD (OR=1.7; 95%CI: 1.1-2.6; p=0.007), and Moderna vaccine (OR=1.5; 95%CI: 1.09-2.2; p=0.014) recipients were positive predictors of patient reported flare. Mycophenolate (OR=0.5; 95%CI: 0.3-0.8; p=0.009) and steroid (OR=0.6; 95%CI: 0.5-0.8; p=0.003) use were protective. Higher frequency of AIRDs reported overall active disease post-vaccination compared to before vaccination (OR=1.3; 95%CI: 1.1-1.5; p<0.001). Flare rates and time to flare were similar across various AIRDs. Prior COVID-19 antibody status did not influence flares. There was a poor agreement between patient and physician reported flares (K=0.403, p=0.022). **Conclusion:** One in ten individuals with AIRDs reported flare following COVID-19 vaccination. The presence of comorbidities especially AID multimorbidity, mental health disorders and the use of Moderna vaccine predicted higher flares.

ICW25-1

Clinical, Laboratory, and Imaging Modality Leading to Diagnosis in Chronic Nonbacterial Osteomyelitis

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Conflict of interest: None

[Objective] Chronic nonbacterial osteomyelitis (CNO) is an aseptic autoinflammatory bone disease of unknown etiology. This diagnosis can be delayed due to the non-specific nature of symptoms, referral patterns to non-rheumatology specialists and normal imaging studies. We evaluated the clinical, laboratory, and imaging characteristics found that can lead to a diagnosis in children. [Methods] Retrospective case series of 32 pediatric patients diagnosed with CNO. They were seen between 2012 and 2022 and treated at the University of Virginia in Charlottesville, Virginia and Bon Secours Mercy Health in Richmond, Virginia. [Results] The average age of diagnosis was 10 (range 2-20) years-old with the average time between onset of symptoms to confirmed radiographic evidence being 26 (range 1-120) months. The most common presenting symptoms were bone pain (100%) and arthritis (52%) with fever (23%) and rash (3%) being less common. Elevated ESR (39%) and CRP (39%) were found at initial visit with rheumatology. Evidence of commonly seen radiographic abnormalities leading to CNO diagnosis was found with regional MRI (65%), bone scan (42%) with some requiring full body MRI (26%) to confirm other lesions. Some patients did have multiple imaging studies including X-ray, CT, bone scan, MRI and bone biopsy in their workup. Treatment history varied from use of NSAIDs, DMARD's, TNF inhibitors, JAK inhibitors to bisphosphonate products. Non-steroidal's were used in 100% of patients. Methotrexate was used in 58% of patients. TNF inhibition was used as follows: Adalimumab in 39%, Etanercept in 16%, Infliximab infusion in 10%. JAK inibition with Tofacitinib was used in 3%. A bisphosphonate, pamidronate was used in 10% of patients. [Conclusions] Advanced imaging studies with full body MRI or regional MRI are often needed to confirm the diagnosis of CNO. Normal x-rays and bone scan can delay proper referral and in turn delay treatment of this autoinflammatory bone disease.

ICW25-2

The role of lung ultrasound in the diagnosis of idiopathic inflammatory myositis-associated interstitial lung disease

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Conflict of interest: None

[Objective] To explore the role of lung ultrasound (LUS) in the diagnosis of idiopathic inflammatory myositis-associated interstitial lung disease (IIM-ILD), and correlation among B-lines score, high-resolution CT (HRCT) score, and pulmonary function tests were investigated. [Methods] Patients with suspected IIM-ILD were consecutively enrolled. Patients underwent LUS, chest HRCT scans, and pulmonary function tests (independently performed within 1 week). The diagnosis of ILD was based on HRCT and the Warrick score was applied to assess severity and extent of ILD. The B-lines score was calculated by summing the number of B-lines on a total of 14 defined intercostal spaces. [Results] Twenty-two patients out of 30 were diagnosed as IIM-ILD by HRCT, with a higher Warrick score and B lines score, worse pulmonary function tests. Taking HRCT as the golden standard of ILD, the sensitivity and specificity of positive B-lines (no less than 6) was 90.9% and 100%, separately. A significant positive correlation was found between the B-lines score and the Warrick score in patients with confirmed ILD (r=0.873, P=0.000). B-lines score was inversely correlated with diffusion capacity for carbon monoxide (r= -0.696, P=0.000), forced vital capacity (r=-0.633, P =0.001) and forced expiratory volume in 1 s (r=-0.516, P=0.010). The median number of B lines between left and right lung did not show significant difference [5.5 (2.0,10.25) vs 3.0 (1.0,9.25), P=0.385]. No significant differences of the median number of B lines were found between anterior, lateral and posterior intercostal spaces, neither. [Conclusions] LUS may represent a useful tool to select IIM patients to be assessed by chest HRCT with a high sensitivity and specificity to detect ILD. B-lines score correlates with HRCT findings and pulmonary function tests, supporting its use as an alternative measure of IIM-ILD severity.

ICW25-4

Radiomics to predict the mortality of patients with rheumatoid arthritis-associated interstitial lung disease: a proof-of-concept study

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) and interstitial lung disease (ILD) have increased mortality compared to the general population and factors capable of predicting RA-ILD long-term clinical outcomes are lacking. In Oncology, radiomics allows the quantification of tumour phenotype by analysing the characteristics of medical images. Using specific software, it is possible to segment organs on High-Resolution Computed Tomography (HRCT) images and extract many features that

may uncover disease characteristics that fail to be detected by the naked eye. Our aim was to investigate whether features from whole lung radiomic analysis of HRCT may alone predict mortality in RA-ILD patients. [Methods] HRCTs of RA patients from January 2012 to March 2022 were analysed. The time between the first available HRCT and last follow-up visit or ILD-related death was recorded. We performed a volumetric analysis in 3D Slicer, automatically segmenting the whole lungs and trachea via the *Lung CT Analyzer.* A LASSO-Cox model was carried out by considering ILD-related death as outcome variable and extracted radiomic features as exposure variables. [Results] Whole line segmentation was fast and reliable. The model included the features *original_firstorder_median (*HR 9.35, 95% CI 1.56-55.86) as positive predictor of death, and *original_firstorder_10 Percentile* (HR 0.20, 95% CI 0.05 - 0.84), *diagnostics_Imageoriginal_Mean* (HR 0.23, 95% CI 0.06-0.82), *original_shape_Flatness* (HR 0.42, 95% CI 0.18-0.98) negatively correlating to mortality, and *original_glcm_Correlation* (HR 1.52 95% CI 0.82-2.83) retained as a confounder. [Conclusions] Radiomic analysis may predict RA-ILD patients' mortality and may promote HRCT as a digital biomarker regardless the clinical characteristics of the disease.

ICW25-5

Glucocorticoids, conventional DMARDs and tocilizumab differently affect 18F-FDG PET metabolic activity in giant cell arteritis patients

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Conflict of interest: None

[Objective] The role of 18F-FDG PET in giant cell arteritis (GCA) patients is still an unmet need. The aim of the study is to evaluate the effect of different treatment regimens, namely glucocorticoids (GC), conventional disease modifying anti-rheumatic drugs (cDMARDs) and tocilizumab (TCZ), on clinical and metabolic activity of GCA. [Methods] Consecutive GCA patients, who underwent to at least 2 consecutive PET scan (a total of 181), were prospectively enrolled. Remission was defined absence of signs and symptoms attributable to GCA and normalization of ESR and CRP. GCA patients were compared according to current treatment regimen: GC monotherapy vs cDMARDs and vs TCZ. For each PET scan the vessel's metabolic activity was evaluated using the Meller's grading and the PETVAS score. [Results] The study included 47 patients exposed to a total of 77 treatment regimens (37 GC, 26 cDMARDs, 14 TCZ). Overall clinical remission rate was 75.7% in GC, 69.2% in cDMARDs and 85.7% in TCZ (p=0.513). All the treatment led to significant reduction of acute phase reactants (GC: ΔESR=-43.3%, ΔCRP=-87.7%; cDMARDs: ΔESR=-152%, ΔCRP=-66.3% and TCZ: ΔESR=-86.7%, ΔCRP=-80.2%). Significant improvement in PETVAS was observed only in TCZ (12vs4, p=0.002, ΔPETVAS -66.7%), while the other treatment approaches resulted not significant (GC p=0.052, cDMARDs p=0.124). Daily prednisone dose at last examination was 4.5 mg/d in the cDMARDs group vs 1.25 mg/d in the TCZ group (p=0.057). Interestingly, at last PET examination low-grade inflammation (Meller 1-2) was observed in 56.8% of GC-treated patients, 57.7% of cDMARDstreated patients and 64.3% of TCZ-treated patients (p=0.884). [Conclusions] 18F-FDG PET is useful in assessing disease activity and monitoring response to therapy. Tocilizumab treatment significantly reduce vessel's metabolic activity over time, compared to conventional treatment. A persistent low-grade uptake during remission is common features in GCA patients, irrespectively of treatment regimens.

ICW25-6

Efficacy of brain magnetic resonance vessel wall imaging in the diagnosis of neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

[Objective] Brain magnetic resonance vessel wall imaging (MR-VWI) detects cerebrovascular abnormalities by examining contrast-enhanced images of the vessel wall. Neuropsychiatric systemic lupus erythematosus (NPSLE) is a disorder seen in a subset of SLE patients and thought to be caused by autoimmune cerebrovascular disorders. The aim of this study is to evaluate the diagnostic value of MR-VWI for NPSLE. [Methods] MR-VWI was performed in SLE patients with neurological or psychiatric manifestations and therefore suspected to have NPSLE from June 2018 to June 2022. NPSLE was classified according to American College of Rheumatology 1999 criteria and diagnosed comprehensively based on clinical symptoms, the examination of spinal fluid, electroencephalography, and MR imaging/MR angiography findings. The patients were divided into two groups according to the findings on MR-VWI: VWI-positive and VWI-negative. We evaluated the association between NPSLE and the abnormal findings on MR-VWI by logistic regression analysis. [Results] This study comprised 35 SLE patients, 32 females (91.4%), with a median age at enrollment of 34 years old (interquartile range: 27-49). Nineteen patients (54.3%) fulfilled the NPSLE criteria while an abnormal finding on MR-VWI was detected in 11 patients (31.4%). There was no specific difference in clinical and laboratory findings between the VWI-positive and -negative groups. In univariate logistic analysis, the abnormal finding on MR-VWI was associated with NPSLE (Odds Ratio (OR): 16.7, 95% C. I: 1.82-152.77, p=0.013). Multivariate logistic analysis confirmed that the abnormal MR-VWI finding was significantly more frequent in patients with NPSLE (OR: 20.6, 95% C. I: 1.75-243.76, p=0.016). MR-VWI showed a sensitivity and specificity of 90.9% and 62.5%, respectively, for the diagnosis of NPSLE. [Conclusions] The abnormal MR-VWI finding was significantly more frequent in patients with NPSLE, suggesting that MR-VWI is useful for the diagnosis of NPSLE.

ICW26-1

Blue-collar jobs are not prevalent in a cohort of Mexican patients with IgG4-related disease

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Conflict of interest: None

[Objective] To assess the prevalence of blue-collar jobs (BCJ) in a Mexican IgG4-related disease (IgG4-RD) cohort. [Methods] We included patients diagnosed with IgG4-RD according to the Comprehensive Diagnostic Criteria and/or the 2019 ACR/EULAR classification criteria assessed between 2018-2022. A standardized questionnaire was applied to obtain work, smoking, and biomass exposure history. The International Standard Classification of Occupations (ISCO88) was used to divide patients into those with white-collar jobs (WCJ) (ISCO88 groups 0-5) or BCJ (ISCO88 groups 6-9). Unpaid household work was classified within group 9. [Results] 95 patients were included with a mean age of 53.8 ± 15.8 years; 48 (50.5%) were men. 78 (82.1%) had a paid job, of whom 63 (66.3%) had WCJ and 15 (15.8%) BCJ. Of the patients without paid occupations, 13 (13.7%) had household work and 4 (4.2%) were students. The proportion of patients with WCJ was higher both when including unpaid domestic work within the BCJ group (66.3% vs. 29.5%) and when excluding it (66.3% vs. 15.8%). When analyzing the cohort without including unpaid domestic work, we found no difference in the proportion of patients with the pancreatobiliary phenotype (14 [22.2%] vs. 5 [33.3%], p=0.40), with pancreatic (29 [46%] vs. 7 [46.7%], p=0.96), or biliary involvement (20 [31.7%] vs. 4 [26.7%], p=0.70), between patients with WCJ and BCJ. When including unpaid domestic work, the same results were found. Patients with BCJ had more lung involvement (18 [29%] vs. 2 [7.1%], p=0.02) and less biomass exposure (12 [19%] vs. 18 [64.3%], p<0.001). There was no difference in the proportion of smoking. [Conclusions] The prevalence of BCJ in a Mexican IgG4-RD cohort is significantly lower than that observed in the Dutch population (29.5% vs 68%). BCJ were not more frequent in patients with pancreatobiliary involvement. These findings indicate that other risk factors influence the development of IgG4-RD in addition to occupational exposure.

ICW26-2

Research of factors that prolong IgG4-related diseases using transcriptome analysis

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Conflict of interest: None

[Objective] IgG4-related disease (IgG4-RD) is a chronic inflammatory disease proposed in Japan. IgG4-RD is widely treated by glucocorticoid but is easy to relapse, leading to prolonged disease and increased total steroid dose. Recent studies suggest that follicular helper T cells, regulatory T cells, and inflammatory factors such as TGF-β, IL-4, and IL-10 are involved in the pathogenesis of IgG4-RD. However, the role of these factors in prolonging the disease is unclear. We performed transcriptome analysis of salivary glands in order to clarify the mechanism of the prolongation of IgG4-RD. [Methods] Salivary gland biopsies were performed among seven patients with IgG4-associated sialadenitis, which consisted of a prolonged group (1 year or longer, n = 3) and an early group (less than 1 year, n = 4). Patients with sialadenitis but not diagnosed with IgG4-RD were assign as a control group (n = 3). RNA-seq was performed using mRNA extracted from specimens by TRIZOL. Gene expression was compared among three groups using DESeq2, and genes satisfying |Fold change|>2 and $p<0.01$ were defined as differentially expressed genes (DEGs). Based on DEGs, pathway analysis was performed using Reactome. [Results] RNA-seq detected 2458 upregulated DEGs and 1003 downregulated DEGs in the early group relative to the control. Many of upregulated DEGs were involved in pathways such as chemokine receptor binding and IL-2 and TNFs signaling. Many of downregulated DEGs were associated with the function of ERBB2 and ERBB4 genes. On the other hand, there were 217 upregulated DEGs and 929 downregulated DEGs between the prolonged group and the early group, and up-regulated DEGs were involved in pathways associated with B-cell receptor activation, complement activation, and activation of immunoglobulin Fc receptors. [Conclusions] We showed a difference in immune response between patients with prolonged IgG4-RD and ones in the early stage. We will report on the difference with a review of the literature.

ICW26-3

IgG4-related disease as a cause of idiopathic constrictive pericarditis

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Conflict of interest: None

[Objective] To determine the number of patients with idiopathic constrictive pericarditis (CP) who meet criteria for IgG4-related disease (IgG4-RD). [Methods] Records of patients with CP attended between 1987-2020 were reviewed. Pericardial biopsies were analyzed in search of dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis. Immunostaining for IgG and IgG4 was done. The number of IgG+ and IgG4+ plasma cells and the IgG4/IgG ratio were determined according to the International Consensus on Pathology (ICP) of IgG4-RD. Cases were classified as highly suggestive, probable histopathological characteristics, or insufficient histopathological evidence. The Comprehensive Diagnostic Criteria for IgG4-RD (CDCI) and the 2019 ACR/EULAR classification criteria (AECC) were also applied. [Results] 66 cases were reviewed, of which 10 had an identified etiology. Of the remaining 56, 12 had a pericardial biopsy. All had been classified as idiopathic. The mean age was 43±14 years; 9 were men. Lymphoplasmacytic infiltrate was found in all, fibrosis in 8, and storiform fibrosis in only 1 case. Obliterative phlebitis was not found. In 2 cases the IgG stains were not assessable, so the IgG4/IgG ratio was calculated in 10. The median number of IgG4+ plasma cells/HPF was 30.5 (IQR 16-41). The median IgG4/IgG ratio was 59.5% (IQR 27-66). All cases had >10 IgG4+ cells/HPF while 7/10 (70%) had an IgG4/IgG ratio >40%. According to the ICP, 1 (8.3%) case was highly suggestive, 6 (50%) had probable histological characteristics, and 5 (41.6%) had insufficient histopathological evidence. 7 (58.3%) met the CDCI for probable IgG4-RD. Only 1 patient met the 2019 AECC for atypical IgG4-RD. [Conclusions] A large number of pericardial biopsies from patients with idiopathic CP have findings suggestive of IgG4-RD and meet at least one set of diagnostic/classification criteria. IgG4-RD should be considered when assessing a patient with CP due to the therapeutic implications.

ICW26-4

Distinct clinical and immunological features of IgG4-related disease by underlying diseases; malignancy and allergy

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Conflict of interest: None

Objectives: Patients with IgG4-related disease (IgG4-RD) frequently complicate malignancy and allergy. In this study, we aimed to clarify the clinical and immunological characteristics of IgG4-RD based on the complications with malignancy or allergy. **Methods:** Consecutive patients with IgG4-RD treated at Keio University Hospital between 2010 and 2021 were divided according to the presence of malignancy or allergy into three groups. The clinical characteristics and 56 immune cell subsets in the peripheral blood were compared among the groups. **Results:** Among 123 patients, 18 (14.6%) had malignancy (malignancy group), 57 (46.3%) had allergy alone (allergy group), and 48 (39.0%) had neither (idiopathic group). In the malignancy group, the patients were older (70.1 vs 54.4 vs 64.9 years, $p<0.001$), male-dominant (83.3 vs 42.1 vs 54.2%, $p=0.008$), and had smoking habits (77.8 vs 42.1 vs 43.8%, $p=0.02$). They also had significant involvement of the aorta/large vessels (33.3 vs. 7.0 vs. 20.8%, $p=0.02$), while the patients in the allergy group tended to have orbital/lacrimal gland involvement. Age ≧ 65, male sex, non-atopic history, smoking habit, and aorta/large vessel involvement were independent risk factors for the presence of malignancy, and the proportion of patients with malignancy significantly increased up to 40% depending on the number of risk factors ($p<0.001$). Remission and relapse rates were not different between the groups; however, overall survival was significantly poorer in the malignancy group ($p=0.02$). Comprehensive immunophenotyping of the peripheral blood demonstrated the increase in CXCR5+CD2-double negative T cells and the decrease in naive CD8 T cells as the significant characteristic of the malignancy group. **Conclusion:** The clinical and immunological phenotypes of IgG4-RD differ depending on the complications with malignancy or allergy. We should screen for malignancy if the patients are the elderly with smoking history and large vessel involvement.

ICW26-5

Peripheral blood CD8 effector memory T cells re-expressing CD45RA is a predictor of disease flare in IgG4-related disease (IgG4-RD)

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Conflict of interest: None

[Objective] Glucocorticoids (GC) are effective in the treatment of IgG4-RD, however, disease relapses are often seen with GC reduction. This study aimed to investigate the long-term treatment outcome of IgG4-RD. [Methods] 60 patients with IgG4-RD who had been treated with GC therapy for at least 1 year were enrolled. Comprehensive immunophenotyping was performed by flow cytometry. [Results] The mean observation period was 2.9 years. The mean initial GC dose was 41.3 mg (PSL equivalent), and 65% (39 patients) received concomitant immunosuppressive therapy. GC treatment resulted in rapid improvement of disease activity and GC dose was reduced in all cases. At a dose higher than 10 mg, there were no disease flares throughout the course. On the other hand, 28.3% (17 patients) showed disease flares when the GC was reduced to 10 mg or less. There was no difference between the mean GC dose for patients who relapsed (3.6 mg) and that for patients who did not (3.9 mg). A comparison of clinical data between patients who relapsed and those who did not

showed that hypocomplementemia at baseline could be a factor for disease flare (C4 level: 15.8 mg/dl vs. 20.1 mg/dl), but not statistically significant (p=0.14). It was difficult to detect disease flare susceptibility from clinical findings, next we investigate immunophenotyping. Similar to previous reports, IgG4-RD patients showed increased levels of effector memory CD4, plasmocytes, and plasmacytoid DCs compared to healthy controls. However, multivariate analysis showed that only the proportion of CD8 effector memory T cells re-expressing CD45RA (TEMRA) was the predictive marker for disease flare (p=0.04). [Conclusions] GC dose reduction below 10 mg is associated with a high risk of relapse. CD8 TEMRA could be a predictor of disease flare in IgG4-RD.

ICW27-1

Subclinical atherosclerosis of carotid arteries in patients with calcium pyrophosphate deposition disease and osteoarthritis

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Conflict of interest: None

Objectives: Assessment of the dynamics of carotid atherosclerosis based on changes of intima-media thickness (caIMT) in pts with CPPD receiving anti-inflammatory therapy (colchicine, methotrexate, hydroxychloroquine). **Methods:** The prospective study included 26 adult pts with CPPD and OA. Exclusion criteria: age >65 yrs, presence of CVD, CA atherosclerosis according to US, high or very high SCORE index. Laboratory tests included: hs-CRP, lipid levels. CA Doppler ultrasonography was performed. The manifestation of subclinical atherosclerosis was diagnosed in case of caIMT increase >0.9 mm. The criteria for the presence of an atherosclerotic plaque in the CA was a local caIMT increase >1.3 mm. CaIMT was measured at the first visit, then, pts with CPPD were administered MTX 15 mg/week or HCQ 200 mg/day or COLCH 1 mg/day. Pts could take NSAIDs to relieve pain. After 26 weeks a second examination was performed. **Results:** 22 pts with CPPD and 19 with OA were examined. The baseline values of caIMT in pts with CPPD and OA didn't differ. By the end of the study, 14 of 22 (64%) pts with CPPD had a decrease in the average values of caIMT, in 2 (9%) pts - an increase, in 6 pts the average values of caIMT didn't change. 7 of 11 pts with CPPD showed normalization of caIMT, 5 of them (45.5%) had a decrease in serum hs-CRP <2 mg/l. A decrease in the number of pts with CPPD and caIMT >0.9 mm from 11 (42%) to 4 (18%) pts was found. In 8 pts with CPPD the serum hs-CRP level significantly decreased: baseline 6.02 [0.69; 6.4] mg/l vs at the end of study period 1.71 [0.78; 2.25] mg/l, p=0.043. Pts with OA demonstrated the constant level: baseline 2.13 [0.22; 2.8] mg/l vs at th end of study period 3.06 [0.39; 6.38] mg/l, p=0.627. A decrease in mean values of caIMT was noted in 5 of 6 (83%) pts took HCQ, in 6 of 9 (67%) pts took COLCH, in 4 of 7 (57%) pts - MTX. **Conclusion:** Therapy with COLCH, MTX and HCQ in pts with CPPD leads to regression of early signs of atherosclerosis.

ICW27-2

Association of preoperative variables of ipsilateral hip abductor muscles with gait function after total hip arthroplasty

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Conflict of interest: None

[Objective] This study aimed to identify association of preoperative variables of ipsilateral hip abductors with gait function after total hip arthroplasty (THA). [Methods] This study enrolled 42 patients who underwent unilateral primary THA for osteoarthritis. Gait speed and Timed Up-and-Go test (TUG) were measured 6 months postoperatively. Preoperative composition of the glutei medius and minimus and the upper portion of gluteus maximus was evaluated by computed tomography. Cross-sectional area ratio of individual composition to the total muscle was calculated. Preoperative variables associated with gait speed and TUG after THA were identified using stepwise regression analysis. [Results] Faster gait speed and shorter TUG correlated with smaller cross-sectional area of low-density lean tissue or intramuscular adipose tissue (low-density lean tissue plus intramuscular fat) in the glutei medius and minimus and lower cross-sectional area ratio of low-density lean tissue to the total glutei medius and minimus. Faster gait speed and shorter TUG also correlated with larger cross-sectional area of lean muscle mass in the gluteus maximus, higher cross-sectional area ratio of lean muscle mass to the total gluteus maximus, and lower cross-sectional area ratio of intramuscular fat or intramuscular adipose tissue to the total gluteus maximus. Faster gait speed additionally correlated with larger total cross-sectional area of the gluteus maximus. From regression analysis, the total cross-sectional area of the gluteus maximus and the low-density lean tissue cross-sectional area of the glutei medius and minimus were the explanatory variables of gait speed and TUG after THA, respectively. [Conclusions] There was potential association between preoperative composition of ipsilateral hip abductors and gait function at 6 months after THA. This study indicates a predictive role of preoperative assessment of ipsilateral hip abductor composition in recovery of gait function after THA.

ICW27-3

Identifying distinct cell types in infrapatellar fat pad during osteoarthritis

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Conflict of interest: None

Objective: Knee osteoarthritis (KOA) is the most common form of arthritis, defined by cartilage degeneration, synovial inflammation, fibrosis, and subchondral bone remodelling. The infrapatellar fat pad (IFP) is the largest FP within the knee however, its role in KOA is not well understood. Furthermore, the cell populations contributing to KOA remain to be fully characterized. This study aims to identify the distinct cell populations within the IFP that may contribute to KOA pathogenesis using single-nucleus RNA sequencing (snRNA-seq). Methods: IFP was obtained from late-stage KOA patients [KL grades III/IV; n=four] undergoing total knee replacement. Nuclei were isolated by fluorescence-activated cell sorting (FACS) based on DNA content and underwent snRNA-seq using droplet-based Chromium Next GEM Single Cell Three' Reagent Kits. cDNA libraries were sequenced on Illumina NextSeq five-hundred-fifty using the one-hundred-fifty bp high output sequencing kit. Data was processed using Cell Ranger and reads were aligned to the human transcriptome (GRChthirtyeight). Samples were merged for clustering and visualization. Clusters were annotated based on canonical markers while differential gene expression testing determined a gene signature. Results: Clustering analysis identified fibroblasts, macrophages, adipocytes, and endothelial cells as major cell populations within OA IFP. Multiple subclusters of macrophages and fibroblasts were identified. Our efforts are now focused on characterizing distinct subtypes of cells identified in IFP using a larger sample size. Furthermore, we are employing advanced bioinformatics and functional assays to understand the function of identified subsets in KOA pathogenesis. Conclusions: Using snRNA-seq, we have identified distinct cell subsets of fibroblasts, adipocytes, macrophages, and other cell types in IFP of patients with KOA. Our ongoing efforts will help characterize the role and function of these identified cell subsets in KOA pathogenesis.

ICW27-4

Determination of urinary and synovial fluid C2C-HUSA levels in total knee arthroplasty patients

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Conflict of interest: None

[Objective] After total knee arthroplasty (TKA), ~30% of knee osteoarthritis (KOA) patients show little improvement. Studies correlate urinary (u) type 2 collagen C terminal cleavage peptide (C2C) with KOA progression but its relation with post-surgical outcomes is still unknown. [Methods] Baseline urine and synovial fluid (sf) were collected from 493 KOA patients at the time of TKA. C2C levels were measured by IB-C2C-HUSA™. Western Ontario and McMaster Universities Osteoarthritis (WOMAC) pain and function subscales at baseline and 1-year post-surgery were used to assess changes between time points, and categories of symptom improvement. Regression models adjusted by age, sex, body mass index, metabolic comorbidity status, and one or more joints affected at baseline were fitted to assess associations between C2C levels and pain/function. [Results] Multivariable linear regression estimates (95% CI; *p*-value) for a 100 unit increase in sfC2C or uC2C, and a 1 unit increase in its ratio were -0.04 (-0.2-0.12; *p*=0.64), -0.37 (-0.7-0.04; *p*=0.029), and 0.16 (3.4e-03-0.32; *p*=0.045) for change in WOMAC pain and -0.21 (-0.76 - 0.34; *p*=0.45), -0.91 (-2.03 - 0.21; *p*=0.11), and 0.60 (0.07-1.14; *p*=0.026) for change in WOMAC function, respectively. Covariate-adjusted odds ratios (95%CI; *p*-value) for a 100 unit increase in sfC2C or uC2C, and a 1 unit increase in its ratio in a cumulative odds model were 0.96 (0.89-1.04; *p*=0.36), 1.15 (0.97-1.36; *p*=0.099), and 0.91 (0.84-0.98; *p*=0.015) for WOMAC pain and 0.97 (0.90-1.05; *p*=0.5), 1.06 (0.91-1.24; *p*=0.44), and 0.92 (0.85-1.00; *p*=0.042) for WOMAC function, respectively. [Conclusions] Baseline uC2C levels were significantly correlated with change in WOMAC pain at 1 year. sfC2C: uC2C levels were consistently associated with changes in WOMAC pain and function at 1 year, regardless of modelling. Thus sf and uC2C levels may be important prognostic factors for surgical OA patient outcomes.

ICW27-5

Identification of distinct cellular populations in the synovium of early and late stage radiographic knee OA using single nucleus RNA sequencing

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Conflict of interest: None

[Objective] Osteoarthritis (OA) is a degenerative joint disease where the synovium has been identified as a key joint tissue involved in the pathophysiology of OA. Minimal research has been done on the synovium in relation to OA pathophysiology. To delineate the synovium's role in OA pathogenesis we sought to identify if distinct cell subtypes exist in the synovium of early (KL1) versus late stages (KL3/4) of radiographic knee OA and in an OA mouse model. [Methods] Synovia from patients with early (KL1; n=5) and late (KL3/4; n=4) stage radiographic knee OA were subjected to single nuclei (sn) RNAseq. Clustering analysis identified cell subtypes and prominent types were re-clustered. Differentially expressed gene (DEG) lists for each subcluster was used to identify canonical cell surface markers which were validated by immunohistochemistry. The destabilization of the medial meniscus (DMM) mouse model was used to identify cell subsets analogous to that from human tissues and to determine their role in OA. [Results] Fibroblasts and macrophages constituted 75% of the cells from the synovium and re-clustering resolved 8 fibroblast and 6 macrophage subclusters. Nuclei proportion differences identified fibroblast clusters 1, 2, 4 and 6 and macrophage clusters 1, 2 and 5 to contribute to early-stage samples while fibroblast clusters 0, 3 and 5 and macrophage clusters 0, 3 and 4 to late-stages. Putative cell surface markers from subclusters were identified from DEGs and confirmed by immunohistochemistry. A pilot study was performed to isolate knee synovia from 6 naïve mice and subjected them to snRNAseq identifying analogous cell types to the human dataset and further studies are being done to track the trajectories of these identified cell subsets at 2 and 10 weeks. [Conclusions] SnRNAseq analysis identified distinct subclusters of fibroblasts and macrophages in human synovia and studies are being done to identify their roles in OA pathophysiology.

ICW27-6

Repairing cartilage defects with the chondrocyte precursors might stop the progress of knee osteoarthritis

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Conflict of interest: None

[Objective] We hypothesized that the cartilage defect on the medial femoral condyle will be deepened and enlarged by cyclic motion of the knee up to 10,000 times a day and lasting for 2 years and repairing the cartilage defect might be helpful to hold the progress of the knee osteoarthritis. [Methods] Chondrocyte precursors (CPs), embedded in atelocollagen were induced from autologous bone marrow stem cells. This surgical graft was implanted onto the defects. Twelve patients fulfilling the criteria for treatment were enrolled. The knee with severer symptoms, such as pain, click, limping and/or refusion, was operated on as experiment one. The contralateral knee was used as control. [Results] Three of the twelve patients were lost during the follow-up period. The remained nine patients maintained good knee functions nine years after operation (IKDC score = 69.8 ± 12.3) vs. the pre-implantation values (*p*-value = 0.0018). Three of the nine untreated contralateral knees had to undergo TKA during the follow-up. Based on the above study, a randomized controlled trial was undergone. Fifteen patients with grade IV cartilage defect on the medial femoral condyle were enrolled and stratified into two groups, undergoing either CPs implantation (n = 10) or microfracture (control group, n = 5), and followed up for two years. Postoperative IKDC scores of the CPs group significantly improved in the second year (IKDC = 73.6 ±13.8, $p < 0.005$) vs. the preoperative condition (IKDC = 47.1 ± 17.0), while the postoperative IKDC scores of the control group in the second year was 52.6 ± 16.4 worse than preoperative IKDC (54.0 ± 9.1). One year after operation, arthroscopy of 13 patients showed smooth appearance at the recipient site of CPs group, whereas the control group showed fibrillated surfaces. [Conclusions] Based on two studies, we demonstrated that cartilage defect treated with CPs resulted in improved knee functions, and stop the progress of osteoarthritis.

ICW28-1

Diabetes mellitus in patients with gout: risk factors and risk-reducing treatment

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Conflict of interest: None

Objectives: To evaluate the influence of RF for DM in pts with gout. **Methods**: 444 pts aged ≧18 years with diagnosis of gout without DM were included. The average duration of observation: 5.66 yrs. To identify the RF, multivariate logistic regression was used. There were included: gender; DM in relatives; age ≧45 yrs; ≧4 attacks of arthritis per yr; presence of tophi; BMI ≧30 kg/m^2; presence of hypertension; allopurinol, febuxostat, GC, diuretics, metformin or colchicine intake; GFR <60 ml/min/1.73 m^2; sUA level ≧420 μmol/l; UA ≧480 μmol/l. **Results**: DM was developed in 108 (24.3%) pts. Pts who developed DM were older than those who did not develop (52.84±10.96 vs 49.72±11.95, p=0.02); they took antihypertensive drugs more often (73.1% vs 50.5%, p=0.0001), also diuretics (27.7% vs 14.8%, p=0.003) and GC (47.2% vs 36.4%, p=0.047). There were more pts with tophi (59.3% vs 29.9%, p=0.001), those who had ≧4 attacks of arthritis per yr (67.6% vs 31.6%, p=0.001), sUA ≧480

μmol/l (71.3% vs 50.8%, p=0.0002), sUA ≧600 μmol/l (34.3% vs 11.8%, p=0.0002). According to a multivariable logistic regression, the risk of DM is increased in case of: ≧4 arthritis attacks per yr (odds ratio [OR] 5.231, 95% confidence interval [CI] 2.978-9.187, p=0.0001; presence of subcutaneous tophi (OR 2.609, 95% CI 1.500-4.537, p=0.001); sUA level ≧480 μmol/l (OR 20.261, 95% CI 1.022-5.004, p=0.144); hypertension (OR 2.577, 95% CI 1.348-4.926, p=0.004); taking diuretics (OR 2.353, 95% CI 1.193-4.64, p=0.014). The risk of developing DM was reduced by taking febuxostat (OR 0.309, 95% CI 0.113-0.844, p=0.022) and metformin (OR 0.49, 95% CI 0.21-1.16, p=0.107). **Conclusion**: The risk of DM in pts with gout is associated with the frequency of arthritis attacks, sUA level ≧480 μmol/l, hypertension and diuretics intake. Therapy with febuxostat or metformin is associated with descended risk of DM.

ICW28-2

Gender Parity in Rheumatology conference speakership: Is the Philippines leading the way ahead?

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Conflict of interest: None

Background: Gender representation at conferences needs to be equitable to facilitate progress in academia. The Philippines is a low to middle-income country in the Asia Pacific, with a relatively egalitarian gender social framework view. We aim to analyze the impact of divergent gender norms on gender equity in rheumatology conference participation, utilizing the data from the annual conferences of the Philippine Rheumatology Association (PRA) and review them with existing studies on other rheumatology conferences. **Methodology**: We used publicly available data from PRA conference materials from 2009 to 2021. Gender was identified based on the information from organizers, online science directory networks, and a name-to-gender inference platform, Gender application program interface (API). International speakers were separately identified. The search results were compared to examine gender parity between PRA and other rheumatology conferences around the world. **Results**: The proportion of PRA female faculty was 47%. Women were more likely to be first authors in abstracts at the PRA (68%). There were more females among new inductees in PRA with Male: Female ratio (M: F) of 1:3. The gender gap among new inductees declined from 5:1 to 2.7:1 from 2010 to 2015. A low female representation was observed among international faculty. (16%). When compared to other available rheumatology society study, EULAR has around 30-48% female moderators and speaker representation, ACR has 43%, and IRACON has 18%. **Conclusion**: Gender parity at the PRA conferences was found to better when compared to other rheumatology conferences. However, a wide gender gap was observed among PRA international speakers. Cultural and social constructs may contribute to gender equity in academic conferences. Further research is recommended to assess the impact of factors on gender parity in academia in other Asia Pacific countries.

ICW28-3

Post COVID-19 Syndrome in patients with autoimmune rheumatic diseases: Results from the COVAD Study

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Conflict of interest: None

Objective Post COVID-19 syndrome (PCS) is an emerging cause of morbidity & poor quality of life in COVID-19 survivors. We assessed prevalence, risk factors, outcomes, association with disease flares of PCS in autoimmune rheumatic diseases (AIRDs) and non-rheumatic autoimmune diseases (nrAIDs), vulnerable groups understudied, using data from 2nd COVID-19 Vaccination in Autoimmune Diseases (COVAD; 106 countries) global multicentre patient self-reported e-survey. **Methods** Survey was circulated from Feb-July 2022, demographics, comorbidities, AIRD/nrAID status, COVID-19 history, vaccination details, & PROMIS physical & mental function were recorded. PCS defined as symptom resolution time >90 days following acute COVID-19. PCS predictors analysed using regression models for different groups. **Results** Out of 7666 respondents, 2650 had COVID-19 infection, and 1677 (45% AIRDs, 12.5% nrAIDs, 42.5% HCs) completed survey >90 days post acute COVID-19. Of these, 136 (8.1%) had PCS. Prevalence of PCS was higher in AIRDs (10.8%) than healthy controls HCs (5.3%) (OR: 2.1; 95%CI: 1.4-3.1, p=0.002). Higher risk of PCS was seen in women (OR: 2.9; 95%CI: 1.1-7.7, p=0.037), with long duration of AIRDs/nrAIDs (OR: 1.01; 95%CI: 1.0-1.02, p=0.016), with comorbidities (OR: 2.8; 95%CI: 1.4-5.7, p=0.005), & those requiring O_2 supplementation for severe acute COVID-19 (OR: 3.8; 95%CI: 1.1-13.6, p=0.039). Among AIRDs, comorbidities (OR: 2; 95%CI: 1.08-3.6, p=0.026), & advanced treatment (OR: 1.9; 95%CI: 1.08-3.3, p=0.024)/intensive care (OR: 3.8; 95%CI: 1.01-14.4, p=0.047) for severe COVID-19 were risk factors for PCS. PCS patients had poorer PROMIS global physical [15 (12-17) vs 12 (9-15)] & mental health [14 (11-16) vs 11 (8-14)] scores than those without PCS. **Conclusions** AIRDs have greater risk of PCS than HCs. Associated comorbidities, & advanced treatment/intensive care unit admission for severe COVID-19 confer a higher risk of PCS. It is imperative to identify risk factors for PCS for multidisciplinary management in anticipation of poor physical & mental health.

ICW28-4

Association between psoriasis risk and antidiabetic drugs in diabetic patients: a nationwide population-base study in Taiwan

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Conflict of interest: None

[Objective] The risk of psoriasis in diabetic patients has rarely been explored. This study aimed to investigate the association between dipeptidyl peptidase-4 (DPP4) inhibitors and the risk of psoriasis in type 2 diabetes mellitus (T2DM) patients. [Methods] We conducted a population-based propensity score-matched cohort study on the basis of Taiwan's National Health Insurance Research Database that included initiators of combination therapy with DPP4i (DPP4i plus metformin) and sulfonylurea (sulfonylurea plus metformin). Psoriasis (PSO) was identified with ≧2 diagnoses. Diabetes complications severity index (DCSI) was calculated. A total

of 22721 DPP4 initiator and 227684 sulfonylurea initiator were identified. A 1:10 matched-pair cohort based on propensity score (PS) was created. PS-stratified Cox proportional hazards models compared the risk of PSO in DPP4i versus sulfonylurea initiator within 2 years, controlling for potential confounders. [Results] After propensity score matching, 9962 patients with T2DM starting DPP4i combination therapy and 39848 starting sulfonylurea combination therapy were selected. The incidence rate of PSO was lower in DPP4i group (188/100000 person- years) than in sulfonylurea group (467/100000 person-years). Risks of incident psoriasis were significantly lower in the DPP4i group versus sulfonylurea with the PS-stratified HR of 0.422 (95% CI 0.273 to 0.716). [Conclusions] DPP4i plus metformin was associated with a reduced risk of psoriasis than sulfonylurea plus metformin. These findings merit further investigation.

ICW28-5

Telemedicine for follow-up of systemic lupus erythematosus in the Covid-19 outbreak: a pragmatic randomised controlled trial

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Conflict of interest: Yes

[Objective] To compare the outcomes of patients with SLE managed by telemedicine (TM) and standard face-to-face consultations during the COVID-19 outbreak. [Methods] This was a 1-year, open-label randomized controlled trial conducted at a regional hospital in Hong Kong. From May 2020, consecutive adult patients with a diagnosis of SLE followed up at the clinic were invited to participate in the study. Participants were randomized 1:1 to either TM (TM group) or standard FU (SF group). Patients randomized to receive TM FU were scheduled for a video consultation via a real-time video conferencing software ZOOM. Patients in the SF group received standard in-person outpatient care. [Results] A total of 144 patients were randomized and 3 patients self-withdrew from the study. At the end of the study, 70 patients in the TM group and 71 patients in the SF completed 1-year FU. There were no baseline differences between the 2 groups. At one year, 80% and 80.2% of the patients in the TM group and SF group were in low disease activity or remission respectively. SLE disease activity indices remained similar between the 2 groups. There were no differences in the SF-36, lupusQoL and HADS scores between the 2 groups at the end of the study. The overall patient satisfaction score was higher in the TM group with a significantly shorter waiting time. The mean out-of-pocket costs of illness were similar between the 2 groups. However, significantly more patients in the TM group requested switch of mode of FU. The proportion of patients requiring hospitalization during the study period was also higher in the TM group. After adjusting for age and prednisolone dosage, not being in low disease activity at baseline was the predictor of hospitalization (OR 3.4, 95%CI 1.20-9.65). [Conclusions] TM delivered care could help maintaining disease control and psychosocial wellbeing during the pandemic, but it might need to be complemented by physical visits, particularly in those with unstable disease.

ICW29-1

Enhanced cellular glycolysis contributes to peripheral B cells hyperactivity induced by IL-27 in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] B cells are essential in rheumatoid arthritis (RA) pathogenesis via antibody-dependent and independent pathways. Considerable efforts have been performed to explore various signaling pathways in regulating B cell biological function. But how these signaling pathways reprogram B cell metabolism to affect the cell fate remains unclear within RA. Glycolysis was increased significantly in RA B cells and glycolysis inhibition downregulated RA B cell proliferation, differentiation, and inflammatory actions. The enhanced cellular glycolysis induced by IL-27 might contribute to B cell hyperactivation by activating the mTOR signaling pathway in RA. Targeting IL-27 or glycolysis may be an efficient therapy to ameliorate the clinical symptoms of RA. [Methods] Here we purified peripheral CD19+ B cells from healthy controls (HC) and RA patients, which were cultured with or without anti-CD40/CpG and glycolysis inhibitor 2-deoxy-D-glucose (2-DG) or mTOR inhibitor rapamycin. Furthermore, the isolated CD19+ B cells were treated by HC serum or RA serum in the presence and absence of recombinant human IL-27 or anti-IL-27 neutralizing antibodies or 2-DG or rapamycin. The B cell glycolysis level, proliferation, differentiation, and inflammatory actions were detected with the analysis of qPCR, flow cytometry or ELISA. [Results] We found that compared to HC B cells, glycolysis was increased significantly in RA B cells and glycolysis inhibition downregulated the proliferation, differentiation, and inflammatory actions of RA B cells. RA serum and IL-27 promoted B cells glycolysis and inflammatory phenotypes, which could be obviously rescued by anti-IL-27 antibodies or 2-DG or rapamycin. [Conclusions] All these results suggested that enhanced cellular glycolysis of RA B cells induced by IL-27 might contribute to B cells hyperactivation through activating the mTOR signaling pathway. Targeting IL-27 or glycolysis may be an efficient therapy to ameliorate the clinical symptoms of RA.

ICW29-2

Tissue-Resident Memory T cell differentiation and pathological relevance to early rheumatoid arthritis -FIRST registry/FLOW study-

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Conflict of interest: None

[Objective] Tissue-Resident Memory T cells (Trm) were identified in the joint localization of rheumatoid arthritis (RA). Trm expresses the surface molecules CD69 and CD103 and survives long-term in peripheral tissues. However, the mechanism of human Trm differentiation and its involvement in the pathogenesis of RA is unclear. We investigated (1) human Trm differentiation mechanisms and functions in vitro, (2) the characterization of Trm in peripheral blood of RA patients based on a large RA cohort (FIRST registry) and comprehensive immunophenotyping (FLOW study). [Methods] We cultured naive $CD8^+$ T cells ($CD45RA^+CCR7^+$) isolated from the peripheral blood of healthy subjects under various stimulations and evaluated cell surface molecules, cytokines/serine protease production, and transcription factor by flow cytometry and PCR. Next, we compared the percentage of CD69-positive cells in peripheral blood $CD3^+$ T cells of RA patients with clinical findings. The study consisted of 310 patients with early-stage (≦12 months) b/ts DMARDs-treat-naive RA (mean age 62.0 years, 71.6% female, mean disease duration 6.2 months) who were enrolled in the FIRST registry between 2003 and 2022 and 30 age-sex matched healthy controls (HC). [Results] (1) $CD8^+CD69^+CD103^+$ T cells (Trm like cells) increased after TCR+TGF-β1+IL-7 or IL-15 stimulation from naïve $CD8^+$ T cells ($p<0.01$). (2) TCR+TGF-β1+IL-15 stimulation increased the expression of Trm characteristic transcription factors RUNX3, BATF, NR4A1, and Blimp-1 and decreased KLRG1 expression in cultured cells ($p<0.01$). (3) Trm like cells produced inflammatory cytokines, granzyme B, and long-term survival in vitro. (4) Patients with refractory RA requiring more than 2 b/ts DMARDs in 3 years had a significantly higher percentage of pretreatment $CD3^+CD4^-CD69^+$ cells ($p=0.028$). [Conclusions] TGF-β1+IL-15 stimulation was essential for Trm differentiation. Peripheral blood Trm like cells may be associated with treatment resistance in RA patients.

ICW29-3

TLR2 causes abnormal CD4+T cell function to participate in the progression of rheumatoid arthritis by promoting ROS production

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease. Activated CD4+T cells induce inflammatory response and participate in the disease process. Previous studies have shown that CD4+T cells express Toll-like receptor (TLR) 2, but its specific function in RA remains unclear. The aim of this study was to investigate the role of TLR2 signaling in CD4+T cells and its influence on the disease progression of RA, so as to provide new strategies for the prevention and treatment of RA. [Methods] Serum samples were collected from RA patients and healthy subjects, and the content of soluble TLR2 (sTLR2) was detected by ELISA. The expression of TLR2 in CD4+T cells and activation of CD4+T cells were detected by FACS. Purified CD4+T cells from RA patients were stimulated by TLR2 ligand P3C, and the activation, cytokine and ROS production levels were detected by FACS. Purified CD4+T cells from RA patients were stimulated with P3C and mitochondrial ROS were removed, and the corresponding functional changes were detected by FACS. [Results] 1. Compared with healthy subjects, serum sTLR2 content in RA patients was higher, and was positively correlated with CRP and RF. The expression of TLR2 was higher in CD4+T cells of RA patients. 2. In CD4+T cells of RA patients, TLR2+ cells expressed higher levels of CD25, CD40L, CD69, PD-1 than TLR2- cells. 3. P3C stimulation of purified CD4+T cells from RA patients can up-regulate activation markers, and promote the production of TNFα, intracellular total ROS and mitochondrial ROS. 4. After P3C stimulation of purified CD4+T cells from RA patients and removal of mitochondrial ROS, the expression of CD25 and CD40L was down-regulated, and the production of TNFα was decreased. [Conclusions] The increased expression of TLR2 in peripheral CD4+T cells of patients with RA can promote abnormal activation of CD4+T cells and secretion of TNFα in a mitochondrial ROS-dependent manner, which is involved in the occurrence and development of RA.

ICW29-4

TSLP mediates the pathogenesis of rheumatoid arthritis mediated by stimulating B cells to produce antibodies by activating T cells

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Conflict of interest: None

[Objective] Thymic stromal lymphopoietin (TSLP) is a cytokine mainly secreted by epithelial cells. Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic synovitis and bone erosion, patients show elevated antibodies, but the pathogenesis of RA is not fully understood, our preliminary results found that TSLP has a certain role in the pathogenesis of RA, this study aims to explore the process and related mechanisms of TSLP participation in RA. [Methods] Collect blood samples of rheumatoid arthritis (RA) and healthy people (HC), and use protein chips and ELISA to detect TSLP levels and related clinical indicators in RA patients and HC serum; The ratio of TSLP to plasma cells, plasma blasts, B reg cells and memory B cells in B cells and T and B co-culture systems was detected by flow cytometry. The effect of TSLP on the expression of IL-6, IL-10 and IL-21 cytokines was detected by PCR technology. RNA sequencing and flow cytometry were used to investigate the effect of TSLP on T cell subpopulation differentiation. [Results] 1. The serum level of TSLP in RA patients was higher than that of normal people, and the TSLP in serum of RA patients was positively correlated with related clinical indicators such as antibodies. 2. TSLP can upregulate the content of antibodies in the T and B co-culture system; 3. TSLP can stimulate the activation of CD4+ T cells, promote proliferation and inhibit apoptosis; 4. RNA sequencing and experimental results showed that TSLP increased IFN-γ secretion, increased the proportion of Th 1 cells, and increased IL-21 and CXCL13 secreted by Tfh cells. [Conclusions] These findings indicate that TSLP has a new mechanistic role in the occurrence and development of RA, which may promote the production of IL-10, IL-21, and other cytokines by Tfh cells by promoting T cell activation, thereby stimulating B cells to produce autoantibodies and promoting the occurrence and development of RA.

ICW29-5

Parsing synovial pathology related to treatment resistance in Japanese rheumatoid arthritis patients by single-cell analysis

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Conflict of interest: None

[Objective] Recent advances in single-cell RNA sequencing (scRNA-seq) technology have improved our understanding of the immunological landscape of rheumatoid arthritis (RA), mainly in non-Asian races. We aimed to stratify the RA synovium from Japanese patients based on single-cell transcriptomics, and gain insight into the pathological drivers related to treatment resistance. [Methods] Synovial specimens were obtained from 31 RA patients using ultrasound-guided needle biopsy. The proportion of 5 immune cell subsets ($CD4^+$ T cells, $CD8^+$ T cells, B cells, NK cells, monocytes) and mesenchymal cells (synovial fibroblasts (SF), endothelial cells, mural cells) were analyzed by flow cytometry. $CD45^+$ and $CD45^-$ live cells were isolated, and scRNA-seq was performed using the 10x chromium system. [Results] Treatment status at the time of biopsy was classified into the following three groups; treatment-naïve, inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs-IR) or biological DMARDs (bDMARDs-IR). The proportion of $CD8^+$ T cells, especially *GZMB*$^+$ *GZMK*$^+$ $CD8^+$ T cells, was lower in csDMARDs-IR patients compared to treatment-naïve patients. This population is characterized by enhanced expression of *IFNG*, the cooperative inducer of IL-6 production from SF. Meanwhile, an increased proportion of SF, especially *THY1*^{low} sublining and *CD34*$^+$ sublining, was observed in csDMARDs-IR and bDMARDs-IR patients. Notably, *THY1*^{low} sublining was indicated to be activated independently of the effects of inflammatory cytokines in the synovium (e.g., TNF-α, IL-1β, IFNs). This SF subpopulation is presumed to be less susceptible to modification by existing therapeutic agents, suggesting the possibility of contributing to treatment resistance. [Conclusion] The synovial analysis has the potential to be useful in elucidating the mechanism of treatment resistance in Japanese RA patients and in searching for novel therapeutic targets.

ICW29-6

Five immunophenotypes of rheumatoid arthritis (RA) with different responses to molecular targeted therapies

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Conflict of interest: Yes

[Objective] Molecular targeted therapies induce different changes in different immune cell phenotypes. We stratified RA patients by immunophenotyping and investigated the response to targeted therapy. [Methods] 533 bio-naive RA patients and 96 healthy controls (HC) were enrolled.

Immune cell profiling (T, B, NK, dendritic cells, and monocyte) was performed by flow cytometric analysis termed "the Human Immunology Project". [Results] CD4 T cell differentiation was mainly affected in RA patients compared to HC, with elevated effector T cells and effector memory T cells re-expressing CD45RA (TEMRA). However, there was no change in the proportion of Th1, Th17, Treg, and Tfh cells. Cluster analysis stratified RA patients into 5 groups. When dimension reduction of their immunophenotypes was performed by UMAP, these groups were clearly separated. While group 1 had an immunophenotype identical to HC, group 2 had fewer Treg cells, and group 3 showed B cell activation. The remaining 2 groups had RA specific phenotypes with little overlap with HC (group 4 and 5). These 2 groups were accompanied by a marked increase in TEMRA with increased effector memory T cells (group 4) and with increased Th1 (group 5). Baseline disease activity and ACPA/RF positivity were similar among the groups. Of note, the clinical efficacy of each targeted therapy was statistically different in each group. Briefly, in group 1 and 2, JAK inhibitors and IL-6R inhibitors were effective, while TNF inhibitors were effective in group 3 and 4. CTLA4-Ig was effective in group 4 and 5. Analysis of immunophenotypes after treatment revealed that the first 3 groups approached the HC phenotype. However, TEMRA remained elevated in TEMRA dominant groups (groups 4 and 5). Interestingly, CTLA4-Ig decreased the proportion of TEMRA. [Conclusions] RA patients can be stratified into 5 groups, each of which benefited from different molecular targeted therapy. Our results could be a milestone in achieving precision medicine.

ICW30-1

Pathologically expanded peripheral CD4+PD-1+Foxp3- T cell subset promotes B cell hyperactivity in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] This study aims to explore the pathogenic characteristics and roles of $CD4^+PD\text{-}1^+Foxp3^-$ T cells in rheumatoid arthritis (RA). [Methods] The frequencies and the characteristics including proliferation, activation, and cytokine-producing profile of peripheral $CD4^+PD\text{-}1^+Foxp3^-$ T cells in RA patients were evaluated by FACS. $CD4^+PD\text{-}1^+CD25^-$ T cells isolated from RA patients by FACS were co-cultured with $CD19^+$ B cells. The differentiation of B cells was analyzed by FACS. The production of immunoglobulin was determined by ELISA. RA $CD4^+$ T cells were treated with different cytokine antagonists. The expansion, activation, and cytokine production of $CD4^+PD\text{-}1^+Foxp3^-$ T cells were tested by FACS. [Results] The frequencies of $CD4^+PD\text{-}1^+Foxp3^-$ T cells were up-regulated in RA patients. The expansion of $CD4^+PD\text{-}1^+Foxp3^-$ T cells was positively correlated with B cell response. Compared with $CD4^+PD\text{-}1^+Foxp3^+$ T cells, RA $CD4^+PD\text{-}1^+Foxp3^-$ T cells exhibited more increased expressions of Ki67 and activation markers including ICOS, CD40L, HLA-DR and CD38 and produced higher levels of IFN-g, IL-4, IL-6, IL-10, and IL-21. Importantly, Compared with $CD4^+PD\text{-}1^+CD25^+$ T cells, RA $CD4^+PD\text{-}1^+CD25^-$ T cells obviously promoted B cell differentiation into plasmablast and secretion of IgM in vitro. The expressions of ICOS, CD40L, IL-6, and IL-21 in RA peripheral $CD4^+PD\text{-}1^+Foxp3^-$ T cells were down-regulated after anti-IL-6R antagonist treatment in vitro. [Conclusions] We confirmed peripheral expanded $CD4^+PD\text{-}1^+Foxp3^-$ T cells in RA patients, which induced B cell hyperactivity. Our findings shed light on the involvement of extrafollicular T-B cell interactions in the pathogenesis of RA.

ICW30-2

Blocking Receptor-type Protein Tyrosine Phosphatase Alpha Ameliorates Mouse Arthritis by Suppressing Migration Activity of Synovial Fibroblasts

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Conflict of interest: None

[Objective] Receptor-type protein tyrosine phosphatase alpha (RPTPα) is one of transmembrane PTPs, which activates SRC kinase and promotes fibroblast-dependent arthritis. We previously showed that *Ptpra* knockout (αKO) mice were protected from serum transfer-induced arthritis (STIA). RPTPα includes an ectodomain, wedge motif and two intracellular catalytic domains (D1 and D2). It remains unknown whether RPTPα mutation in D1 domain or wedge motif, deletion of D2 domain (dD2) and blocking ectodomain reduce migration activity of synovial fibroblasts (SF) and arthritis. The purpose of this study is to investigate the effects of RPTPα modifications on SF migration in vitro and arthritis in mice. [Methods] SF lines were isolated from wild type (WT), *Ptpra* KO (αKO) or *Ptpra* C469S (CS) (catalytic domain D1 mutation) mice. In vitro, CS SF or αKO SF transfected with WT *Ptpra*, P201L/P211L (P210) *Ptpra* (wedge motif mutation) or dD2 *Ptpra* constructs were assessed by several microscopic technologies (super-resolution microscopy, FRET technologies) and/or migration assays. A RPTPα ectodomain-blocking antibody (2F8 antibody) was used against WT SF in vitro. STIA mouse model was used to assess the effects of CS mutation and 2F8 antibody on arthritis severity. [Results] A catalytically-inactivating CS mutation reduced SRC activation in SF and protected mice from arthritis. αKO SF with P210 and αKO SF with dD2 reduced RPTPα-RPTPα clustering and RPTPα-SRC association. The same mutations also reduced recruitment of RPTPα to actin-rich structures and suppressed SRC activation and SF migration. 2F8 antibody, which de-clustered RPTPα, also reduced RPTPα-SRC association and SRC activation. Furthermore, 2F8 antibody suppressed SF migration and joint damage in arthritic mice. [Conclusions] Impaired RPTPα catalytic activity or blocking RPTPα clustering suppresses SF migration and arthritis via SRC inactivation.

ICW30-3

The potential role of the IFN-gamma-CCL17 axis in rheumatoid arthritis

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Conflict of interest: Yes

[Objective] The chemokine CCL17 is implicated in rheumatoid arthritis (RA). Previous studies using arthritic mice demonstrated that the receptor for CCL17 is expressed on Th2 and Th1 cells and that granulocyte macrophage colony-stimulating factor (GM-CSF) stimulates monocytes/macrophages and promotes CCL17 production; however, studies in humans are scarce. In this study, we aimed to examine which clinical parameters as well as cytokines are associated with CCL17 levels in patients with RA. [Methods] RA patients who visited Kyoto University Hospital between April 2020 and March 2021 and gave written informed consent to this study were cross-sectionally enrolled. Medical records were retrospectively reviewed. Plasma levels of CCL17 and cytokines, including IL-1β, IL-6, TNFα, IFN-γ, IL-4, IL-17A, and GM-CSF were evaluated by Luminex Discovery Assay (R&D systems). Association between CCL17 levels and clinical parameters was assessed by multiple linear regression analysis or Pearson correlation analysis after normality test. [Results] A total of 66 RA patients were enrolled. The median age was 68 years (IQR 59-73), females were dominant (83.3%), and median DAS28-CRP was 1.58 (1.29-2.29). RF and anti-CCP antibodies were positive in 47 (71.2%) and 46 patients (69.7%), respectively. Methotrexate, prednisolone, bDMARDs or tsDMARDs were concomitantly used in 46 (69.7%), 19 (28.8%), 36 (54.5%), and 1 patients (1.5%), respectively. Among clinical

parameters, plasma CCL17 levels were significantly associated with DAS28-CRP (P=0.03). Then, we examined the association between plasma CCL17 levels and cytokines. Plasma CCL17 levels were significantly associated with IFN-γ (P=0.01), particularly in RF-positive patients (P=0.0005), but not associated with GM-CSF (P=0.40). [Conclusions] Our study results suggest that CCL17 level can be a marker of disease activity of RA and that IFN-γ-CCL17 axis may form a vicious cycle through Th1 cell recruitment particularly in seropositive RA.

ICW30-4

Immunological profiling identified clinical correlates and predictors of rheumatoid arthritis

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Conflict of interest: Yes

[Objective] Rheumatoid arthritis (RA) patients are heterogeneity in their clinical phenotype and in response to molecular targeted therapies. To identify immunological correlates of clinical phenotypes and predictors of treatment response, we performed peripheral blood multi-omics profiling of RA patients initiating abatacept treatment. [Methods] In the PREDICTABA study, we have recruited 104 RA patients starting abatacept treatment. Peripheral blood mass cytometry analysis was performed in discovery and validation cohorts (n=79 and 22). In total, 10 million T and B cells were clustered. After accounting for the effects of age, sex, CDAI disease activity, anti-CCP antibody titer, and donor batch effects, immune cell clusters were tested for their association with baseline treatment and future abatacept treatment response (CDAI improvement at 6 months) using logistic mixed model. Peripheral blood RNA-seq identified immune cell signatures and immune pathway signatures. [Results] At baseline, median age was 73 years. 80% were female and 80% were seropositive. Median CDAI improved from 17 to 5 after 6 months of abatacept treatment. RNA-seq immune cell gene signatures validated mass cytometry immune cell cluster frequencies. Naive CD8 T cells were negatively associated with age (odds ratio (OR) 0.57 and 0.32, *P*-values<0.001). Naive B cells were negatively associated with baseline prednisolone use (OR 0.53 and 0.25, *P*-values<0.001). Plasmablasts were negatively associated with baseline methotrexate use (OR 0.59 and *P*-value<0.001), and with IL6_JAK_STAT3 signaling gene signature (Rho=-0.36, *P*-value<0.001). Finally, $CD25^{+}CD8^{+}$ T cells showed suggestive association with CDAI improvement after abatacept treatment (OR 1.4 and 1.6, *P*-values 0.01 and 0.07). [Conclusions] B cell subsets are associated with conventional RA treatments. Abundance of $CD25^{+}CD8^{+}$ T cells may be predicative of good abatacept response.

ICW30-5

Relationship of Semaphorin 3A to the pathogenesis of rheumatoid arthritis

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Conflict of interest: Yes

[Objective] Semaphorin 3A (SEMA3A) plays pleiotropic roles in neural development, angiogenesis, the immune system, and bone protection. The purpose of this study is to determine the function of SEMA3A in the pathogenesis of rheumatoid arthritis (RA). [Methods] SEMA3A expression in the synovial tissues was evaluated by immunostaining. To investigate the cellular source of SEMA3A, fibroblast-like synovial cells (FLS) and osteoblast cell lines (IDG-SW3 cells) were stimulated with proinflammatory cytokines such as TNF-α, IL-6, and GM-CSF, followed by real-time PCR and Western blotting. The effects of SEMA3A on FLS survival, migration, and cytokine production were evaluated by flow cytometry, transwell assay, and ELISA, respectively. Serum concentrations of SEMA3A were measured in patients with rheumatic diseases including RA (n=46), systemic lupus erythematosus (n=20), Sjögren's syndrome (n=17), systemic sclerosis (n=22), ANCA-associated vasculitis (n=85), and in healthy controls (n=29) by ELISA. Bio-plex assay was also performed to evaluate the various serum cytokine levels. [Results] In RA synovial tissues, SEMA3A is expressed on CD55-positive fibroblasts. mRNA expression levels of *sema3a* in CD55-positive FLS were significantly decreased upon stimulation with TNF-α or IL-6. GM-CSF induced the secretion of SEMA3A from IDG-SW3 cells. SEMA3A suppressed the migration of FLS via its receptors Nrp-1 and Plexin-A1. The levels of serum SEMA3A, especially a form of SEMA3A with potent biological activity, in patients with RA were significantly higher compared with those in patients with other rheumatic diseases. Active SEMA3A levels were positively correlated with RA disease activity and proinflammatory cytokine levels such as TNF-α, IL-6, and GM-CSF. [Conclusions] SEMA3A is produced by osteoblasts in RA patients with high disease activity. SEMA3A acts protective in the pathogenesis of RA by suppressing synovial cell migration via Nrp-1 and Plexin-A1.

ICW30-6

Expansion of pathological and highly cytotoxic SLAMF4+ CCR5+ effector memory CD4+ T cells in rheumatoid arthritis

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Conflict of interest: None

[Objective] Conventional CD4+ Foxp3- T cells (Tconv) play a key role in the inflammatory process involved in rheumatoid arthritis (RA). SLAMFs (Signaling lymphocytic activation molecule) represent a family of nine receptors able to upregulate the Tconv response, whose involvement in the control of the Tconv response remains largely unexplored in RA. Our objective was to determine the role of SLAMFs in the shaping of the pro-inflammatory response of Tconv in RA. [Methods] We analyzed by flow cytometry the expression of SLAMFs by different subpopulations of Tconv. For this purpose, peripheral blood mononuclear cells (PBMC) from RA patients (n=64) and healthy donors (HD) (n=14) were used. After cells sorting (BD FacsARIA II), the transcriptome of SLAMF4+ CCR5+ Tem was compared to that of their SLAMF4- counterpart (RNAseq). Expression of cytokines, molecules related to cytotoxic activity, and chemokine receptor expression by SLAMF4+ Tem were studied by flow cytometry. [Results] Among the different SLAMFs and subpopulations of Tconv studied, only the frequency of SLAMF4+ cells among Tem was positively correlated with disease activity. Furthermore, our results show that among SLAMF4+ Tem only those expressing the chemokine receptor CCR5 were related to RA activity (DAS28-VS vs % of SLAMF4+ CCR5+ cells among Tem, R=0.65, p<0.0001). Results of RNAseq experiments and associated analyses, highlighted an overexpression by SLAMF4+ CCR5+ Tem of genes associated with cytotoxic activity (GZMA, GZMB, GZMH, GNLY, PRF1, FASLG, KLRD1...). Our data confirmed at the protein level that SLAMF4+ CCR5+ Tem correspond to a Th1-like subpopulation of cytotoxic Tconv. [Conclusions] This study describes for the first time a new subpopulation of cytotoxic Tconv, the SLAMF4+ CCR5+ Tem, and reveals its close link with the pathophysiology of RA. Further studies will be needed to determine how to target SLAMF4+ CCR5+ Tem, and to evaluate their involvement in the response to targeted therapies in RA.

ICW31-1

MS4A4A expression in peripheral blood monocytes of patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] Membrane Spanning 4-Domains A4A (MS4A4A) is a tetraspanin transmembrane protein expressed on monocytic cells and was identified as a disease activity-related gene in rheumatoid arthritis (RA). The aim of this study was to identify the MS4A4A protein expression in monocytes subsets in relation to RA. [Methods] Peripheral blood mononuclear cells (PBMCs) were cross-sectionally collected from healthy donors (HD), polymyalgia rheumatica (PMR) patients and RA patients. Classical ($CD14^{hi}CD16^{-}$), intermediate ($CD14^{hi}CD16^{+}$) and non-classical ($CD14^{lo}CD16^{+}$) monocyte were analyzed by flow cytometry. [Results] We enrolled 17 HD, 18 PMR, and 79 RA patients. Median age [interquartile range] was 32 [27, 37], 77 [69, 84], 65 [55, 77] with female (rate) 8 (47.1%), 13 (72.2%) and 68 (86.1%), respectively. Frequency of MS4A4A positive monocyte was 7.3 [2.8, 9.4] %, 7.2 [4.6, 9.7] %, 12.2 [7.9, 20.4] %, respectively, demonstrating specific and significant increase in RA ($p<0.001$). Distribution of classical, intermediate ($CD14^{hi}CD16^{+}$) and non-classical monocytes ($CD14^{lo}CD16^{+}$) was similar among the 3 groups. Although MS4A4A positive rate in classical and non-classical monocyte was similar among the 3 groups, marked elevation was observed in non-classical monocytes from RA (HD; 39.8 [22.8, 49.0] %, PMR; 44.2 [29.2, 63.6] %, RA; 64.9 [45.5, 82.6] %, $p<0.001$). However, frequency of MS4A4A positive non-classical monocytes did not correlate with collected RA clinical information; age ($p=0.31$), gender ($p=0.62$), anti-CCP antibody titer ($p=0.054$), RF titer ($p=0.67$), DAS28-ESR ($p=0.75$), methotrexate dose ($p=0.89$), or steroid dose ($p=0.52$). [Conclusion] Cross-sectional analysis of MS4A4A protein expression in peripheral monocytes did not relate with RA clinical information including disease activity. However, specific increase in frequency was observed in non-classical monocyte indicating the involvement of MS4A4A in the pathogenesis of RA.

ICW31-2

Filgotinib Inhibits the Differentiation and Function of Tumor Necrosis Factor alpha and Interleukin-6- Induced Osteoclasts Derived from Peripheral Blood Monocytes in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Janus kinase (JAK) inhibitors compose a new class of drugs, among which filgotinib has been approved for the treatment of rheumatoid arthritis (RA). We have recently reported that stimulation of human peripheral blood monocytes (PBMs) with TNF-α and IL-6 induces differentiation of osteoclasts (OCs) with bone resorption activity in vivo and in vitro. Additionally, the number of TNF-α and IL-6-induced OCs generated from PBMs was significantly associated with the magnitude of joint destruction in RA patients, however, that of RANKL-induced OCs was not. We undertook this study to clarify whether filgotinib could inhibit the differentiation of TNF-α and IL-6-induced OCs using PBMs collected from patients with RA. [Methods] PBMs derived from RA patients and healthy donors were stimulated by TNF-α and IL-6 or RANKL with or without 10-1000 nM filgotinib. The number of tartrate-resistant acid phosphatase-positive multinucleated cells induced with TNF-α and IL-6 or RANKL were assessed. A pit formation assay on dentine slices was performed. [Results] PBMs collected from patients with RA showed higher TNF-α and IL-6- or RANKL-induced OC differentiation potentials compared with those from healthy donors. Filgotinib inhibited the differentiation of TNF-α and IL-6-induced OCs derived from PBMs of RA patients in a dose-dependent manner. The same concentrations of filgotinib did not inhibit osteoclastogenesis induce by RANKL. Stimulation of PBMs by TNF-α and IL-6 with filgotinib inhibited generation of resorption pits compared to findings in those PBMs without filgotinib. In contrast, stimulation by RANKL with filgotinib showed resorption pits in a manner similar to those generated by RANKL without filgotinib. [Conclusions] Our results suggest that the prevention effect of progressive bone destruction by filgotinib in RA patients may involve inhibition of TNF-α and IL-6-induced OC differentiation, as well as suppression of osteoclastic bone resorption activity.

ICW31-3

Solid Dispersion Formulation Enhanced Dissolution Efficacy of Rheumatoid Arthritis Pain Management Drug - Ketoprofen

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Conflict of interest: None

Objective: Ketoprofen (KETO) is effectively used in moderate to severe pain associated with rheumatoid arthritis. It is a BCS class-II drug bearing poor water solubility, and therefore shows a low dissolution rate and systemic absorption. Aim of the present study was to improve the solubility and dissolution rate of KETO by solid-dispersion approach. **Methods**: Solid dispersions were prepared by using polyvinylpyrrolidone K30 (PVP K30) and D-mannitol in different drug-to-carrier ratios. Dispersions with PVP K30 were prepared by kneading and solvent evaporation techniques, whereas solid dispersions containing D-mannitol were prepared by kneading and melting techniques. These formulations were characterized in the liquid state by phase-solubility studies and in the solid state by Differential Scanning Calorimetry (DSC), Fourier Transform Infrared (FTIR) spectroscopy, X-ray diffraction (XRD) and Scanning Electron Microscopy (SEM). **Results**: The aqueous solubility of KETO was favored by the presence of both carriers. The negative values of Gibbs free energy illustrate the spontaneous transfer from pure water to the aqueous polymer environment. Solid state characterization indicated KETO was present as fine particles in D-mannitol solid dispersions and entrapped in the carrier matrix of PVP K30 solid dispersions. In contrast to the very slow dissolution rate of pure KETO, dispersions of drug in carriers considerably improved the dissolution rate. This can be attributed to increased wettability and dispersibility, as well as decreased crystallinity and an increase in the amorphous fraction of the drug. **Conclusion**: Solid dispersions prepared with PVP K30 showed the highest improvement in the dissolution rate of KETO. Even physical mixtures of KETO prepared with both carriers also showed better dissolution profiles than those of pure KETO.

ICW31-4

Composition of Intestinal Bacteria and Disease Activity in Rheumatoid Arthritis Patients

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Conflict of interest: None

[Objective] Microbiome study gain attention in the study of rhaumatoid arthritis (RA). Study of dysbiosis in RA using animal models, mostly performed to established its role in conjunction with other risk factors for developing clinical RA. Human study mostly comparing microbiome composition between RA and non-RA group. Intestinal microbiome mainly consists of Firmicutes and Bacteroidetes (80-90%) followed by Actinobacteria and Proteobacteria comprising <15%. Our preliminary study aim to obtain number of dominant microbiome phylae in different disease activity state of RA subjects. [Methods] Twelve subjects divided into remission-low disease activity group and moderate-high disease activity group, were consecutively selected for DAS-28 ESR assessment and fecal 16S rRNA sequencing. [Results] Of 12 subjects, 10 were females, age ranging from 28 - 73 years old, 4 subjects were in remission, 2 in low disease activity and 6 in moderate disease activity. Mean percentage of Actinobacteria, Proteobacteria, Bacteroidetes and Firmicutes in remission-low disease activity were 2.5 (0.9-4.0), 9.7 (2.0-18.0), 51.5 (30-63), and 33.3 (27-50)% respectively, while in moderate-high disease activity were 2.1 (0.5-3.0), 6.8 (2-17), 49.2 (43-57), and 39.5 (33-50)% respectively. This preliminary study shows no similar pattern of 4 phylae compositions in regards of disease activity, several confounding factors include treatment and dietary compositions and other influencing factors were not assessed. Microbes interact one another to maintain the environment through *quorum sensing* mechanism. Microbiome studies should include affecting factors (i.e. SCFA production) to identify role of dysbiosis. [Conclusions] This study

does not find similar pattern of 4 phylae composition in RA patients based on disease activity. Further studies required and should include other affecting parameters and surrogate parameters.

ICW31-5

Identification of CD4+T-cell subsets critically involved in clinical characterization of early rheumatoid arthritis

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Conflict of interest: None

[Objective] Pathophysiological mechanisms of early rheumatoid arthritis (RA) are still largely unknown due to the lack of studies which performed the detailed analysis of immune cell subsets in treatment-naïve patients. In this study, we aimed to identify CD4+T-cell subsets important for clinical characterization of early RA in a large cohort of treatment-naïve patients. [Methods] Treatment-naïve, active patients with early RA (n=48) and healthy controls (HC, n=20) were included. A total of 34 subsets of CD4+T cells in peripheral blood were analyzed with flow cytometry. Composite measures such as simplified disease activity index were calculated to assess disease activity. [Results] Our comprehensive immunophenotyping identified 10 subsets to be significantly increased in early RA, while 6 subsets to be significantly decreased compared with HC. Among them, the increased proportion of CCR5+T helper type 2 (Th2) subset was positively correlated with disease activity indices. On the other hand, the increased proportions of CCR5+T follicular helper type 2 (Tfh2) subset and TIGIT+Tfh2 subset were positively correlated with titers of rheumatoid factor and anti-CCP antibody, respectively. Notably, the proportions of CCR5+Tfh2 and TIGIT+Tfh2 subset were increased in seropositive patients as compared with seronegative patients, while seronegative patients exhibited higher proportion of T helper type 17 (Th17) subset than seropositive patients. Furthermore, patients with interstitial lung disease showed the increased proportions of CCR5+Tfh2 compared with those without. [Conclusions] Our results suggest that different CD4+T-cell subsets, CCR5+Th2, CCR5+Tfh2, TIGIT+Tfh2 and Th17, are involved in pathogenesis of distinct clinical features in patients with early RA.

ICW31-6

Immunogenicity of adjuvanted recombinant herpes zoster subunit vaccine in rheumatoid arthritis patients treated with anti-rheumatic drugs

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Conflict of interest: None

Objective: Herpes zoster (HZ) develops due to a decline in varicella-zoster virus (VZV)-specific cell-mediated immunity with increasing age and immunosuppressive therapies, resulting in the reactivation of VZV. Disease-modifying anti-rheumatic drugs (DMARDs), particularly Janus kinase inhibitors, are known to increase the risk of HZ in patients with rheumatoid arthritis (RA). The recently approved adjuvanted recombinant VZV glycoprotein E (gE) subunit vaccine (RZV) has been shown to be effective in healthy elderly populations. However, the immunogenicity of RZV in RA patients treated with DMARDs remains unclear. Therefore, this study was undertaken to determine whether RZV is still immunogenic to RA patients treated with DMARDs. Methods: This is a longitudinal prospective study enrolling 53 RA patients treated with DMARDs (csDMARDs, n=20; bDMARDs, n=23; and tsDMARDs, n=10) and 11 individuals without immunosuppressants as controls. Cell-mediated immunity and humoral immunity to RZV were assessed before and three months after the first administration of RZV by flow cytometry, enzyme-linked immunosorbent assay, and enzyme immunoassay. Information on baseline characteristics, disease activities, flares, and adverse effects was also collected. Results: Patients' age and disease duration were 70 years old and 11 years, respectively. DAS28-CRP score at the time of enrollment was 1.39. Thirty-five percent of RA patients had a history of HZ before the administration of RZV. After RZV administration, significant induction of gE-specific CD4-positive T cells ($P<0.0001$, Wilcoxon signed-rank sum test) and an increase in the VZV-IgG titer ($P<0.0001$) were observed. No serious adverse effects were observed, and no patient developed HZ during the observation period. The incidence rate of disease flares after vaccination was 3.8%. Conclusion: RZV can significantly induce gE-specific cell-mediated immunity and humoral immune responses in RA patients treated with anti-rheumatic drugs.

ICW32-1

T follicular helper cells in blood mirror salivary gland-infiltrating T cells in primary Sjögren's syndrome (pSS)

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Conflict of interest: None

[Objective] To examine which T cell subsets in blood share the same T cell receptor (TCR) αβ with T cells infiltrated at labial salivary gland (LSG) in patients with pSS, and evaluate mechanisms of their differentiation. [Methods] 1) TCR repertoires of each T cell subset (Th, Tfh, Treg) in blood and LSG-infiltrating T cells were analyzed by TCR sequence. 2) The proportion of each T cell subset in blood was compared between pSS (n=30) and healthy controls (HC) (n=20). 3) The proportion of each T cell subset between blood and LSG was evaluated in pSS (n=7). 4) Based on the above results, Tfh-related gene mRNA expressions were evaluated in LSG of pSS. 5) The conditions of Tfh differentiation in pSS were examined. 6) Cytokine production from $CD4^+$T cells differentiated under Tfh conditions in pSS were examined. [Results] 1) LSG-infiltrating T cells, and peripheral Th1, Tfh1, and Tfh2 cells showed higher clonality than Th17 and Tfh17. Peripheral Tfh1 and Tfh2 were the two most frequent subsets comprised by the same T cell clones infiltrating in LSG. 2) Peripheral Tfh subsets were all significantly increased in pSS than in HC. The proportion of $PD\text{-}1^+ICOS^+$Tfh1 cells was correlated with titers of anti-nuclear, anti-SS-A, and anti-SS-B antibody in pSS. 3) The proportions of Tfh subsets, especially Tfh1, were significantly increased in LSG compared with blood in pSS. 4) Expression levels of CXCR5, IL-6, IL-21, and TGFβ in LSG were significantly higher in pSS than HC. TGFβ was significantly and positively correlated with CXCR5 expression in pSS. 5) $CD4^+$T cells stimulated with CD3/28 beads and TGFβ significantly increased CXCR5 expression, and Tfh1 population. 6) Production of IL-21, IL-2, and TNFα were significantly increased after CD3/28 beads and TGFβ stimulation. [Conclusions] Tfh1 cells in blood shared the same TCRαβ with LSG-infiltrating T cells in pSS. They proliferated under TGFβ-enriched environment like LSG and their proportion was positively correlated with autoantibody production in pSS.

ICW32-2

CX3CR1+ cytotoxic T cells are involved in distinct organ involvements in primary Sjögren's syndrome and IgG4-related disease

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Conflict of interest: None

[Objective] Primary Sjögren's syndrome (pSS) and IgG4-related disease (IgG4-RD) are heterogenic diseases that primarily affect lacrimal and salivary glands. Since the pathology of these diseases are not uniform, different mechanisms are presumably involved in formation of individual organ lesions. Recent studies suggest that cytotoxic T cells contribute to pathogenesis of both diseases, however, their association with clinical manifestations remains unknown. In this study, we demonstrated the possible involvement of CX3CR1+T cells in development of distinct organ involvements in pSS and IgG4-RD with a large cohort. [Methods] Consecutive patients with pSS (n=57), IgG4-RD (n=54) and healthy controls (HC, n=40) were included. Whole blood samples were stained for CX3CR1+CD4 and CX3CR1+CD8 T cells and analyzed by flow cytometry.

[Results] Proportions of CX3CR1+CD4 and CX3CR1+CD8 T cells were significantly increased in pSS and IgG4-RD compared with HC. A significant positive correlation was observed between proportions of CX3CR1+CD4 and CX3CR1+CD8 T cells in both diseases. Particularly, pSS patients with interstitial lung disease showed higher proportions of both CX3CR1+CD4 and CX3CR1+CD8 T cells than those without, whereas patients with other extraglandular involvements showed no difference. IgG4-RD patients with retroperitoneal fibrosis/aortitis exhibited higher proportions of CX3CR1+CD4 and CX3CR1+CD8 T cells compared with those with Mikulicz's disease. Moreover, proportions of CX3CR1+CD4 and CX3CR1+CD8 T cells decreased after glucocorticoid therapy along with clinical improvements in IgG4-RD. Of interest, higher proportions of CX3CR1+CD4 and CX3CR1+CD8 T cells at baseline predicted higher relapse-free survival in IgG4-RD. [Conclusions] CX3CR1+T cells were increased in both pSS and IgG4-RD and were associated with their distinct organ involvements. Our data raise the possibility that CX3CR1+T cells are involved in pathogenesis of distinct clinical phenotypes.

ICW32-3

Alveolar macrophage subpopulations and immature neutrophils are hallmark of progressive pulmonary fibrosis in connective tissue disease-associated interstitial lung disease patients

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Conflict of interest: Yes

[Objective] Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a serious complication of autoimmune diseases. Although some patients develop progressive pulmonary fibrosis (PPF) despite treatment, it is difficult to predict PPF before treatment. The objective of this study is to find characteristics of PPF in CTD-ILD. [Methods] We collected BALF and blood before treatment from 6 rheumatoid arthritis (RA), 8 dermatomyositis (DM), 5 Sjögren syndrome (SS), 7 systemic sclerosis, 4 ANCA-associated vasculitis patients who complicated ILD, and 12 idiopathic interstitial pneumonia (IIP) patients as controls. Twelve out of 42 patients fulfilled PPF criteria (Raghu, *Am J Res Crit Care Med* 2022) in 1 year period. We applied Seq-Well, a portable platform of single-cell RNA sequencing, to analyze immune cells in BALF and blood. We compared the distribution of immune cells and differential gene expressions in BALF and blood between PPF and non-PPF patients in CTD-ILD. [Results] In BALF, we found more neutrophils in RA patients, while T cells increased in DM patients and B cells and T cells in SS patients. We further classified alveolar macrophages and neutrophils into more detailed subsets based on their gene expression patterns and compared them between diseases. In PPF patients, we found increased $CXCL10^{+}$ macrophages and $CXCL8^{+}$ macrophages in BALF. Moreover, we found increased interferon-induced proteins with tetratricopeptide repeats $(IFIT)^{+}$, $MMP\text{-}9^{+}$ and immature neutrophils, which were reported to be associated with severe COVID-19 pneumonia, in the blood of PPF patients. Differentially expressed gene analysis revealed high levels of high mobility group box (HMGB)-2 and IL-1β in PPF patients. [Conclusions] We found that some macrophage subsets increased in BALF while neutrophil subsets increased in blood of PPF patients In CTD-ILD. These cell subpopulations and up-regulated genes would be potential biomarkers and therapeutic target of PPF in CTD-ILD patients.

ICW32-4

FcgR3A activation-mediated glycolysis alters MDSCs modulation of Sjögren Syndrome in CD4+ T cell subsets

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Conflict of interest: None

[Objective] Our and other researchers' previous studies found that myeloid-derived suppressor cells (MDSCs) were increased and showed pro-inflammatory effects in SS. However, the key factors and mechanisms leading MDSCs to be inflammatory remain unclear. [Methods] Healthy control or SS MDSCs were co-cultured with PBMCs. Then, $CD4^{+}$T cell subsets and Th1/Th2 and Th17/Treg ratio were analyzed. The correlation between SS MDSCs and serum IgG and Fcg receptor (FcgR) 3A expression on MDSCs were analyzed. The function and glycolysis level of MDSCs, treated with or without IgG or glycolysis inhibitor 2-DG or heat-aggregated IgG (HAIG), were detected by RT-qPCR or FCM or co-culturing with PBMCs. Furthermore, $FcgRIV^{+}$MDSCs, MDSC glycolysis levels and T cell subsets of SS-like NOD mice were detected by FCM. [Results] We found that SS MDSCs down-regulated Th1/Th2 ratio and up-regulated Th17/Treg ratio. MDSCs were positively correlated with IgG and highly expressed FcgRIIIA and showed high levels of p-mTOR, HIF-1a, Glut1, HK2, LDHA and glucose uptake capacity in SS patients. HAIG increased the expression of Arg-1, IL-10, IL-6, COX2, IL-4 and glycolysis relevant molecules in MDSCs and induced them to disturb Th1/Th2 and Th17/Treg balances, which could be obviously rescued by IgG or 2-DG. $FcgRIV^{+}$MDSCs, MDSC glycolysis levels, Th1/Th2 and Th17/Treg ratio increased in SS-like NOD mice. [Conclusions] Our studies indicated that SS MDSCs showed pro-inflammatory phenotypes by inducing $CD4^{+}$T cell subsets alteration. MDSCs pro-inflammatory effects might be directly linked to the enhanced glycolysis mediated by FcgRIIIA activation.

ICW32-5

The relevance of increase in effector Treg to better outcome in sarcoidosis

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Conflict of interest: None

[Objective] Sarcoidosis (SA) is an inflammatory disease in which some patients experience spontaneous remission, while others are treatment-refractory. To aid in clarifying how the clinical course of SA relates to immunophenotype, we analyzed regulatory T (Treg) cell proportions in SA patients with different clinical outcomes. [Methods] We recruited 23 new-onset SA patients and 10 age- and gender-matched rheumatoid arthritis (RA) patients. Peripheral immunophenotypes were determined using the standardized NIH/FOCIS flow cytometry and immune cell classification protocol. Differences in immunophenotypes and clinical variables between SA and RA patients, and SA patients with and without spontaneous remission were determined. [Results] Nine SA patients (39.1%) had no active ocular, cardiac, or neurological lesions, and thus received no treatment. All nine patients had spontaneous remission without relapse. Conversely, of the patients who received treatment, five relapsed (21.7%). SA patients had a higher proportion (6.5±3.8%) of effector Treg (eTreg) cells ($CD3^{+}$ $CD4^{+}$ $CD45RO^{+}$ $FoxP3^{hi}$) than RA patients (0.9±0.7%, $p < 0.01$ in $CD3^{+}$ $CD4^{+}$ cells). Moreover, a higher proportion of eTreg cells (5.0±0.4%) was observed in spontaneously remitting SA patients than that in non-remitting patients (2.8±1.8, $p<0.01$), but there were no differences in other clinical features or immune cell subsets between the two groups. In the treatment group, relapsed patients had a higher proportion of non-Treg cells ($CD3^{+}$ $CD4^{+}$ $CD45RO^{+}$ $FoxP3^{lo}$) compared with non-relapsed patients (n=19) (relapsed groups: non-relapsed groups=13.3±13.3: 4.8±1.8 (% in $CD3^{+}CD4^{+}$cells, p=0.01). [Conclusions] The activation of Treg cells may play a role in SA pathology and clinical course, suggesting that Treg cell abundance could help to guide therapeutic strategy.

ICW32-6

Similarities and Differences among Peripheral Blood Immunophenotypes of Mixed Connective Tissue Disease, Systemic Lupus Erythematosus, Scleroderma, and Idiopathic Inflammatory Myopathy

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Conflict of interest: None

[Objective] Mixed connective tissue disease (MCTD) is considered a subtype of scleroderma (SSc); however, its manifestations, such as pulmonary hypertension, often respond well to immunosuppressive therapy, leading to the hypothesis that MCTD has an immunological background similar to systemic lupus erythematosus (SLE). To examine this, we performed peripheral blood immunophenotypic analysis in patients with different autoimmune diseases. [Methods] Patients with autoimmune disease and healthy controls were recruited at our institution from May 2011 to May 2022. Hierarchical cluster analysis was performed using the top 11 principal components (PCs) of counts of 46 cell types obtained by flow cytometric analysis of peripheral blood mononuclear cells. We then compared the distribution into clusters by disease (Fisher's exact test, significance level: Bonferroni-corrected $p<0.05$). Finally, hierarchical cluster analysis was performed using Euclidean distances between the centroids of the 5 groups in the top 11 PCs. [Results] In total, 781 individuals were included in the study: 55 with MCTD, 198 with SSc, 311 with SLE, 140 with idiopathic inflammatory myopathy, and 77 controls. These 5 groups were classified into 4 clusters. Comparing the distribution to clusters pairwise, only MCTD vs. SSc and MCTD vs. SLE showed no significant differences ($p = 0.102$, 0.265, respectively). This was true even when MCTD was restricted to the 40 cases that were negative for both anti-Sm and anti-ds-DNA antibodies ($p = 0.181$ and 0.175, respectively). MCTD was placed in the cluster with SLE, and SSc with controls. [Conclusion] MCTD patients were distributed into 4 clusters, which were not significantly different from that of SSc or SLE, suggesting that MCTD has an immunophenotype intermediate between SSc and SLE. Furthermore, MCTD was classified into the same cluster as SLE, suggesting that the immunophenotype of MCTD is similar to that of SLE.

ICW33-1

The treatment outcome of TNF inhibitors in patients with ankylosing spondylitis

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Conflict of interest: None

[Objective] To examine the treatment outcome of TNF inhibitors in patients with ankylosing spondylitis (AS). [Methods] Sixteen cases (9 men and 7 women) in patients with AS were registered. The average age was 41 years old (15 to 67 years old). All cases were fulfilled with modified New York diagnostic criteria. Adalimumab (ADA) was firstly administered for 14 cases, and infliximab (IFX) for 2 cases. Human leucocyte antigen (HLA), the time course of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and C-reactive protein (CRP) were examined. Adverse events were also examined. [Results] HLA-B62 was maximum in 6 cases, followed by B27 and B52 in 5 cases. BASDAI significantly decreased from 6.7 on the administration of the first TNF inhibitors to 4.4 on 6 months ($p<0.001$), 5.0 on 12 months (not significant), and 5.0 on 24 months ($p<0.01$). CRP significantly decreased from 2.0 mg/dl on the administration to 0.37 mg/dl on 6 months ($p<0.05$), 0.53 mg/dl on 12 months (not significant), and 0.54 mg/dl on 24 months (not significant). For adverse events, purulental bursitis of knee (1 case), elevation of liver enzyme (1 case), and irregular menstruation (1 case) were detected. No cessation case of TNF inhibitors due to adverse events was detected. [Conclusions] TNF inhibitors significantly decreased BASDAI up to 24 months after the administration for our cases with AS, suggesting that TNF inhibitors are effective.

ICW33-2

Efficacy and Safety of Tofacitinib in Spondyloarthritis

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Conflict of interest: None

Objective: Recently tofacitinib has been approved for the treatment of SpA by FDA. Though, safety and efficacy data for tofacitinib in SpA are very limited. So this study was aimed to see the treatment response and safety of tofacitinib in SpA patients. **Methodology:** SpA patients who fulfilled the inclusion and exclusion criteria were enrolled in this study after a written consent. All the clinical details were collected including disease activity before and after 2 months of tofacitinib therapy. Side effects of tofacitinib like drug intolerance, thrombotic event, infection etc were also monitored actively. **Inclusion criteria** 1. SpA patients diagnosed as per ASAS classification criteria. 2. Juvenile Idiopathic Arthritis-Enthesitis Related (JIA-ERA) diagnosed as per ILAR classification criteria (age >18 years). 3. Patients with high or very disease activity (calculated as per ASDAS-ESR or CRP). **Exclusion criteria:** 1. Active or chronic infection 2. Past history of thrombotic events (DVT or thrombotic stroke or CAD) **Results:** Total 35 patients (M:F=33:2) were recruited in this study. Mean age of the study population was 31 years. In this study 27 adult SpA (77%), 6 JIA-ERA (17%) and 2 reactive arthritis (6%) patients were enrolled. Axial symptoms, peripheral joint, uveitis and HLA-B27 positivity was reported in 100%, 51%, 8.5% and 94% respectively. Disease activity calculated as per ASDAS-ESR or CRP was reported very high, high, moderate and inactive disease in 37%, 67%, 0% & 0% and 3%, 17%, 40% & 40% pre and post treatment respectively. Treatment response reported as major improvement, clinically significant improvement and no improvement in 37%, 49% and 14% of the patients respectively. Only one patient (3%) had reactivation of herpes zoster. **Conclusion:** Tofacitinib is effective and safe drug for the treatment of SpA patients.

ICW33-3

Effectiveness and Safety of Secukinumab Prefilled Syringe and Sensoready Pen in Patients with Psoriatic Arthritis or Ankylosing Spondylitis: Data from a Post-marketing Surveillance Study

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Conflict of interest: Yes

Objectives Secukinumab (SEC) is an anti-IL-17A monoclonal antibody approved for the treatment of psoriatic arthritis (PsA), psoriasis and ankylosing spondylitis (AS) in various countries. A post-marketing surveillance (PMS) was performed to evaluate efficacy and safety of SEC injection, prefilled syringe, and sensoready pen in PsA and AS patients (pts) in routine clinical practice. **Methods** This 12wk or 24wk multicentre, non-interventional PMS in Korea enrolled pts (>18 years) with AS or PsA who have been prescribed and continuing SEC before or after the site initiation, after signing consent form. Key assessments included TJC and SJC in PsA pts and BASDAI in AS pts. Final efficacy was assessed as "improved", "no change", or "aggravated" by investigator at wks12 or 24. Effectiveness and safety were also evaluated in special pts including elderly (>65 years) and long-term use pts. **Results** Efficacy assessments included 41 PsA and 98 AS pts while safety assessments included 41 PsA and 107 AS pts. At baseline (BL), the mean±SD TJC and SJC were 7.8±5.8 and 6.1±4.2, respectively in PsA pts while BASDAI was 5.6±2.3 (n=92) in AS pts. The mean change in TJC from BL to 12 wks and 24 wks were -3.9±4.6 (n=30) and -5.6 ± 4.1 (n=30), respectively; corresponding SJC was -3.2±3.1 (n=12) and -4.8±3.8 (n=15) (all $p<0.0001$). In AS pts, mean BASDAI change was -2.5±2.3 (n=74) and -2.4±2.6 (n=47) (both $p<0.0001$). Based on efficacy assessment 37 (90.2%), 4 (9.8%) and 0% PsA pts and, 89 (90.8%), 4 (4.1%) and 5 (5.1%) AS pts were assessed as "improved", "no change" and "aggravated". Efficacy rate was 83.3% (5/6 elderly) and 94.7% (36/38 long-term use) in PsA pts and 100% in elderly (2/2) and 95.4% (83/87 long-term use) AS pts. Serious adverse events, including the serious adverse drug reaction, were reported in 2.4% (PsA) and 3.7% (AS) pts. No deaths were reported during the period. **Conclusion** SEC showed improvements in signs and symptoms especially in

long-term use pts in routine clinical practice.

ICW33-4

Inflammation is associated with incident hypertension in patients with axial spondyloarthritis: a longitudinal cohort study

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Conflict of interest: None

[Objective] To elucidate the risk factors for the development of incident hypertension (IHT) in patients with axial spondyloarthritis (axSpA) over a period of 20 years. [Methods] We conducted a retrospective cohort study in axSpA patients who were recruited from 2001-2019 from a university clinic in Hong Kong. Patients with HT and/or anti-hypertensive drug use at baseline were excluded. They were followed until the end of 2020. The outcome was IHT, defined by a diagnosis and a prescription for an antihypertensive drug. Baseline and time-varying Cox regression analyses adjusting for age, sex, and body mass index (BMI), were used to assess the relationship between drug history, inflammatory burden and IHT. [Results] 413 patients [age: 34 (25-43) years, male: 319 (77.2%)] were recruited. After a median follow up of 12 (6-17) years, 58 patients (14%) developed IHT (IHT+group). Among all the baseline variables, disease duration was the only independent predictor for IHT based on the Cox regression model. In the time-varying multivariate Cox regression analysis, baseline disease duration remained as the only significant independent predictor to increase risk of future IHT. ESR level as an inflammatory marker had only borderline statistical significance in predicting the development of IHT, while ESR≧20, the use of csDMARDs, sulfasalazine or paracetamol were no longer statistically significant. [Conclusions] Higher inflammatory burden as reflected by a longer disease duration was a predictor associated with IHT after adjusting for traditional CV risk factors. Higher ESR level may also play a role in the development of IHT in these patients.

ICW33-5

Disease Burden in Patients with Rheumatoid Arthritis or Spondyloarthritis: Data from COVAD patient-reported e-survey

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Conflict of interest: None

[Objective] Understanding health and functional status of patients with either Rheumatoid arthritis (RA) or spondyloarthritis (SpA) is crucial to provide personalized management strategies. To this end, we aimed to compare disease burden in patients with RA and PsA utilizing Patient-Reported Outcome Measurement Information System (PROMIS) Physical Function (PF) data obtained in the COVAD study, an international e-survey assessing the safety of COVID-19 vaccines in AIRDs. [Methods] COVAD e-survey data regarding demographics, diagnosis, disease activity, Visual Analogue Scale (VAS) fatigue, VAS pain, and PROMIS PF-10a were extracted for patients with self-reported RA or SpA (either Psoriatic Arthritis, Axial SpA or Ankylosing Spondylitis). Active disease was defined as the patient's perception of their disease as active in the four weeks before COVID-19 vaccination. Paramentric on non-parametric tests were used (whichever was appropriate) to compare continuous variables between groups, [Results] From April to December 2021, n. 1334 patients with RA, female 87.2% (1160/1134), with mean age ±SD) 50.57±13.68, and n. 421 patients with SpA, male 40.15% (169/421), with a mean age of 44.74±12.53 years, responded to the COVAD e-survey. In those with active disease, PROMIS PF-10a was lower in RA patients than in SpA patients (37.17±8.86 VS 38.25±8.36 respectively, p=0.02). Nevertheless, no difference in terms of PROMIS PF-10a score was found between groups considering those with inactive disease (42.71±7.15 VS 42.76±7.53 respectively, p=0.95). Conversely, patients with active SpA experienced worse pain (4.58±2.48 VS 4.30 ± 2.46 respectively, p=0.03). No difference in VAS fatigue was shown between RA and SpA patients with active disease (4.81±2.50 VS 4.78±2.52 respectively, p=0.84). [Conclusions] Disease burden is roughly comparable in patients with RA or SpA. Patients with active SpA may experience worse pain but better functional status than those with active RA.

ICW33-6

Abnormal kynurenine levels contribute to the pathological bone features of ankylosing spondylitis

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Conflict of interest: None

Ankylosing spondylitis (AS) is typically characterized by new bone formation and systemic bone loss. Although abnormal Kynurenine (Kyn), a tryptophan metabolite, has closely linked to the disease activity of AS, the distinct role of pathological bone features is unknown. Kyn sera levels were measured by ELISA from healthy control (n=22) and AS (n=87). In AS group, the kyn levels were compared with mSASSS scores, MMP13, and OCN. Various bone-forming activities of AS-osteoprogenitors were evaluated by cell proliferation, alkaline phosphatase (ALP) activity, bone mineralization (alizarin red s (ARS), von kossa (VON), and hydroxyapatite (HA) staining), and mRNA expression. The TRAP staining was used for the osteoclast formation of RAW264.7 cells. KYN sera levels were significantly elevated in the patient group with AS compared to the healthy control group. Also, Kyn sera levels were correlated with mSASSS (r=0.0388, p=0.067), MMP13 (r=0.0327, p=0.093), and OCN (r=0.0436, p=0.052). During osteoblast differentiation, treatment with Kyn showed no difference in cell proliferation and ALP activity but promoted ARS, VON, and HA staining for bone mineralization. Intriguingly, Osteoprotegerin (OPG) and OCN expression were obviously augmented in the presence of Kyn treatment during differentiation. KYN treatment showed induction of OPG mRNA and protein expression and AhR response genes in osteoprogenitors. The secreted OPG protein was found in the supernatant of Kyn-treated osteoprogenitors. Notably, the supernatant addition to osteoclastogenesis interrupted the osteoclast formation of RAW264.7 cells accompanied by a reduction of osteoclast differentiation markers. Our results exhibit that elevated Kyn levels increased the bone mineralization of osteoblast differentiation in AS and decreased RANKL-mediated osteoclast differentiation by inducing OPG expression, suggesting a potential therapeutic target that abnormal Kyn levels could be involved in pathological bone features of AS.

ICW34-1

Spleen tyrosine kinase inhibitor attenuates pro-inflammatory cytokine production from Fc gamma receptor IIb deficient macrophages, an intervention for lupus adjunctive treatment

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Conflict of interest: None

[Objective] The exacerbation of lupus through macrophage activation after the presence of lipopolysaccharide (LPS) and glucan in the blood that transfers from the gut (gut leakage), is previously mentioned. Fostamatinib, a spleen tyrosine kinase (SYK) inhibitor, has been studied in many chronic immunologic conditions such as chronic immune thrombocytopenic purpura (ITP), Rheumatoid Arthritis (RA) and IgA nephropathy. Although this drug has recently approved by the US FDA for the treatment of ITP, the data that demonstrate a potential effect of fostamatinib on systemic lupus erythematosus (SLE) are still too less. Thus, we sought to determine the efficiencies of this drug to inhibit cytokine production from macrophages, a crucial impact of innate immunity toward the lupus exacerbation, from Fc gamma receptor IIb (FcgRIIb) knockout mice, a lupus model that represent FcgRIIb dysfunction polymorphisms commonly found in in Asia. [Methods] GM-CSF differentiated bone marrow derived macrophages (BMDM) were prepared from wild-type (WT) and FcgRIIb knockout (KO) mice. The combination of LPS and glucan were used to activate both BMDMs in conditions with and without SYK inhibitor. The expression of SYK activation was performed using western blotting, as well as cytokine release was measured by ELISA, respectively. [Results] Activated KO BMDMs exhibited significantly higher production of tumor necrosis factor alpha (TNF-a) than WT BMDMs (616.5±146.9 ng/mL; n=4 vs. 389.9±74.3 ng/mL; n=4). With SYK inhibitor, TNF-a release from both KO and WT BMDMs was significantly reduced (KO BMDMs, n=4: 616.5±146.9 ng/mL vs. 273.9±152.6 ng/mL and WT BMDMs, n=4: 389.9±74.3 ng/mL vs. 224.2±99.5 ng/mL). Additionally, SYK inhibitor could inhibit SYK activation observed by western blotting (phosphor-SYK/SYK intensity: 0.36±0.01 vs. 0.21±0.05). [Conclusions] Our work supports the use of SYK inhibitorfor the adjunctive treatment of SLE via the reduction of inflammatory cytokine production.

ICW34-2

The effects and molecular mechanisms of TRAF5 on pulmonary vascular remodeling in patients with systemic lupus erythematosus associated pulmonary arterial hypertension

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Conflict of interest: None

[Objective] Pulmonary arterial hypertension (PAH) is one of the most important complications that seriously threatens the prognosis of patients with systemic lupus erythematosus (SLE). We aim to investigate candidate biomarkers and targeted therapy for the early diagnosis and timely treatment of SLE-PAH patients. [Methods] 1) In order to screen susceptible genes of SLE-PAH, a number of 150 peripheral blood from SLE-PAH patients were subject to the whole-exome sequencing and the genome-wide association analysis was performed by comparing to 1000 healthy controls. 2) Intervention experiments on pulmonary artery endothelial cells (PAEC) were performed to figure out the potential pathogenicity of the selected genes in vitro. RNA-seq and gene ontology were applied to identify the downstream pathways. 3) Established by pristane injection and hypoxia induction, SLE-PAH mice model were used to confirm the pathogenicity of selected genes and evaluate their therapeutic value. The level of pulmonary vascular remodeling (PVR) in each group was estimated. 4) The transcriptional expression levels in peripheral blood PBMC of SLE-PAH patients were examined to evaluate the clinical diagnosis values of the selected genes. [Results] 1) The tumor necrosis factor receptor-associated factor 5 (*TRAF5*) was identified as a susceptible gene of SLE-PAH. 2) Knockdown of *TRAF5* significantly induced the apoptosis of PAEC and triggered the pathogenesis of pulmonary vascular remodeling (PVR) through distinct pathways. 3) Tail-intravenous injection of TRAF5-overexpression vector attenuated the mean pulmonary artery pressure and immune inflammation of SLE-PAH mouse model. 4) The significant reduction on mRNA level of peripheral blood PBMC of SLE-PAH patients were confirmed. [Conclusions] *TRAF5* plays a key role in the connection between the immune inflammatory response and PAEC abnormality in the PVR of SLE-PAH, and it could be a candidate marker for diagnosis and therapy of SLE-PAH patients.

ICW34-3

Phospholipase D 4 positive B cells are toll-like receptor-stimulated, potentially autoreactive, and expanded ones in systemic lupus erythematosus

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Conflict of interest: Yes

[Objective] Autoantibodies or autoreactive B cells play significant roles in systemic lupus erythematosus (SLE). Detecting distinct phenotypes of such autoreactive ones would lead to more specific treatment. [Methods] 19 healthy donors (HD) and 40 SLE patients were recruited. Using monoclonal antibodies against human phospholipase D 4 (PLD4), flow cytometry analysis was done to compare the frequency of PLD4-positive (PLD4+) B cells. Also, to investigate if cell activation would cause the induction of PLD4+ B cells, PBMC from HDs were stimulated in vitro with toll-like receptor (TLR) ligands or anti-B cell receptor (BCR) antibodies. [Results] PLD4+ B cells were significantly expanded in SLE (median (IQR): 0.54% (0.065, 2.1) in HD vs 8.8% (4.7, 17) in SLE, $p < 0.001$). PLD4+ B cells contained more transitional B cells, memory B cells, and double negative B cells, and less naive B cells, plasmablasts than the entire CD19+ B cells. In vitro stimulation assay revealed that while BCR engagement alone did not induce PLD4+ B cells, TLR7 or 9 stimulation could substantially induce PLD4+ B cells. In some SLE patients, double negative 2 B cells (DN2) were expanded. PLD4+ B cells overlapped with DN2, sharing large cell sizes, surface phenotypes, and the increased expression of intracellular T-bet. [Conclusions] PLD4+ B cells are uniquely expanded in SLE. They are likely TLR-stimulated ones, therefore they possibly contain autoreactive ones, which is further supported by overlapping with DN2. Thus, PLD4 is a promising novel surface marker of SLE treatment.

ICW34-4

cGAS-STING activation induces enhanced production of IFN-alpha via GATA4 in lupus monocytes

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Conflict of interest: None

[Objective] Enhanced interferon α (IFNα) production is associated with the pathogenesis of systemic lupus erythematosus (SLE). We previously reported that IFNα production by monocytes activated with stimulator of IFN genes (STING) pathway is enhanced in patients with SLE. We aimed to clarify the mechanism of enhanced IFNα production in SLE monocytes by transcriptome analysis. [Methods] Monocytes isolated from peripheral blood of SLE patients and healthy control (HC) were stimulated with 2'3'-cGAMP, a ligand of STING pathway. IFNα positive/negative cells were FACS-sorted and processed for RNA-sequence (RNA-seq) analysis. SLE and HC monocytes were untreated or stimulated with 2'3'-cGAMP, and relative gene expression of several genes were quantified by real-time PCR analysis. The role of GATA4 on the IFNa producing capacity of monocytic cell line (U937) was assessed by using GATA4 expressing plasmid targeting GATA4. The role of GATA4 on the IFNα producing capacity of monocytic cell line (U937) was assessed by overex-

pressing GATA4 by a plasmid transfection. [Results] Differentially expressed gene (DEG) analysis revealed that in IFNα positive SLE monocytes, the expression of GATA4 was upregulated, a gene related to the enhanced cytokine production in senescent cells. The expression of CDKN2A, a novel marker gene of cellular senescence was upregulated in SLE monocytes at steady state and further increased upon STING stimulation. IFNαproduction of U937 was enhanced by GATA4 overexpression. [Conclusions] SLE monocytes displayed the senescent-like phenotype and this was enhanced by STING activation. The overexpression of senescence-associated GATA4 may be responsible for enhanced production of IFNαin SLE monocytes.

ICW34-5

Deficiency of serum short-chain fatty acids promotes differentiation into plasmocyte in systemic lupus erythematosus

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Conflict of interest: None

[Objective] Microbiota and microbiota-derived metabolites play an important role in the pathogenesis of SLE as an environmental factor. However, the underlying mechanism is still unclear. [Methods] $CD19^+$ B cells were isolated from the peripheral blood of healthy controls. The effect of gut microbiota-derived metabolites on B cell differentiation was investigated. Serum short-chain fatty acids (SCFAs) concentrations were measured in healthy controls and lupus patients by high-performance liquid chromatography. [Results] B cells were differentiated into plasmocytes after CpG stimulation with BCR cross-linking. However, among the various gut microbiota-derived metabolites, B cell differentiation and immunoglobulin production were suppressed by the addition of SCFA. In the process, SCFA suppressed the expression of the differentiation-promoting factor, Blimp1, and increased the expression of the repressor Bach2. This effect was recapitulated by an agonist of the SCFAs receptor GPR43 and the effect of SCFAs was canceled by GPR43 antagonists. GPR43-mediated signaling is known to regulate cAMP concentration. We found that both SCFAs and GPR43 agonist increased cAMP levels in B cell cytoplasm. In addition, B cell differentiation and expression of Blimp1 were inhibited by apremilast which can increase the cAMP concentration. Next, SCFAs promoted the phosphorylation of protein kinase A, downstream of cAMP, and consequently inhibited the NF-kB phosphorylation. Moreover, pNF-kB inhibitor suppressed plasmocyte differentiation. These findings suggested that SCFAs regulated B cell differentiation via modulation of cytoplasm cAMP. Finally, the concentration of SCFA, butyrate, statistically decreased in the serum of lupus patients. [Conclusions] SCFAs suppressed plasmocyte differentiation through GPR-mediated regulation of cytoplasm cAMP levels and subsequent inhibition of NF-kB phosphorylation. Our results indicate that SCFA could be one of the important environmental factors for SLE.

ICW34-6

Fine-tuning of T cell subsets by Janus kinase inhibitors (Jakinibs) in systemic lupus erythematosus (SLE)

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Conflict of interest: None

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

ICW35-1

Rheumatoid Arthritis - A model Rheumatology HOT clinic at a tertiary care hospital in Peshawar Pakistan

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Conflict of interest: None

Objective To share a model for the management of Rheumatoid Arthritis in a Rheumatology Outpatient clinic in Peshawar, Pakistan. **Methods** The rheumatology HOT clinic service at North West General Hospital Peshawar has been in place since April 2018. Patients with Rheumatoid Arthritis are seen in clinic usually within 48 to 72 hours. Patients undergo assessment, investigations and commencement of disease modifying anti rheumatic drugs (DMARDs) usually the same day. Patients with Rheumatoid Arthritis are reviewed regularly with the patient having the autonomy to book the appointments as per their individual needs. Drug monitoring is done on all patients commenced on DMARDs as per international guidance. **Results** The Rheumatology HOT clinic has improved the management of patients with Rheumatoid Arthritis in particular. In the rheumatology HOT clinic patients have a clinical diagnosis along with appropriate investigations and commencement of drug treatment on the same day. This helps improve patient care and achieve better disease control. Patients with disease flare can access the clinic urgently as well which helps improve clinical care of the patients. Treat to target approach helps achieve better disease control and improves the quality of life of patients with Rheumatoid Arthritis. **Conclusions** Working in a lower middle income country like Pakistan where there is a lack of healthcare resources and financial constraints provision of a HOT rheumatology clinic services is in line with the future vision of the international bodies including the Royal College of Physicians (RCP) London to introduce innovation in outpatient clinic care. With the patients having autonomy to decide the future appointments clinical care of the patients is improved. This model has the potential to be applied in other departments as per individual needs.

ICW35-2

Post COVID-19 Auto-Immune Rheumatic Diseases (AIRDs) and Their Outcome: A Tertiary Care Centre Experience

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Conflict of interest: None

Objective: The aim of this study was to know the association of various types of AIRDs after COVID-19 infection and their prognosis. **Methodology:** Consecutive, previously healthy, post-COVID-19 patients with history of musculoskeletal problems were subjected for autoimmune screening tests (RF, Anti-CCP, ANA By IIF, ANCA by IIF, ENA by LIA and HLA-B27 & B5). Those patients who fulfilled the inclusion and exclusion criteria were enrolled in this study. Inclusion criteria: 1. History of symptomatic COVID-19 infection confirmed by RTPCR test. 2. Auto-Immune Rheumatic Diseases (AIRDs) symptoms within 2 months of symptomatic COVID-19 infection. 3. Patient fulfilling criteria of AIRDs as per existing classification or diagnosed by expert rheumatologist. Exclusion criteria: 1. Any symptoms suggestive of AIRD prior to COVID-19 infection. **Results:** Total 17 patients who had evidence of AIRDs were enrolled in this study. Male to female ratio was 8:9. Six patients fulfilled the criterion for rheumatoid arthritis (RA), 3 patients for granulomatosis polyangiitis (GPA), 2 patients for axial spondyloarthritis SpA), one each for dermatomyositis, possible Behchet's disease, urticarial vasculitis, seronegative arthritis, nonspecific tenosynovitis and enthesitis. Three RA patients were positive for RF & ACPA and three were negative for both antibodies. All three GPA patients were anti PR-3 positive. All patients responded well with conventional treatment regime except one GPA patient who initially responded to induction therapy but had relapse after 6 months and succumbed to his illness. **Conclusion:** Almost every type of AIRDs can be triggered by COVID-19 infection and most of them have good response with conventional treatment regime.

ICW35-3

ANCA-associated vasculitis with high white blood cell count characterized by serum G-CSF and IL-6

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Conflict of interest: None

[Objective] The white blood cell count (WBC) at diagnosis of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) has been reported to be one of the prognostic factors for the long-term survival in the multivariable analysis in the European cohort study. We aimed to elucidate the difference in the clinical characteristics between AAV patients with and without WBC higher than the normal range and specify the cytokine associated with the difference in WBC. [Methods] We retrospectively analyzed 60 patients newly diagnosed with AAV from March 2010 to April 2022 with preserved sera. We collected medical records from baseline variables at diagnosis, including clinical symptoms and laboratory data, treatments, and outcomes. We compared these indices between the patients with and without WBC higher than 10,000/μL. Multiplex cytokine and chemokine bead assays were performed using preserved serum supernatants. Serum samples from 101 healthy donors define the normal cytokine and chemokine levels. [Results] Of the 60 patients, 31 had WBC >10,000/μL at diagnosis; this group had significantly higher body mass index, higher Birmingham Vasculitis Activity Score (BVAS), higher platelet count, higher neutrophil percentage, lower lymphocyte percentage, and higher CRP compared to patients with WBC =<10,000 /μL. There were no differences in the treatments (initial prednisolone dose, methylprednisolone pulse therapy, intravenous cyclophosphamide, and rituximab) and the prognosis (relapse and death). Patients with WBC >10,000/μL demonstrated higher granulocyte-colony stimulating factor (G-CSF) and higher interleukin-6 (IL-6) than those with WBC =<10,000/μL and healthy donors. [Conclusions] WBC >10,000/μL at diagnosis could be a simple indicator of high disease activity. In addition, higher G-CSF and IL-6 in patients with WBC >10,000/μL provided a reasonable explanation for the higher neutrophil percentage and CRP and might suggest heterogeneity in the pathophysiology of AAV.

ICW35-4

Our Experience with Undifferentiated Connective Tissue Disease (UCTD) In Northern Pakistan

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Conflict of interest: None

Objective: To provide a foundation for the clinical, serological, and epidemiologic characteristics of Undifferentiated Connective Tissue Disease (UCTD) in the Nothern Pakistani population. **Methods**: A case-series study of 46 patients was carried out at Dr. S Khan's clinic, Peshawar, from January 2019 to August 2022, which provides a catchment for rheumatology patients of Northern Pakistan and neighboring Afghanistan. The diagnosis of UCTD was made using Preliminary Classification Criteria. **Results:** Most of the patients were female (89.1%) and were distributed throughout the region with no geographical preference. The most common presenting complaint was arthritis (67.2%), followed by arthralgia (55.2%). ANA was positive in most of the cases, (89.61%) followed by Anti-RNP (26.09%). The majority of patients responded well to NSAID treatment, while others were treated with corticosteroids, hydroxychloroquine, and methotrexate. **Conclusion**: Rare rheumatologic conditions are largely unexplored in Pakistan and UCTD is no exception. While its clinical features can differ widely among different populations, antibody profiles and treatment responses are generally comparable.

ICW35-5

Ibuprofen for polymyalgia rheumatica (PMR)

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Conflict of interest: None

Objectives The incidence of PMR is increasing as society is aging. The first-line therapy has been steroid, which would be best avoided for elderly susceptible to PMR. We have successfully treated some PMR patients with ibuprofen without steroid. How many and what type of patients might get remission with ibuprofen were studied. ***Methods*** Patients diagnosed with PMR by EULAR/ACR criteria in our hospital from 2015 to 2020 were studied for therapies including ibuprofen, colchicine, prednisolone (PSL), and methotrexate (MTX). Patients recovered with ibuprofen (including additional colchicine) without either PSL or MTX were compared with those who had either of them for sex, age, serum CRP level and disease duration. ***Results*** Forty-three patients (28 females and 15 males, 74.6±4.5 years old) were included, among whom 31 had 600 mg/day ibuprofen. 5 patients (all females) among the 31 recovered without PSL and/or MTX. Other NSAIDs than ibuprofen prescribed beforehand for the 4 out of the 5 had not worked; for the 1, ibuprofen was the first NSAID. Among the remaining 26 (17 females and 9 males), 25 had a steroid and 1 had MTX early. It showed that sex or age (75.0±1.7 vs 77.5±4.9 years old) did not differ significantly nor did the CRP level (7.36±3.79 vs 8.28±4.93 mg/dL). On the other side, the duration from symptom onset to ibuprofen introduction was significantly shorter in the 5 than in the 26 patients (1.40±0.65 vs 3.28±2.98 months, $p<0.05$). ***Discussion*** Early ibuprofen introduction elicited a good response. In Japan, the officially approved recommended dosage of ibuprofen is up to 600 mg/day. It is substantially lower than that (400-800 mg, 3-4 times a day) in western countries. Even if our patients are petite by western standard, the dosage is still too small. Nevertheless, a good response was obtained. Compared to other NSAIDs, ibuprofen might have another potency at least for PMR. ***Conclusion*** The earliest ibuprofen administration is recommended for PMR patients.

ICW36-1

The impact of biologic therapy on development of malignancy in patients with HLA-B27-positive ankylosing spondylitis

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Conflict of interest: None

[Objective] Biologic disease-modifying antirheumatic drugs (bDMARDs), such as tumor necrosis factor-α inhibitors (TNFi), have been authorized for patients with ankylosing spondylitis (AS). However, the impact of bDMARDs on development of malignancy *in patients with*human leukocyte antigen B27 (HLA-B27)- positive *AS remains unclear*. Through investigating an extended long-term follow-up data, we aim to determine the incidence of malignancy in HLA-B27-positive AS patients and to identify whether bDMARDs or other risk factors are associated with development of malignancy. [Methods] From 2006 to 2021, 1,445 HLA-B27-positive AS patients were reviewed retrospectively. Among them, 112 patients received bDMARDs therapy. Patients were compared via propensity score (PS) matching and factors associated with malignancy were analyzed. [Results] During 8,253 person-years of follow-up, 38 (2.6%) new malignancy were reported. The most common was lung cancer (N = 7), followed by hepatocellular carcinoma (N = 5), breast cancer (N = 4), and colon cancer (N = 4). The risk of malignancy was significantly higher in bDMARDs group when compared to the PS- matched groups treated with conventional synthetic DMARDs (csDMARDs) and non-steroidal anti-inflammatory drugs groups (hazard ratio [HR] 4.064, p = 0.010 and HR 5.620, p = 0.003, respectively). In the multivariate logistic regression model, receiving bDMARDs-including therapy, bDMARDs in combination with csDMARDs therapy, and age at diagnosis of AS older than 30 years were independent risk factors for developing malignancy (adjusted HRs 3.358, p = 0.039; adjusted HR 3.910, p = 0.022; and adjusted HR 5.669; p = 0.006, respectively). [Conclusions] The risk of new malignancy development increased in AS patients who were diagnosed after age 30 or received bDMARD treatment. Further study is required to confirm our findings.

ICW36-2

Stage 1 hypertension may carry excessive cardiovascular risk in axial spondyloarthritis patients: a 12-year longitudinal cohort study

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Conflict of interest: None

[Objective] To ascertain whether stage 1 hypertension at baseline is a predictor of future cardiovascular event (CVE) in patients with axial spondyloarthritis (axSpA). [Methods] We conducted a retrospective cohort study in axSpA patients who were recruited from 2001-2017. Patients with at least 2 years of follow-up and without prior CVE were divided into three groups according to the calculated mean BP over the first 2-year period (adjusted mean BP) (≧140/90 mm Hg, 130-139/80-89 mm Hg and <130/80 mm Hg). They were followed from baseline until the end of 2020 or occurrence of a first CVE. Multivariate Cox regression analyses adjusting for baseline and time-varying variables were used to assess the relationship between mean BP and with CVE. [Results] Out of the 458 patients fulfilling the inclusion criteria, 56 (12.2%) and 141 (30.8%) had an adjusted mean BP ≧140/90 mm Hg and 130-139/80-89 mm Hg respectively, and 261 (57.0%) were normotensives. After a median follow-up of 12 [7-18] years, 56 (12.2%) CVE were documented. The incidence rates were 21.4, 14.2 and 5.9 per 1000 patient-years for the three groups respectively. A adjusted mean BP of 130-139/80-89 mm Hg was independently associated with the occurrence of CVE after adjusting for the baseline covariates as well as time-varying inflammatory burden. This association was not significant after adjustment for time-varying traditional cardiovascular risk factors. [Conclusions] Stage I hypertension at baseline is associated with increased risk of developing CVE in axSpA patients. This association may be mediated by other traditional cardiovascular risk factors.

ICW36-3

The whole body MRI analysis of non-radiographic spondyloarthritis (SpA) and rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] The radiological findings are essential to classify SpA and RA. However, X-ray analysis can not detect some early-stage lesions. Whole body MRI (WBMRI) is an alternative method which can detect very early arthritis/enthesitis. In this study, we performed WBMRI analysis for non-radiographic SpA and RA to elucidate the early-stage SpA and RA characteristics. [Methods] We enrolled non-radiographic SpA and RA patients in the study. The diagnosis and classification of SpA were according to the Assessment of Spondyloarthritis international Society (ASAS) criteria and modification of the New York criteria grade 0-1, and RA patients are defined based on the 2010 ACR/EULAR criteria, Steinbrocker classification of stage I. We retrospectively reviewed their WBMRI images at Hokkaido University Hospital between 2007 and 2018. We examined joints, bones, and tendons in the whole body with short-term inversion recovery (STIR) and contrast-enhanced MRI imaging. Abnormal signals such as synovitis, bone erosions, bone marrow edema, and synovial bursitis were evaluated and statistically analyzed with Fischer's test. [Results] 30 patients were enrolled in this study. Eight had SpA (three with axial SpA, five with peripheral SpA: pSpA) and 22 with RA (13 with seropositive RA, nine with seronegative RA). Enthesitis was seen in 72.7% of RA patients. Hands lesions were seen in all of the pSpA patients (axial SpA 0% vs pSpA 100%, p=0.0179). 91.7% of seropositive RA patients had abnormal MRI signals on the feet compared to 44.4% of seronegative RA. [Conclusions] Foot lesions are seen in the majority of the early-stage RA patients; therefore, MRI analysis for the foot lesions is especially helpful for the assessment of early-stage RA. The majority of the early-stage RA patients had enthesitis same as in the early-stage SpA patients, which suggests the existence of enthesitis can not exclude the diagnosis of RA in the early stage.

ICW36-4

Time-dependent csDMARDs use and inflammatory burden can predict cardiovascular risk in patients with ankylosing spondylitis: a population-based study

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Conflict of interest: None

[Objective] To examine whether inflammatory burden and drug use over time increase major adverse cardiovascular events (MACE) independent of traditional cardiovascular (CV) risk factors in ankylosing spondylitis (AS) patients. [Methods] Patients who had been diagnosed with AS (ICD-9: 720.0) from 2006 to 2015 were recruited in a retrospective cohort study. They were followed until the end of 2018. The primary outcome was a first incidence of MACE. Time-varying Cox proportional hazard models were used to assess whether inflammatory burden (c-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]), and drug use (non-steroidal anti-inflammatory drugs [NSAIDs] and disease modifying anti-rheumatic drugs [DMARDs]) can predict the development of first MACE. [Results] Totally 3827 patients (age: 45.2±15.0 years, male: 2911 [76.1%]) were recruited. 135 patients (13.2%) developed a first MACE. ESR level (including ESR≧20 mm/h and ESR≧30 mm/h, HR: 2.07-2.41), CRP level (including CRP>3 mg/dl, HR: 1.20-8.77) and use of steroid (HR: 3.48) were associated with a significantly higher risk of MACE during follow-up. Whereas the use of sulfasalazine (SLZ), bDMARDs and non-COXII inhibitor were associated with reduced risk of MACE. After adjusting for time-fixed CV risk scores in the multivariable models, only ESR level (including ESR≧30 mm/h, HR: 1.02-1.94) and CRP level (including CRP>3 mg/dl, HR: 1.14-5.43) remained significant predictor for increased risk of MACE, while SLZ (HR: 0.41-0.52) was protective against MACE. [Conclusions] Increased inflammatory burden was associated with increased risk of MACE, while the use of SLZ may reduce risk of future MACE in patients with AS.

ICW36-5

Comparative Profiling of Serum Protein Biomarkers and Disease Activity Across Various Disease Domains in patients With Psoriatic Arthritis (PsA)

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Conflict of interest: None

Introduction Psoriatic Arthritis (PsA) is a complex, heterogeneous disease with chronic inflammation. Disease manifestations include the peripheral joint inflammation, dactylitis, enthesitis and skin psoriasis. Chronic inflammation is associated with structural damage, which jeopardize long-term functional ability. Sensitive biomarkers reflecting disease activity in various disease domains are lacking. **Objective** To define the molecular basis of inflammation in different disease domains through comparative profiling of serum proteins **Method** This is a cross-sectional study in patients with PsA. Clinical assessment of inflammation in the peripheral joint (clinical Disease Activity in Psoriatic Arthritis [cDAPSA] and swollen joint count), dactylitis digit count, skin (Psoriasis Activity and Severity Index [PASI]) and enthesis (Leeds enthesitis index) were performed. Blood samples were collected for biomarker assay including 48 cytokines, chemokines, growth and angiogenic factors using the Bio-Rad Bioplex assay1 (Table 1). Levels of selected serum proteins were compared between different disease activity scores across various domains using adjusted linear regression with least absolute shrinkage and selection operator (LASSO) modeling. **Results** 100 PsA patients were recruited (age: 51±11 years, male: 52 (52%), disease duration: 9.0±3 years). The cohort had moderate disease activity (DAPSA: 24.4±14.6; PASI: 6.0±7.2). 53 (53%) and 11 (11%) patients were using conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) and biologic DMARDs (bDMARDs) respectively. Using LASSO regression analysis, biomarkers correlating with peripheral joint inflammation were IFN-γ, IL6, SCF and MCP1, while MIP-1α and β-NGF were related to dactylitis. Biomarkers correlating with skin severity were IP10, M-CSF and eotaxin, while IL8, M-CSF and CTACK were related to enthesitis. Details of biomarkers independent predicting various disease severity are listed in table 2-3.

ICW37-1

Role of M1 and M2 monocytes in the pathogenesis of systemic sclerosis

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Conflict of interest: None

[Objective] The progression of systemic scleroderma (SSc) is associated with three pathologies: fibrosis, autoimmunity, and vascular damage. M1 macrophages are said to be involved in inflammation and M2 macrophages are known that M2 implicated in non-inflammation and fibrosis. In addition to macrophages, M1 and M2 subsets are also present in monocytes. The aim of this study is to clarify the relationship between the M1/M2 subset of monocytes and the pathogenesis of SSc. [Methods] By flow cytometry, we analyzed M1 monocytes (CD14-positive, and CD68-positive, and CCR2-positive cells) and M2 monocytes (CD14-positive, CX3CR1-positive, and CD163-positive cells). Next, CD14-positive cells were extracted from PBMCs of SSc patients using the Beads method, and a multiplex bead array assay was performed to comprehensively measure cytokines/chemokines. CD14-positive cells were isolated from PBMCs of healthy controls by FACS sorting, among which CX3CR1-positive CD163-positive cells were isolated as M2 monocytes and others as not-M2 monocytes. TGF-β1 in the supernatant was measured by multiplex bead array assay. Finally, functional analysis of healthy human M1 and M2 monocytes was performed by co-culture with dermal fibroblasts. [Results] The M2/M1 ratio in peripheral blood was significantly higher in the systemic scleroderma patient group compared to healthy controls. Cytokines/chemokines assay revealed that M2/M1 ratio was collarated with the secretion of MCP-1 and MIP-1α from monocytes. TGF-β1 secretion from extracted M2 monocyte was significantly higher as compared those from non-M2 monocytes. Moreover, co-culture with M2 monocytes showed tendency to increase the expression of COL1A2 and CTGF analyzed by real-time PCR. We also plan to report the investigation of αSMA expression by immunofluorescence staining. [Conclusions] Our present study suggested that M2 monocytes may be associated with pathogenesis of SSc by promoting chemokines/growth factors production and causing fibrosis.

ICW37-2

Prognosis of Patients with Systemic Sclerosis-related Interstitial Lung Disease on the Lung Transplantation Waiting List and Receiving Lung Transplantation; a single center retrospective study

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Conflict of interest: None

[Objective] Although lung transplantation (LT) is a potential therapeutic option for advanced systemic sclerosis-associated interstitial lung disease (SSc-ILD), the data on LT for SSc-ILD is still insufficient, especially in non-Western countries. We aimed to assess survival of patients with SSc-ILD on the waiting list for deceased LT and post-transplant outcomes for SSc-ILD in one of the highest-volume LT centers in Asia. [Methods] A single-center retrospective study. Using the LT candidate database at Kyoto University Hospital, patients with SSc-ILD who were registered for deceased LT were identified. To investigate post-transplant outcomes, recipients who underwent LT for SSc-ILD were also identified from the LT recipient database. Clinical data and outcomes were analyzed. [Results] 29 patients were identified from LT waiting list from 2010 to 2022. 10 received deceased donor LT (34%), 2 received living-donor LT (7%), 7 died while waiting for LT (24%) and the remaining 10 survived on the list (34%). The median duration from LT registration to the outcome date was 28.9 months in patients who received deceased LT and 6.5 months in those who died or received living-donor LT. Pulmonary hypertension was associated with mortality or switching to living-donor LT while waiting for deceased LT (Hazard ratio 10.1, 95%CI 1.26-81.1). In post-transplant analysis, 15 patients received LT for SSc-ILD between February 2002 and April 2022. LT improved forced vital capacity percent predicted (%FVC) significantly: the median %FVC was 55.1% at baseline, 65.8% at 6 months (P<0.001), and 80.3% at 12 months (P=0.001). The estimated 5-year re-transplant free survival of SSc-ILD with LT and that of idiopathic pulmonary fibrosis were 86.2% and 55.3%, respectively (log-rank P=0.33). [Conclusions] LT is an acceptable and practical therapeutic option for selected patients with severe SSc-ILD. Therefore, the appropriate timing of referral to LT centers for SSc-ILD patients should be sought.

ICW37-3

Beneficial effects of nintedanib on cardiomyopathy in patients with systemic sclerosis: a pilot study

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Conflict of interest: None

[Objective] Nintedanib is an inhibitor of tyrosine kinases with anti-fibrotic and anti-inflammatory activities that has been shown to slow the progression of interstitial lung disease (ILD) associated with systemic sclerosis (SSc). Since nintedanib was also effective for myocardial fibrosis in animal models, this study aimed to explore the effect of nintedanib on cardiomyopathy (CM) in patients with SSc. [Methods] This was a single-center prospective observational study performed at Hokkaido University Hospital. Twenty patients with SSc-ILD were enrolled and followed. The semiannual rate of change in cardiac magnetic resonance (CMR) parametric mapping, including myocardial extracellular volume

(ECV), was primarily evaluated. Other endpoints, including changes in CMR functional parameters were also evaluated. [Results] Nintedanib was administered in 10 patients, whereas the other 10 were treated without nintedanib or watched, according to ILD severity and progression. Five patients continued nintedanib at full dosage (300 mg/day). Baseline values of CMR parameters were not different between the two groups. The semi-annual rate of change in myocardial ECV was largely different between the nintedanib group and the control group (-1.62% vs. +2.00%, p = 0.0001). Myocardial ECV was increased in the control group, compatible with SSc-CM progression over time. Conversely, it was rather decreased in the nintedanib group, suggesting beneficial effects of nintedanib on myocardial inflammation and/or fibrosis. Among other endpoints, the change in right ventricular ejection fraction was significantly different between the two groups (+1.00% vs. -2.93%, p = 0.02), with a preferential change in the nintedanib group. [Conclusions] Beneficial effects of nintedanib on CM are for the first time suggested in patients with SSc. The current data would represent the cornerstone of a future therapeutic strategy for the treatment of SSc-CM, one of the unmet medical needs in modern rheumatology.

ICW37-4

Characteristics of nail fold capillary abnormalities in anti-RNA polymerase III antibody-positive systemic sclerosis

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Conflict of interest: None

[Objective] There are not enough reports on differences in nailfold capillary (NFC) abnormalities by autoantibody, especially anti-RNA polymerase III (RNA) antibodies. The purpose of this study was to evaluate whether autoantibodies affect the score of NFC abnormalities in patients with systemic sclerosis (SSc). [Methods] We retrospectively investigated patients who visited Hiroshima University Hospital from May 2018 to December 2021 and underwent nailfold video-capillroscopy (NVC) test. Among them, they were grouped into anti-centromere antibody (ACA), anti-Scl-70 antibody (Scl), RNA, and negative (Neg). SSc was defined as meeting the 2013 ACR/EULAR classification criteria. Exclusion criteria were multiple autoantibody-positive cases and immunosuppressive treatment and pulmonary hypertension treatment introduced before the first evaluation. NFCs were evaluated using a NVC, and enlaged capillaries (E), giant capillaries (G), hemorrhage (H) were quantitatively evaluated according to the criteria of Cutolo et al. Data were presented as medians and interquartile ranges. Wilcoxon's signed-rank test was used for the test. [Results] 452 patients were tested, and 159 were ACA, 36 were Scl, and 14 were RNA. SSc was diagnosed in 82 cases (51.6%) for ACA, 30 cases (83.3%) for Scl, 12 cases (85.7%) for RNA, and 21 cases were negative. 62 ACA, 15 Scl, 9 RNA, and 13 negative cases were evaluated. The NVC scores were as follows; ACA: E 1.50 (0.88-2.13), G 0.50 (0.22-1.41), H 0.56 (0.25-1.00), Scl-70: E 1.50, (1.00-2.00), G 0.50 (0.25-1.00), H 0.38 (0.13- 0.63), RNA: E 1.25 (0.69-1.50), G 0.13 (0.06-0.50), H 0.38 (0.31-0.56), Neg: E 1.50 (0.50-2.25), G 0.50 (0.13-1.38), H 0.75 (0.19-1.13). The comparison between RNA and other was as follows; E 1.25 v.s. 1.50 (0.88-2.03) p=0.15, G 0.13 v.s. 0.50 (0.13-1.25) p=0.056, H 0.38 v.s. 0.50 (0.25-0.91) p=0.47. [Conclusions] Anti-RNA polymerase III antibody-positive SSc tended to have a lower score for giant capillaries than others.

ICW37-5

Pulmonary veno-occlusive disease triad of the chest CT is correlated with pulmonary haemodynamics in pulmonary arterial hypertension associated with systemic sclerosis

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Conflict of interest: None

[Objective] Systemic sclerosis (SSc) associated with both pulmonary arterial hypertension (PAH), and pulmonary veno-occlusive disease (PVOD), that in part shares the haemodynamics with PAH. It remains unclear whether the pulmonary haemodynamic abnormalities of SSc derive from two distinct pathological entities, remodeling of the pulmonary artery/vein or a spectrum of pulmonary vascular disease. We aimed to reveal the relation between clinical features of PVOD and pulmonary haemodynamic severity in SSc patients. [Methods] This study comprised 51 SSc patients with PVR >2 WU, suggested to have pulmonary vascular remodeling. PVOD triad of the chest computed tomography was defined as (1) mediastinal lymph node enlargement, (2) thickened interlobular septal wall, and (3) ground glass opacity, and patients were divided into two groups, the 0-1 group and the 2-3 group, according to the number of PVOD triad. Pulmonary haemodynamics, pulmonary function test, and mortality were compared between the two groups. [Results] The 0-1 group and the 2-3 group contain 37 and 14 patients, respectively. The 2-3 group had significantly higher mPAP 24 mmHg vs. 34 mmHg (p=0.02), and lower %DLco/VA 54% vs. 39% (p=0.01) than the 0-1 group. Mortality in the 2-3 group tend to be lower than in the 0-1 group (the 5-year survival rate is 67% vs. 53% for the 0-1 group and the 2-3 group respectively). Pulmonary oedema following pulmonary vasodilator therapy occurred in two (14%) and none (0%) patients in the 0-1 group and the 2-3 group, respectively. [Conclusions] Clinical features of PVOD positively correlated with pulmonary haemodynamic severity in SSc patients, indicating that SSc-PAH may reflect spectrum of vascular disease that ranges from the pulmonary artery to vein.

ICW38-1

A novel molecular mechanism of vascular fibrosis in Takayasu arteritis: macrophage-derived GPNMB promoting adventitial fibroblast extracellular matrix production in the aorta

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Conflict of interest: None

[Objective] To explore role of glycoprotein non-metastatic melanoma protein B (GPNMB) in regulating the function of aorta adventitial fibroblasts (AAFs) and potential medications targeting this effect on vascular fibrosis in Takayasu arteritis (TAK). [Methods] In TAK patients, GPNMB expression was detected in the plasma, macrophage culture supernatants, and aortic tissue by ELISA and immunohistochemistry staining. The correlation between GPNMB and extracellular matrix (ECM) expression was examined in vascular adventitia. Co-localization of GPNMB, $CD68^+$ macrophages, and $CD90^+$ fibroblasts was detected by immunofluorescence staining. Co-immunoprecipitation (Co-IP) was performed to detect the expression of the GPNMB receptor on AAFs. Downstream signaling pathways were detected by western blot and validated with corresponding inhibitors. Potential immunosuppressant suppressing GPNMB effects was explored in cell culture and patients with TAK. [Results]: GPNMB was positively correlated with adventitial ECM (e.g., fibronectin and collagen I) expression. GPNMB was increased in vascular $CD68^+$ macrophages, which were closely located with $CD90^+$ fibroblasts in the fibrotic adventitia of TAK. THP-1-derived macrophages with GPNMB overexpression promoted ECM expression in AAFs. Co-IP assay and siRNA or inhibitor intervention demonstrated that integrin αVβ1 was the receptor for GPNMB which mediated downstream Akt and Erk activation to promote the GPNMB effect in AAFs. Leflunomide treatment inhibited GPNMB-mediated fibrosis in AAFs, as well as GPNMB expression in macrophages, which was also partially validated in leflunomide-treated patients. [Conclusions] Macrophage-derived GPNMB promotes AAFs ECM expression via the integrin αVβ1 receptor and Akt/Erk signaling pathway. Leflunomide might play an anti-fibrotic role in TAK by interfering with the macrophage-derived GPNMB/AAFs axis.

ICW38-2

Serum C3 levels are associated with CRP level, but inversely associated with disease severity and renal function in microscopic polyangiitis: Results from the REVEAL cohort

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Conflict of interest: Yes

[Objective] Recent studies have shown that inhibition of the complement pathway is highly effective for microscopic polyangiitis (MPA). Thus, complement activation is substantially involved in the pathogenesis of MPA. In this study, we aimed to examine whether serum C3 levels were associated with clinical characteristics, disease severity, treatment, and prognosis in the Kansai multicenter REVEAL cohort. [Methods] Patients with MPA whose C3 levels were measured at diagnosis were enrolled. The diagnosis of MPA was based on the 2012 revised Chapel Hill consensus criteria. Patients were divided into three groups: low C3 (<86 mg/dL), normal C3 (86-130 mg/dL) and high C3 (>130 mg/dL) groups, and clinical characteristics were compared. Analysis of variance or the Kruskal-Wallis test was used when the variates were numeric, while the chi-squared test or Fisher's exact test was used when variates were categorical. [Results] A total of 158 patients (low C3: 28, normal C3: 90, high C3: 40 patients) were enrolled. Baseline characteristics did not differ between the three groups in age at onset, sex, smoking history, and MPO-ANCA positivity. Serum C3 levels (P<0.001) as well as C4 (P<0.001) and CH50 levels (P=0.0013) were significantly lower in the low C3 group. In addition, hemoglobin (P=0.0058), platelets (P<0.001), and serum CRP levels (P=0.002) were significantly lower in the low C3 group, while serum creatinine levels (P=0.001), BVAS (P=0.039), and five factor score (P=0.005) were significantly higher in the low C3 group. Notably, the proportion of patients who fulfilled the 2022 revised ACR/EULAR classification criteria for MPA was significantly lower in the low C3 group (P=0.039). Initial prednisolone dose and survival did not differ between the three groups. [Conclusions] Low C3 levels are associated with severe disease and renal dysfunction, while high C3 levels are associated with elevated CRP levels. Serum C3 levels may be useful in predicting disease state.

ICW38-3

Combination of monoclonal anti-MPO antibodies forms complexes to induce small-vessel vasculitis

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Conflict of interest: Yes

[Objective] There have been no studies showing monoclonal antibodies can induce ANCA-associated vasculitis. In this study, we developed a mouse model of vasculitis using monoclonal antibodies and investigated the mechanism by which ANCA induces the pathogenesis of the disease. [Methods] 37 MPO-KO mice were immunized with recombinant MPO proteins. Splenocytes were harvested on day 42 and splenic B cells were subjected to single-cell culture to obtain monoclonal anti-MPO antibodies. Purified antibodies were injected into wild-type mice to examine their potential to induce glomerulonephritis. To assess neutrophil extracellular trap (NET) formation, mouse bone marrow neutrophils were seeded onto 96-well plates. SYTOX green dye was then added to non-fixed live cells to detect extracellular DNA. Formation of immune complexes was detected by Size Exclusion Chromatography (SEC), immunostaining for mouse IgG, and Native-PAGE. [Results] Based on the amino acid sequence of IgG expressed by B cells, 10 different antibodies were purified as high-affinity antibodies to MPO. Each antibody alone did not cause glomerulonephritis in wild-type mice. One specific combination of three monoclonal antibodies was able to induce severe glomerulonephritis. These antibodies significantly enhanced NET formation. SEC analysis showed that large immune complexes were formed when recombinant MPO proteins were mixed with this antibody cocktail. The antibodies were captured on the surface of activated neutrophils, and the deposition of IgG increased when the combination of antibodies was used. Native-PAGE showed that the antibodies formed larger immune complexes than control antibodies. [Conclusions] In this study, we successfully developed a novel ANCA-associated vasculitis mouse model using monoclonal anti-MPO antibodies. Our data provide new insight into the pathogenesis of small-vessel vasculitis by suggesting that immune complexes on the surface of neutrophils are required.

ICW38-4

Clinical features of motor neuropathy associated with eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] This study aimed to determine the clinical features of motor neuropathy associated with eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] Consecutive patients with EGPA who visited our department between 2006 April and 2022 September were included in our study. We examined the following clinical features in the presence and absence of motor neuropathy: the presence of ANCA, and the worst blood test values (such as white blood cell count (WBC), WBC differentiation, and C-reactive protein (CRP), IgG, IgE, ANCA levels) before the initial therapy. Motor neuropathy was evaluated by using the manual muscle test (MMT). The MMT score was evaluated by 10 bilateral muscles (deltoid, biceps brachii, triceps brachii, wrist flexors, wrist extensors, iliopsoas, quadriceps, hamstring, anterior tibialis, gastrocnemius) on a scale of 0 to 5, for a total score of 100. We evaluated the MMT score before treatment. [Results] A total of 24 patients with EGPA were identified. Among them, 15 patients had motor neuropathy. Presence of ANCA was not associated with motor neuropathy. Between the patients with EGPA with and without motor neuropathy, WBC and CRP levels were significantly higher in those with motor neuropathy than those without (WBC 15200±2325 vs. 21800±1801/μL (p=0.03), CRP 6.16±0.97 vs. 2.15±1.25 mg/dL (p=0.02)) before the initial therapy. A negative correlation was suggested between WBC levels and MMT score (r=-0.57, p=0.03), CRP levels and MMT score (r=-0.57, p=0.03). [Conclusions] We determined the clinical feature of motor neuropathy associated with EGPA. Worst WBC and CRP levels before the initial therapy can be a poor prognosis factor for motor neuropathy in patients with EGPA. Therefore, EGPA patients with high WBC and CRP levels need to be paid more attention to because of possible development of severe motor neuropathy.

ICW38-5

Exploration of poor prognostic factors for respiratory-related mortality in microscopic polyangiitis complicated by interstitial lung disease: the multicenter REVEAL cohort study

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Conflict of interest: None

[Objective] To explore poor prognostic factors for respiratory-related mortality in microscopic polyangiitis (MPA) complicated by interstitial lung disease (ILD) using the clinical characteristics in the multicenter cohort of Japanese patients with MPA (REVEAL cohort). [Methods] We enrolled 116 MPA patients with ILD, who were treated immunosuppressive therapy from 2005 to 2021, in the REVEAL cohort. We evaluated demographic, clinical, laboratory, and radiological findings, treatments. The presence of honeycombing at 1 cm above the diaphragm were also evaluated on high-resolution computed tomography (HRCT) on admission. We explored the risk factors predictive of respiratory-related mortality. [Results] Out of 116 patients, 26 cases were died due to respiratory related diseases during the follow-up. 18 cases (69%) were dead due to respiratory infection, and 3 cases (12%) were diffuse alveolar hemorrhage (DAH), and 5 cases (19%) were exacerbation of ILD. The median age and the prevalence of presence of honeycombing at 1 cm above the diaphragm in right lower lobe were significantly higher, and the percent forced vital ca-

pacity (%FVC) was significantly lower in the dead group than in the survival group (P = 0.003, 0.020, 0.003, respectively). Seventy nine years at onset and %FVC≦ 79.6% were determined to be the best cut-off value indicating a poor prognosis using receiver operating characteristic curve analysis. The 5-year survival rate was significantly lower in patients with aged ≧79 years, %FVC≦ 79.6%, and presence of honeycombing at 1 cm above the diaphragm in right lower lobe than patients without those (P= <0.0001, 0.001, 0.01, respectively). [Conclusions] Higher age and low percent FVC and the presence of honeycombing in right lower lobe were associated with respiratory-related death in patients with MPA-ILD.

ICW38-6

Short-term effectiveness and safety of rituximab versus cyclophosphamide for severe ANCA-associated vasculitis: a Japanese nationwide retrospective cohort study and a propensity-score matched analysis

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Conflict of interest: None

Objectives: Severe ANCA-associated vasculitis (AAV) with rapidly progressive glomerulonephritis (RPGN) and/or alveolar hemorrhage (AH) has a poor prognosis. Rituximab (RTX) has been shown to be as effective as cyclophosphamide (IVCY) in remission induction therapy, but the effectiveness and safety of RTX have not been established in severe AAV with RPGN and/or AH cases. We aimed to investigate the short-term effectiveness and safety of RTX in severe AAV with RPGN and/or AH cases. **Methods:** Records of severe AAV with RPGN and/or AH cases that were treated with RTX or IVCY during hospitalization between Apr 2018 and Mar 2020 were extracted from a Japanese nationwide inpatient database. Propensity score matching (PSM) (1:1) was performed. Effectiveness and safety were evaluated by the 30/60-day survival rate and the incidence of infections after RTX or IVCY administration. **Results:** A total of 687 cases were included original study. After PSM, 400 cases were included in the matched cohort. The median age (years) was 70.9. There were 337 cases with RPGN and 106 cases with AH. 46 deaths, 25 renal deaths, and 214 incidences of infections after RTX or IVCY use were observed. 263 cases (65.8%) were treated with glucocorticoid (GC) pulse. 87 cases (21.8%) and 79 cases (19.8%) were performed with plasma exchange (PEx) and hemodialysis. 30/60-day survival rates were 91.2/85.0% in the RTX group and 89.2/82.7% in the IVCY group, respectively. There was no significant difference in survival between the two groups (p-value = 0.60). As for the incidence of infection, there was also no significant difference between the RTX group (49.5%) and the IVCY group (57.5%) (p-value = 0.13). Age: odds ratio (OR) 1.03 [95% confidence interval (CI), 1.01-1.06], GC pulse: OR 2.71 [95% CI, 1.55-4.81] and PEx: OR 2.38 [95% CI, 1.06-5.59] were associated with the incidence of infections. **Conclusions:** RTX has similar short-term effectiveness and safety compared to IVCY for severe AAV with RPGN and/or AH.

ICW39-1

From Juvenile Idiopatihc Arthritis to Pachydermoperiostosis (Touraine-Solente-Gole Syndrome)- not a fairy tale with few therapeutic options!

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Conflict of interest: None

[Objective] We present the case of a 19-year-old man, presented in April2021 in our Clinic for polyarticular painless swellings, especially in the knees. In 2018 he was diagnosed with Juvenile idiopathic arthritis (JIA) and treatment with Methotrexate started (15 mg/wk), stopped becauase of nausea by the patient. [Methods] At the time of evaluation we found multiple skin lesions - facial seborrhea, acnee, highly marked skin creases in the forehead, thickened eyelids, skin ankles sweating Osteoarticular system with clubbing of the fingers and toes, enlergement of bilateral forearm and legs, effusion of bilateral knee joints. Biologically mild anemia with biologic inflammatory syndrome. Immunology RF, anti-CCP, ANA negative, normal levels of IgA, M, G X rays of the hands and forearms showed enlargement of distal ulna and radius with cortical thickening, carpitis. Pelvis x rays with cortical thickening of the femur. Knee x rays decreased joints space. Diagnostic and therapeutic arthrocentesis was perfromed. Results showed negative cultures, exsudates characteristics, citology negative for the presence of ragocytes. [Results] The patient is discharged with the following treatment: Methylprednisolone 16 mg/day, potassium and Vitamin D3 supplements, colchicine 1 mg/day, Sulfasalazine 3 mg/day. Endocrinological evaluation was performed with Somatomedin C (IGF-I), thyroid hormone within normal limits. He returns to our clinic after 6 months, and at the time of the evaluation we find in addition to the previous evaluation the appearance of a typical skin manifestation -tick transversely folded skin of the scalp-cutis verticis gyrate. Also he had significant effusion of bilateral knee joins. The imaging investigations are completed with skull x ray-skull. [Conclusions] The final diagnosis was established: pahidermoperiostosis -complete form. What therapeutic options should we take into consideration for this rare case, considering only few cases reported using NSAIDs, cortisone, colchicine and bisphosphonates?

ICW39-2

Multisystem Inflammatory Syndrome in Children (MIS-C) Post-COVID-19 infection: A Case Series of Patients in Singapore

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Conflict of interest: None

Objective: MIS-C was first reported in Singapore in Oct 21. We aim to describe a series of patients diagnosed with MIS-C in a local tertiary referral hospital and identify best markers of treatment response. **Method**: Clinical charts of paediatric patients diagnosed with MIS-C (by CDC case definition) from Oct 21-May 22 were retrospectively reviewed. **Results**: 12 patients were diagnosed at median 5 days of symptoms (range (R):4-8). Mean age was 4.5 yrs (R:21 mths-8 yrs); M: F ratio=0.7:1. All but one had symptomatic COVID-19 infection at mean 32 days (R:17-52) before MIS-C onset. All had fever and at least 1 criteria of Kawasaki Disease; conjunctivitis, rash, oro-mucosal changes were most common. Cardiovascular (n=11), gastrointestinal (n=10), haematologic systems (n=9) were most commonly involved. At presentation, mean C-reactive protein (CRP), procalcitonin (PCT), ferritin and erythrocyte sedimentation rate were 128 mg/L, 6.3 ng/mL, 498 μg/L and 34 mm/h respectively. Nine (75%) had thrombocytopenia and 5 (42%) lymphopenia. Raised troponin I, CKMB and NT-proBNP were seen in 42%, 17% and 92% respectively. 3 (25%) needed inotropes. None had invasive ventilation. All received intravenous immunoglobulin (IVIg) 2 g/kg and steroids. Initial methylprednisolone dose was 2-30 mg/kg/day. None required biologics. Following treatment, fever lysed after mean of 2 days (R:1-5). CRP and PCT were quickest blood markers to improve: halving 3 days after treatment (R_{CRP}:2-5; R_{PCT}:1-5). Ferritin halved over 12 days (R:4-47) and NT-proBNP over 3 days. Lymphopaenia resolved after 2.5 days and thrombocytopaenia after 4 days. 6 (50%) had abnormal echo at diagnosis. 10 (83%) and 11 (92%) had normal echo by wk2 and wk4-6 respectively, including all 3 who had inotropes. **Conclusion**: Though younger than previously described cohorts, our patients showed excellent outcomes with IVIg and early systemic steroids. Nearly all achieved normal echo at 4-6 weeks post diagnosis. CRP, PCT and NT-proBNP were quickest blood markers of improvement.

ICW39-3

Spectrum of clinical phenotypes associated with myositis-specific antibodies in juvenile idiopathic inflammatory myositis is variable across age and ethnicity: our experience from North-India

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Conflict of interest: None

Background: Idiopathic Inflammatory Myositis (IIM) are a heterogenous group of disorders with distinct clinical phenotypes associated with specific myositis-specific antibodies (MSA). Objective: To evaluate the frequency, pattern, and associations of MSA in a large Indian cohort of juvenile IIM (JIIM). Methods: A review of medical records of all patients diagnosed to have JIIM during the period January 1992 - October 2022 in Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India was done and children with JIIM having significant positivity for MSA by myositis immunoblot were analyzed. Results: Of the 151 children with JIIM, MSA immunoblot was carried out in 66 patients. Myositis antibody was positive in 54/66 (81.8%) cases and 15 of them were positive for multiple antibodies. Most common MSA was anti-NXP2 18 (27.2%) followed by anti-MDA5 9 (13.6%), anti-Mi2 9 (13.6%). Anti-TIF-gamma, anti-Ro52, anti-PM-Scl positivity was found in 8 (12.1%) cases each. We observed 4 (6%) cases of anti-SAE1, all of them having cutaneous disease predating muscle disease and the myositis responded briskly to immunosuppressants. Anti-SRP positivity was noted in a child with polymyositis. Calcinosis-predominant presentation with no clinical muscle involvement was seen in 4/18 (22.2%) cases with anti-NXP2 antibody group. While severe and relapsing cutaneous disease is more commonly noted in anti-TIF-gamma group, cutaneous ulcers, arthritis and interstitial lung disease (ILD) were noted at higher rates in anti-MDA5 group. However, we have not noted amyopathic form or rapidly progressive form of ILD in anti-MDA5 JDM in our cohort. Conclusions: Spectrum of MSAs and clinical phenotypes within the particular category of MSAs in our cohort varies from other reported cohorts from eastern and western world. Anti-NXP2 is the commonest MSA. Anti-MDA5 subgroup had more arthritis presentation and no amyopathic form was noted in this group.

ICW39-4

Successful Management with Tofacitinib in Adult and Juvenile Dermatomyositis

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Conflict of interest: None

[Objective] A subset of DM patients present with resolved muscle involvement but continue to have skin disease. In these cases, first and second line treatments are sometimes insufficient, necessitating escalation of treatment. Several recent studies have investigated the response of tofacitinib in DM. [Methods] Seven patients with DM without evidence of current muscle involvement and four patients with active muscle disease began treatment with Tofacitinib 5 to 11 mg daily. They had failed or had adverse effects to first- and second-line immunosuppressive agents. Four of the patients had Juvenile DM (JDM). Their skin disease was measured at every visit by the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI). The follow up interval was not timed and was based on usual care. Throughout their treatment patients were monitored for the necessity of additional treatment. Adverse effects to Tofacitinib were monitored. [Results] Ten of eleven patients within the case series showed improvement of their cutaneous disease, indicated by reduction of CDASI activity score by 7-16 points, over the first 6 months of treatment. Patient 2 required use of low dose oral Prednisone and Patient 4 required IVIG. Patient 5 and Patient 6 flared when Tofacitinib was tapered, however, both regained response when it was restarted. Patient 7 required one dose of IVIG because of a flare. Patient 9 (with JDM) did not respond to Tofacitinib after 2 months and was taken off this medicine. Patient 11 continued to require use of Methotrexate due to inflammatory arthritis. The patients that required additional treatment had extra-cutaneous manifestations of JDM/DM. No adverse effects including cardiovascular events or infections were noted with Tofacitinib use. Ten out of eleven patients continue Tofacitinib for their myositis. [Conclusions] Ten of the eleven patients within this retrospective study showed significant improvement of cutaneous disease with Tofacitinib use.

ICW39-5

Longitudinal trends of somatic mutation rates and single-cell functional analysis in cryopyrin-associated periodic syndrome somatic mosaic patients

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Conflict of interest: None

[Objective] Cryopyrin-associated periodic syndrome (CAPS) is an autoinflammatory disease caused by gain-of-function mutations in the *NLRP3* gene. Although reports of CAPS caused by *NLRP3* somatic mosaicism have increased, the precise mechanism is unclear. The purpose of this study is to analyze the longitudinal trends of somatic mutation rates and to elucidate the mechanism of how the small number of mutant cells form a robust inflammatory pathology in CAPS mosaic patients. [Methods] The mutation rates from dried umbilical cord (DUC), blood cell, and buccal mucosa of the patients were analyzed using digital PCR. Single-cell IL-1β secretion real-time imaging (LCI-S) was performed by the patient's monocytes before and after anti-IL-1β therapy. IL-1β-producing cells were picked up and analyzed to see whether they had genetic mutations. [Results] A total of 16 cases was analyzed (mutation rate 1.0-35.0%). 8 cases were the most severe form, 7 cases were the intermediate form and one case was NLRC4-related. In the 13 Early-onset cases, the mutation rates were generally the same in various tissues and tended not to change over time including the DUC of 5 cases available for analysis. In the 3 Late-onset cases, the mutation rates were high in myeloid cells such as neutrophils and monocytes and low in other tissues. In one case, DUC could be analyzed and no mutations were found. LCI-S showed IL-1β hypersecretion in the patient's monocytes which was ameliorated by anti-IL-1 therapy. The sequence of the patient's IL-1β producing cells revealed that, though the percentage of mutant cells was enriched, the majority of the IL-1β-producing cells were mutation-negative. [Conclusions] In the Early onset type, mutations occur relatively early after fertilization. In the Late onset type, mutations occur significantly in myelomonocytic blood cells. The patient's mutant-negative cells could be activated and produce a large amount of IL-1β under the influence of mutant cells.

ICW39-6

Differentiate Kawasaki Disease Among Febrile Children by Machine Learning Approach

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Conflict of interest: None

[Objective] Early awareness of Kawasaki disease (KD) helps physicians administrate appropriate therapy to avoid acquired heart disease in children. Still, the diagnosis of KD is challenging and depends on subjective diagnostic criteria. We aimed to develop a prediction model using machine learning with objective parameters to differentiate KD from febrile children. [Methods] We performed a retrospective study that enrolled febrile children presented to pediatric emergency departments during January 2010 to December 2019. These children were labeled as KD or febrile controls (FC) accordingly. The demographic data and objective laboratory values, including complete blood cell with differential count, urinalysis, and biochemistry, were collected as possible predictors. The extreme gradient boosting (XGBoost) machine learning method was applied to establish a prediction model. The confusion matrix and likelihood ratio were used to evaluate the performance of our prediction model. [Results] A total of 1142 KD and 73499 FC with age not older than five years old from four different hospitals were included in our study. The KD group is male predominant (60.2% vs 56.4%, p=0.011) with younger age (1.08 ±

0.84 vs 1.55 ± 1.36, p<0.001) than the FC group. Among all variables, pyuria or not, the count of white blood cell in urine, C-reactive protein, alanine aminotransferase, and percentage of eosinophil are the top-5 important features in the predicting model. The best performance of our model in the testing set could achieve 92.5% of sensitivity, 97.3% of specificity, and 97.2% of accuracy with a positive likelihood ratio of 34.0, indicating outstanding performance. The area under the receiver operating characteristic curve is 0.980 in our prediction model. [Conclusions] Machine learning with XGBoost can help physicians differentiate KD among febrile children at the pediatric emergency department with excellent sensitivity, specificity, and accuracy.

Workshop

W1-1

Safety of sarilumab in Japanese elderly patients with rheumatoid arthritis: Data from an interim analysis of a post-marketing surveillance

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Conflict of interest: Yes

[Objective] To investigate the safety of sarilumab (SAR) in elderly patients (pts) with rheumatoid arthritis (RA) using data from an interim analysis of a post-marketing surveillance (PMS). [Methods] This interim analysis enrolled pts who initiated SAR between June 2018-2021 in Japan. We analyzed data collected by 12 January 2022, with adverse events monitored over 52 weeks. [Results] Of 972 pts included in the safely analysis, 59.2% and 27.8% were aged ≧65 and ≧75 years, respectively. The majority of pts (≧65 years, 93.6% and ≧75 years, 91.1%) received the standard 200 mg dose of SAR as the initial dose. Adverse drug reactions (ADRs) were reported in 24.6% (239/972) of pts (≧65 years, 23.1% [133/575]; ≧75 years, 25.2% [68/270]). Serious ADRs were observed in 6.4% (62/972) of pts (≧65 years, 7.0% [40/575]; ≧75 years, 7.8% [21/270]). Serious infections were comparable between elderly pts (≧65 years, 2.6% [15/575]; ≧75 years, 3.0% [8/270]) and the total population (2.3%; 22/972). No apparent difference in decrease of absolute neutrophil count was observed between pts with serious and non-serious infections. No malignancy was observed across all age groups. [Conclusions] SAR therapy was well tolerated with no new safety signals reported in elderly pts with RA in this interim analysis.

W1-2

Efficacy and safety of sarilumab (SAR) in patients with rheumatoid arthritis (RA) stratified by age (<65 and ≧65 years): a post-hoc analysis of Japanese phase 3 clinical trials

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Conflict of interest: Yes

[Objectives] To assess efficacy and safety of SAR in elderly patients with active RA. [Methods] A post-hoc analysis of KAKEHASI (NCT02293902) and HARUKA (NCT02373202) trials, stratifying patients by age (<65 and ≧65 yrs). Treatment arms were: KAKEHASI, SAR+MTX and placebo; HARUKA, SAR alone and SAR+DMARDs. Efficacy was assessed by ACR20/50/70, CDAI, DAS28-CRP, or HAQ-DI response rates. For safety, AEs, serious AEs, and AEs of special interest were analysed. [Results] Approximately 20% of patients were aged ≧65 yrs in treatment arms across both trials, except in the SAR+DMARDs arm (40%, 12/30). SAR response rates btw age groups up to Wk 52 were generally similar, except for the HAQ-DI response rate in the SAR alone arm at Wk 24 (<65 yrs, 66% [31/47]; ≧65 yrs, 36% [5/14]; nominal P=.04). Wk 24 ACR20 response rates by age (<65 and ≧65 yrs) were respectively: SAR+MTX, 64% (79/124) and 59% (22/37), P=.6 (nominal, same below); SAR alone, 66% (31/47) and 79% (11/14), P=.4; SAR+DMARDs, 78% (14/18) and 75% (9/12), P=.7. Safety profiles were similar btw age groups except for higher incidence of serious AEs reported in patients aged ≧65 yrs in SAR+MTX and SAR+DMARDs arms. [Conclusion] No clear difference in efficacy or safety was observed btw Japanese patients with RA

aged <65 and ≧65 yrs.

W1-3

The effects of sarilumab (SAR) as monotherapy and in combination with non-methotrexate (non-MTX) disease-modifying anti-rheumatic drugs (DMARDs) on unacceptable pain (UP) in patients (pts) with rheumatoid arthritis (RA): a post-hoc analysis of HARUKA

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Conflict of interest: Yes

[Objectives] To investigate post-hoc the effect of SAR as monotherapy or in combination with non-MTX DMARDs on UP and inflammation control in pts with active RA. [Methods] In the HARUKA phase 3 study (NCT02373202), pts received SAR (150 mg, n=31; 200 mg, n=30) or SAR with non-MTX DMARDs (SAR 150 mg, n=15; SAR 200 mg, n=15). UP was defined as Visual Analogue Scale >40 mm and inflammation was measured using plasma C-reactive protein (CRP). [Results] Overall, 78.0% (71/91) of pts presented with UP at baseline (BL). SAR and SAR+DMARDs respectively showed fast onset of action with reductions in UP frequency to 55.9% (33/59) and 34.5% (10/29) by Week (Wk) 4 (P<0.01 vs BL in both regimens). The reduction was sustained through Wk 52, at frequencies of 15.5% (9/58) for SAR and 0 (0/24) for SAR+DMARDs (P<0.0001 vs BL in both regimens). At BL, the frequency of pts with both UP and CRP≧1 mg/dL was 39.6% (36/91). This was reduced with SAR and SAR+DMARDs by Wk 2, to frequencies of 6.6% (4/61) and 3.3% (1/30), respectively. The reduction was sustained through Wk 52, to frequencies of 0 (0/58) and 0 (0/24) for SAR and SAR+DMARDs, respectively. [Conclusion] SAR as monotherapy and in combination with non-MTX DMARDs reduced UP and inflammation with fast onsets of action in pts with RA in Japan.

W1-4

Evaluation of efficacy and safety in long-term administration of IL-6 inhibitor sarilumab

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Conflict of interest: Yes

[Objective] We evaluated the efficacy and safety of the IL-6 inhibitor sarilumab. [Methods] 165 patients were included. Disease activity evaluation was evaluated by CDAI. [Results] In 165 patients with sarilumab (143 females, mean age 59.1 years), the average number of treatment weeks was 48.2 weeks. Treatment retention rate was 82.5% at 12 weeks and 70.5% at 24 weeks, and there was no significant difference between the phase II and the phase III initiation group (Log-rank p=0.6197). CDAI improvement rate was 75.6% at 12 weeks and 76.8% at 24 weeks. There was no significant difference in CDAI improvement rate between these groups (Wilcoxon p>0.05). Sarilumab monotherapy without concomitant csDMARDs such as MTX was administered to 62 patients (37.6%). There was no significant difference in continuation rate (Log-rank p=0.3170) and CDAI improvement rate (Wilcoxon p>0.05) regardless of the presence or absence of MTX. Sarilumab monotherapy was administered to 7 patients with MTX-LPD, but no relapse of LPD was observed during the mean treatment period of 99.4 weeks. [Conclusions] Sarilumab shows early and sustained efficacy regardless of treatment phase. It was effective with or without concomitant MTX, suggesting that it was unaffected by prior b/tsDMARDs in Phase III treatment.

W1-5

continuation rate and efficacy of sarilumab with or without methotrexate

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Conflict of interest: None

[Objective] We estimated the effect on concomitant use of methotrexate in RA patients treated with sarilumab. [Methods] We finally analyzed 72 RA patients treated with sarilumab. Thirty-three patients were combined with methotrexate (MTX group) and 39 patients were not combined with methotrexate (nonMTX group). The purpose of this study was to evaluate the continuation rate and efficacy at 52 weeks after sarilumab treatment in each group. [Results] NonMTX group was older, longer disease duration, and lower eGFR than MTX group (p<0.01, respectively). The continuation rate was not different between MTX group and nonMTX group (56.4 vs 74.4%, p=0.08). In MTX group, DAS28-ESR were 5.0, 3.9, 3.0, 2.9, 3.2, 3.0, SDAI were 20.4, 15.0, 11.3, 10.9, 11.7, 11.2, and CDAI were 18.0, 14.5, 11.1, 10.6, 11.3, 10.9 at 0, 4, 12, 24, 36, 52 weeks. In nonMTX group, DAS28-ESR were 5.3, 3.8, 3.2, 3.2, 3.2, 3.1, SDAI were 23.2, 15.1, 11.2, 10.9, 11.4, 10.3, and CDAI were 21.2, 14.8, 10.9, 10.7, 11.3, 10.2 at 0, 4, 12, 24, 36, 52 weeks. Improvement rate of DAS-ESR (p=0.35, p=0.91, p=0.75, p=0.65, p=0.68), CDAI (p=0.65, p=0.98, p=0.99, p=0.61, p=0.47) at 4, 12, 24, 36, 52 weeks were not different between groups. [Conclusions] Sarilumab treatment for RA was effective even so patients without methotrexate.

W1-6

Clinical usefulness of sarilumab at24 weeks in 43 patients

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Conflict of interest: Yes

[Object] Clinical usefulness and treatment continuation following 24 weeks of Sarilumab (SAR) in rheumatoid arthritis (RA) patients were investigated. [Methods] Subjects were 43 analyzable patients introduced to SAR at the author's institution from Dec. 2018 to Mar. 2022. Mean age was 58.7 years, mean duration of illness 11.8 years. Most of the patients (40 patients) were switched from patients inadequate response to TNF inhibitors. 24 patients were treated with MTX and 19 patients were not treated with MTX. The course of DAS28 (ESR), HAQ and remission rate were analyzed. [Results] Overall DAS28 (ESR) remission rate showed clinical remission in 57% of patients from 4 weeks, and achieved 86% from 12 weeks, after that this condition continued. Overall HAQ remission rate at 24 weeks was 64%, which is considered a good result considering the average disease duration of 11.8 years, and the large number of Stage 4 and switch cases. [Conclusions] SAR is effective even in patients without MTX and with inadequate response to TNF inhibitors, and the time to onset of effect is rapid.

W2-1

Interval prolongation of ozoralizumab (a Novel anti-TNF-alpha multivalent NANOBODY® compound) in rheumatoid arthritis patients who sustained low disease activity

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Conflict of interest: Yes

[Objective] To evaluate the efficacy and safety of ozoralizumab (OZR), a novel anti-TNFα multivalent NANOBODY® product, with extended dosing interval. [Method] Among the patients who completed the Phase II/III study (OHZORA trial) with methotrexate (MTX) or the Phase III study (NATSUZORA trial) without MTX and enrolled in the long-term extension study (HOSHIZORA trial), patients who sustained low disease activity (LDA; DAS28-ESR < 3.2 at the last two time points) with OZR 30 mg Q4W changed the dosing interval to Q8W at the discretion of the investigator. We evaluated the dosing continuation rate, efficacy, and safety in patients with OZR Q8W for 24 weeks after changing the interval to Q8W. [Results] Of the 32 subjects who sustained LDA and changed the interval to Q8W, 28 (87.5%) continued to receive OZR Q8W for 24 weeks. At 24 weeks after changing the interval to Q8W, the proportion of subjects who achieved LDA was 84.4% (27/32). There were no safety concerns for 24 weeks in the Q8W group. [Conclusions] RA patients who sustained LDA with OZR 30 mg Q4W maintained efficacy (84.4%) and showed well tolerability for 24 weeks after changing the interval to Q8W.

W2-2

Efficacy and safety of ozolalizumab (a Novel anti-TNF-alpha multivalent NANOBODY® compound) in rheumatoid arthritis patients, the results of treatment for 2 years

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Conflict of interest: Yes

[Objective] To evaluate the efficacy and safety of ozoralizumab (OZR), a novel anti-TNFα multivalent NANOBODY® product, the results of treatment for 2 years (104 weeks). [Method] Efficacy and safety of OZR after treatment for 104 weeks, including after transition to a long-term extension study (HOSHIZORA trial), were evaluated in the patients who enrolled the Phase II/III study (OHZORA trial; n=381) with methotrexate (MTX) or the Phase III study (NATSUZORA trial; n=140) without MTX. [Results] The proportion of subjects who achieved SDAI remission (non-response imputation) in OZR 30 mg continuous group (n=246), which was randomly allocated OZR 30 mg at initial allocation was 28.5% at week 52 and was maintained through week 104 (26.0%). There were no specific safety concerns during 104 weeks of treatment in all subjects treated with OZR (n=513). [Conclusions] Treatment with OZR demonstrated efficacy for up to 2 years and was well tolerated.

W2-3

Single-site results in OHZORA Trial of ozoralizumab in combination with MTX

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Conflict of interest: Yes

[Objective] This study will evaluate the efficacy and safety of subcutaneous ozoralizumab (OZR) 30 mg or 80 mg plus methotrexate (MTX) in patients with highly active rheumatoid arthritis (RA). [Methods] Overall, 381 patients were assigned to placebo, OZR 30 mg or OZR 80 mg in this multicenter, double-blind, parallel-group, placebo-controlled Phase II/III trial. Six patients at our institution entered, three of whom were assigned to the 30 mg group and three to the 80 mg group. OZR was administered subcutaneously with MTX every 4 weeks for 24 weeks. [Results] The mean age was 65.5 years, and the mean disease duration was 7.3 years. One patient in the 30 mg group discontinued at 20 weeks due to pneumonia. The change of SDAI averaged -9.58 in the 30 mg group and -5.50 in the 80 mg group on Day 3, -11.4 in the 30 mg group and -12.6 in the 80 mg group on Week 1, and -17.4 in the 30 mg group and -17.6 in the 80 mg group on Week 4. These results suggested that improvement in the number of painful joints and pain VAS may have contributed to the improvement. [Conclusions] OZR may demonstrate clinical effect relatively early, including patient reported outcome, in combination with MTX.

W2-4

Clinical Effects and safety of a Novel Anti-TNF-alpha Agent (Ozoralizumab)

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Conflict of interest: None

[Objective] Following the approval of ozolalizumab (OZR), the sixth drug in a series of advanced anti-TNF agents for Rheumatoid Arthritis in Japan, we report on the clinical progress of patients enrolled at our institution under the clinical trial. [Methods] Four patients (Study 3000-JA) and four patients (Study 3001-JA) who have rheumatic disease activity participated in these trials. Placebo in 3000-JA study were assigned to OZR 30 mg or 80 mg after 24 weeks. Efficacy and safety were evaluated up to 52 weeks. [Results] In combination with MTX, DAS28-CRP changes (DAS28) was -3.19/-3.40 and -1.45/-2.28 at 4/24 weeks after transition from placebo to OZR, showing improvement in both cases. A patient in OZR 80 mg group improved early in treatment with DAS28 (4 weeks/20 weeks) -1.49/-3.36. A patient in OZR 30 mg group improved early with DAS28 (4 weeks/16 weeks) -1.98/-4.86. In the without MTX group, one of the two patients in the OZR 30 mg group showed improvement with DAS28 (4 weeks/52 weeks) -2.74/-3.29. One of the two patients in the OZR 80 mg group improved to DAS28 (4 weeks/52 weeks) -0.66/-1.92. [Conclusions] Clinical improvement was achieved with or without MTX in patients treated with OZR.

W2-5

Factors contributing to the pharmacokinetics (PK) of a novel anti-TNF-alpha multivalent NANOBODY® compound, ozoralizumab (OZR) in Japanese patients with rheumatoid arthritis (RA): Analysis using population pharmacokinetic (PopPK) modeling

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Conflict of interest: Yes

[Objectives] A PopPK analysis was performed to evaluate the PK of OZR in patients with RA and to explore the background factors that affect the PK. [Methods] We used 3412 observations from 494 patients from two studies (with/without methotrexate) in which 30 or 80 mg of OZR was administered subcutaneously every 4 weeks for 52 weeks to Japanese patients with RA. The PopPK analysis was conducted using NONMEM ver 7.4.3. [Results] Plasma OZR concentrations could be described by a one-compartment model with 1st-order absorption and 1st-order elimination processes. The inter-individual and intra-individual variation were assumed to be proportional error models, and a covariance was set for the inter-individual variation between apparent clearance (CL/F) and apparent volume of distribution (Vd/F). Covariates included in the model were as follows: body weight, gender, presence of anti-drug antibodies, eGFR and use of methotrexate, for CL/F, body weight and gender for Vd/F. PK parameters estimated from the model were CL/F 9.2 mL/h, Vd/F 4.91 L, 1st-order absorption rate constant 0.0343 h^{-1}. Sensitivity analysis indicated that PK of OZR was mainly affected by body weight. [Conclusions] The PopPK model of OZR in Japanese RA patients was obtained, and PK of OZR were mainly affected by body weight.

W2-6

Unique structure of Ozoralizumab, a trivalent anti-TNF-alpha NANOBODY® compound, offers the potential advantage of mitigating the risk of Immune Complex induced inflammation

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Conflict of interest: Yes

[Objective] Large immune complexes (ICs) and aggregates of biologics are recognized by immune systems, resulting in induction of an unwanted immune response, such as the injection site reaction (ISR). Ozoralizumab is a trivalent, bispecific NANOBODY® compound that differs structurally from IgGs. Treatment with ozoralizumab has been shown to provide comparable beneficial effects to other TNFα inhibitors in the treatment of RA. Reported ISRs were very few (2%). [Methods] To elucidate whether the unique structure of ozoralizumab is associated with a reduction in the unwanted immune response, we investigated the stoichiometry of twoTNFα inhibitors (ozoralizumab and adalimumab, an anti-TNFα IgG) ICs and induction of Fcγ receptor (FcγR)-mediated immune response. And also we developed an IC-induced subcutaneous inflammation model. [Results] Ozoralizumab-TNFα ICs which are smaller in size than adalimumab-TNFα ICs and lack an Fc portion did not activate neutrophils. And ozoralizumab-TNFα ICs did not induce any significant inflammation at injection site. [Conclusions] The results of our studies suggest that ozoralizumab is a promising candidate for the treatment of RA, with a lower risk of IC-mediated cell activation that can lead to unwanted immune responses.

W3-1

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 aimed to investigate whether sleep health status affects the development of neuropsychiatric symptoms (NPSLE) in systemic lupus erythematosus (SLE). Methods: Subjects were SLE patients aged 6-40 years within 1 year of onset, enrolled by PLEASURE-J study (A Prospective cohort study on the short and long-term prognosis, including pregnancy outcomes, of young patients with systemic lupus erythematosus in Japan). Patients were divided into two groups according to the cutoff value of 5.5 points on The Pittsburgh Sleep Quality Index (PSQI): sleep disorder group (5.5 points or higher) and control group (below the cutoff value). The prevalence of NPSLE at the onset of SLE was compared in the two groups as the primary endpoint. Results: This study comprised 167 patients including 117 patients in sleep disorder group. 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). In a post hoc analysis, high PSQI score at enrollment was significantly associated with NPSLE development up to 1 year after in the multivariate logistic analysis (P=0.01). Conclusion: PSQI score in SLE patients might be a predicting factor for developing NPSLE up to 1 year thereafter.

W3-2

The Effect of Gender and the Big Five Personality Traits on Systemic Lupus Erythematosus Patients' Trust in Their Attending Physicians: The TRUMP2-SLE STUDY

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Conflict of interest: Yes

[Objective] Gender and personality characteristics affect how doctors communicate with patients, and doctor-related factors can affect doctor-patient trust. In this study, we examined the impact of physician gender and personality on SLE patients' trust in physician. [Methods] Cross-sectional study involving SLE patients at five facilities. Factors were gender combination of physician-patients and physician personality characteristics measured by the TIPI-J scale. The outcome was trust in physician, measured by shortened version of the 5-item WFPT scale. Adjustment variables included physician-patient age difference, SLEDAI, duration of illness, periods with the physician, and position of physician. [Results] Among 502 patients, mean age was 47 and 88% female. The physician's mean age was 40 and 24% female. The trust in physician increased with the higher level of physician's extroversion and agreeableness (2.3 points per point increase [95% CI 1.0 to 3.6], 2.7 points per point increase [95%CI 1.3 to 4.0]) while decreased with higher level of diligence (-1.2 points per point decrease [95% CI -1.6 to -0.8]). [Conclusion] The doctor's extroversion and agreeableness increased patient trust, whereas excessive diligence could diminish trust by asking the patient to be diligent as well.

W3-3

Do personality characteristics (grit) of the primary care physician and the SLE patient influence shared decision-making in medical care?: TRUMP2-SLE study

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Conflict of interest: None

[Objective] Shared decision-making (SDM) is important in the long-term treatment of SLE. Last year, we reported that LLDAS was less likely to occur when the physician's grit was high. In the present study, we investigated how physician and patient Grit is related to SDM in order to examine the mechanism. [Methods] Cross-sectional study of 481 SLE patients from 5 centers. Exposure was physician and patient Grit, using mean Grit-S scores (1-5 points). Outcome was SDM using SDM-Q-9 (0-100 points). To estimate the relationship between patient and physician personality characteristics and SDM, we used a general linear model with the attending physician as a cluster, adjusted for physician and patient age and gender, physician job title, patient education, income, marital status, duration of illness, and disease activity. Multiple completion was used to address missing measures. [Results] Grit was higher for physicians than for patients (3.1 vs. 3.4, p<0.001). Patient Grit per point increase was associated with higher SDM (3.1 points [95%CI 0.2 to 6.0]) and physician Grit with lower SDM (-3.6 points [95%CI -5.8 to- 1.3]). [Conclusions] Consistent with previous studies, too high primary physician perseverance was shown to be associated with inadequate SDM.

W3-4

The association of hypocomplementemia and infectious disease complication in systemic lupus erythematosus (the second report): a retrospective observational study of the LUNA registry

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Conflict of interest: None

[Objective] To analyze the association between hypocomplementemia and infectious disease complications in SLE. [Methods] We divided the patients registered in the multicenter SLE registry "LUNA" into two groups by the lower limit of standard CH50 value and compared the clinical parameters. The risk of complications of infection requiring hospitalization in the past year was analyzed by binomial logistic regression analysis with age, sex, disease activity (SLEDAI), anti-ds-DNA antibody titer, prednisolone (PSL) use, and belimumab (BLM) use as adjustment variables. [Results] Of the 922 patients, 83 (9.0%) belonged to the low CH50 group. The low CH50 group showed significantly higher SLEDAI (6.6 ± 5.2 vs 4.0 ± 4.1, $p < 0.001$), higher titers of anti-ds-DNA antibodies (52.5± 159.6 vs 14.6±29.1 IU/ml, $p < 0.001$), higher PSL dosage (7.0 ± 4.1 vs 5.1 ± 3.9 mg/day, $p < 0.001$), and higher BLM usage rate (14.5% vs 5.2%, $p = 0.003$) compared to the non-low CH50 group. In binominal logistic regression analysis, the odds ratio of the low CH50 group to the non-low CH50 group for complications of infection requiring hospitalization in the past year was 3.33 ($p = 0.027$). [Conclusions] In SLE, hypocomplementemia is an independent risk factor for complications of infection requiring hospitalization.

W3-5

Relationship between the number of attending physicians and damage index in SLE patients: Cross-sectional study, the LUNA registry

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Conflict of interest: None

[Objective] The purpose of this study was to cross-sectionally investigate whether the number of attending physicians changes after the onset of Systemic Lupus Erythematosus (SLE) is associated with the progression of disability. [Methods] Patients with SLE enrolled in the 14-center multicenter registry (LUNA) were included. The exposure was the number of attending physicians. The primary outcome was SDI (0 point / >=1 point). We also conducted a multiple logistic regression to estimate a regression coefficient with a 95% CI between the exposure and the outcome variable to adjust for potential confounders, including age, sex, disease duration, and the number of hospitalizations due to SLE, and emotional health. [Results] Of the 709 participants (median age, 46 years [IQR35-58]), 86.5% were women. The median disease duration was 7.3 years [4.3-11.8], the median number of hospitalizations due to SLE was 1 [1-2], the median number of changes of attending physician was 1 [1-3], the median SDI was 0 points [0-1]. The primary outcome, odds ratio was 1.14 (95%CI 1.04-1.25, P=0.006), which was significantly different. [Conclusions] This study is the first report indicating that the more attending physicians a patient experiences, the more disability progresses in patients with SLE.

W3-6

Association between photosensitivity and headache in systemic lupus erythematosus: a multi-institutional study (LUNA)

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Conflict of interest: None

[Objective] In this multi-institutional study, we investigated the implication of photosensitivity (PS) in headache (HA) or HA-related disability in systemic lupus erythematosus (SLE). [Method] We conducted a longitudinal study using the clinical information, including PS, HA, and Migraine Disability Assessment Scale (MIDAS) scores, enrolled in the LUNA cohort. Logistic regression analyses were performed for exploring the implications of PS, along with other manifestations, in the development of HA and moderate or higher HA-related disability in daily life (HA-disability). HA-disability was defined at 11 or more MIDAS scores. [Results] This study included 369 patients (335 women [90.8%], median age 45 [IQR 36-55]). Patients with HA significantly had higher frequencies of PS (68.1% vs. 51.2%, p=0.002), skin rash, mucosal ulceration, Sjögren's syndrome, and lower age than those without HA. Multivariate analysis indicated PS was associated with HA appearance (odds ratio 2.0 [95% confidence interval 1.23-3.26], p=0.006). PS was not correlated with HA-disability. [Conclusion] PS may lead to the development of HA in patients with SLE.

W4-1

Investigating non-achieving factors associated with sustained DORIS remission and LLDAS in systemic lupus erythematosus

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Conflict of interest: None

[Objective] We investigated the achievement status of LLDAS and DORIS remission lasting 6 months at our hospital, and background factors for DORIS remission and achievement of LLDAS were examined. [Methods] Of 104 patients with SLE who were evaluable for LLDAS and DORIS remission at least three times since May 2021 and had been on treatment for at least one year, those who achieved DORIS remission or LLDAS for at least six consecutive months were compared with those who did not achieve remission. Analyses were performed using some background factors. [Result] 36.5%and 66.3% of patients achieved 6-month consecutive DORIS remission and LLDAS, respectively. In univariate analysis, history of cyclophosphamide use for DORIS remission (p=0.0263), and serositis for LLDAS was a non-achieving factor (p=0.0174). In multivariate analysis, history of cyclophosphamide use (p=0.0018) and hematological abnormalities (p=0.0314) for DORIS remission and serositis (p=0.0169) for LLDAS contributed to non-achievement. [Conclusions] The presence of hematologic abnormalities has been reported in previous reports as a factor associated with non-achievement of remission. This may suggest that severe cases requiring cyclophosphamide may be difficult to achieve DORIS remission even if LLDAS can be achieved.

W4-2

Relapse at 2 years in SLE patients fulfilling DORIS 2021 remission and LLDAS

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Conflict of interest: None

[Objective] In patients with SLE, to evaluate the relationship of the new definition of remission in SLE (DORIS) and Lupus Low Disease Activity State (LLDAS) with 2-year relapse rate. [Methods] The subjects were SLE patients who visited our hospital from July to October 2019. We measured and analyzed the DORIS remission, LLDAS, patient characteristics, 1 and 2-year relapse rate. Relapse was assessed as BILAG category A or B. [Results] Analysis was performed on 180 subjects both DORIS and LLDAS data of whom were available. The mean age was 45.6 years, 89.4% were female. Of the 132 LLDAS-achieved patients, 91 (68.9%) achieved DORIS remission. Relapse rates in the DORIS remission and non-remission groups were 22.5% vs 30.6% (p=0.24) at 1 year, 27.9% vs 34.1% (p=0.41) at 2 years. Relapse rates in the LLDAS and non LLDAS groups were 22.0% vs. 38.3% (p=0.04) at 1 year, 26.6% vs. 42.6% (p=0.06) at 2 years. Relapse rates in the DORIS remission group, LLDAS only group, and other groups were 22.7%, 20.5%, and 39.1% (p=0.10) at 1 year, 28.2%, 23.1%, and 43.5% (p=0.10) at 2 years, respectively. [Conclusions] Patients who met the new DORIS remission had a similar 1 and 2-year relapse rate as those who met LLDAS, but there was no significant difference from the non-remission group.

W4-3

The association of relapse of systemic lupus erythematosus (SLE) and obesity: a retrospective observational study of the LUNA registry

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matology, [10]Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, [11]Department of Rheumatology, Yokohama Rosai Hospital, [12]Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, [13]Department of Rheumatology, Tokyo Kyosai Hospital, [14]Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, [15]Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University (TMDU)

Conflict of interest: None

[Objective] To analyze the association between relapse of SLE and obesity. [Methods] The patients registered in the multicenter SLE registry "LUNA" were divided into two groups, the standard body weight group (18<=BMI<25) and the obesity group (BMI>=25). We compared the incidence of relapse during one year. [Results] Of the 1127 registered patients, 280 (24.8%) belonged to the obesity group. There were no significant differences between the two groups in age, sex, disease duration, past maximal dose of Prednisolone (PSL), SLEDAI score, and the usage of other immunosuppressants and Hydroxychloroquine (HCQ). The rate of relapse (13.3% (113/847) vs 8.9% (25/280), p=0.051) tended to be higher in the standard body weight group than in the obesity group, although there was no significant difference between the two groups. The multivariate analysis, which was adjusted for age, sex, past maximal dose of prednisolone, SLEDAI score, and the usage of HCQ, showed no significant difference in the relapse rate during the one year between the two groups. [Conclusions] We could not find an association between relapse of SLE and obesity. We plan to analyze with larger sample size and more extended observation in the future.

W4-4

Is it possible to achieve steroid-free clinical remission in systemic lupus erythematosus?

Hiroshi Oiwa
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Conflict of interest: Yes

[Objective] To investigate the achievement of clinical remission off corticosteroids (CR off C) in our cohort of SLE patients. [Methods] The enrolment criteria were (1) SLE patients who visited our department between January 2012 and August 2022 and met the ACR or EULAR/ACR classification criteria, (2) started or increased the dose of steroids during this period due to active SLE, and (3) followed up for at least one year. CR off C was defined as a clinical score of 0 on the SLEDAI without corticosteroids, allowing for residual serological activity and the use of hydroxychloroquine, immunosuppressive or biological agents. Univariate analysis was performed to determine factors predicting CR off C in baseline data. Non-steroid medications, used when CR off C was achieved, was compared with the concomitant agents in the non-achieving group. [Results] 55 patients were enrolled and 11 (20%) achieved CR off C. Baseline factors predictive of achieving CR off C were men and presence of IC (crude hazard ratios of 8.3 and 14.7, respectively). No non-steroid medications were associated with CR off C. [Conclusions] 20% of SLE patients achieved CR off C. Men and presence of IC were predictive of CR off C, although non-steroid medications contributing to this goal were not identified.

W4-5

Lupus Impact Tracker in patients with systemic lupus erythematosus (SLE) in our hospital

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Conflict of interest: None

Aim: The Lupus Impact Tracker (LIT) is a patient-centered outcome measure that assesses the impact of SLE on daily life. This study aims to evaluate the impact of SLE on organ damage and the use of medications on patient quality of life. Methods: The LIT was collected from 300 patients. Results: Patient background was as follows: mean age 51.1 ± 15.0 years, 88.6% female. Compared to non-arthritis patients, arthritis patients had significantly higher scores for limitation of usual activities due to fatigue (P=0.0043) and anxiety (P=0.041). Arthritis patients were limited in fulfilling family responsibilities due to physical effects (Spearman correlation coefficient rs= 0.71 [95%Cl 0.46-0.85 P<0.0001]), and SLE had an impact on scheduling activities and events (Spearman correlation coefficient rs =0.79 [95%Cl 0.59-0.89 P<0.0001]), and a positive correlation was found between scores on each of the two items and total LIT scores. There were no significant differences in scores for hair loss or erythema, nor were there significant differences in scores for fatigue, anxiety, or concern about appearance. Discussion: Arthritis contributes to fatigue and anxiety, and improvement in daily life disability due to arthritis may lead to improvement in health-related quality of life.

W4-6

Association of Health-related quality of life and treatment of SLE

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Kuwana City Medical Center

Conflict of interest: None

[Objective] Investigation about the health-related quality of life (HRQOL) of our SLE patients in terms of disease activity and therapeutic agents. [Methods] We made a survey to our SLE patients, who visited our department from the end of September 2022 for one month, about the Japanese LupusPRO (A cross-cultural validation of an outcome measure for lupus. Lupus, 26 (8), doi: 10.1177/ 0961203316682100) and our questionnaires. [Results] 40 cases. The mean age was 46.2 ± 16.3 year. 77.5% were prescribed hydroxychloroquine, 37.5% glucocorticoids, 75% immunosuppressants. Physical Health Domain score of the LupusPRO was 80.9 ± 23.5. The score was significantly higher in patients without corticoid use and with biologic use (Wilcoxon p=0.0353). [Conclusions] Aggressive glucocorticoid reduction and discontinuation with biologic agents, depending on need, contributes to improved HRQOL.

W5-1

Leucine-rich alpha-2 glycoprotein as a potential biomarker for large vessel vasculitides

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Conflict of interest: None

[Objective] No reliable biomarkers for reflecting activity of large vessel vasculitides (LVV) have been established. In this study, we investigated whether serum leucine-rich α-2 glycoprotein (LRG), a known biomarker in several inflammatory diseases, could be a useful biomarker in patients with LVV. [Methods] Forty-nine LVV patients were enrolled. Serum concentrations of LRG were measured with enzyme-linked immunosorbent assay. The disease activity was determined based on the medical records. [Results] The serum LRG levels were higher in patients with active disease than those in remission, and decreased after the treatment. Receiver operating characteristic curve analysis revealed that a cut-off value of LRG was 21.5 mg/ml. LRG levels were positively correlated with both CRP and erythrocyte sedimentation rate. Eleven out of 35 CRP-negative patients had positive LRG. Among the 11 patients, two had active disease and the other nine were in remission. About the 30 patients in remission, the rate of disease relapse during the following four years was 22% in initially LRG-positive patients, while 14% (3/21) in initially LRG-negative ones. [Conclusions] LRG could be used as a complementing biomarker for LVV. Elevated LRG may reflect latent vascular inflammation.

W5-2

Immunohistological evaluation of temporal artery biopsy in patients with giant cell arteritis based on transcriptome analysis

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Conflict of interest: Yes

[Objective] The pathogenesis of giant cell arteritis (GCA) remains unclear. This research aims to explore the potential factor related to the pathogenesis of GCA. [Methods] Eighteen temporal artery biopsy specimens (TABs) were collected from three hospitals (n = 16, ten GCA, six non-GCA). Based on the transcriptome analysis of mRNA extracted from the TABs, we performed an immunopathological evaluation of TABs. [Results] We categorized TABs into two groups, the inflammatory profile group (n = 8, all GCA) and the non-inflammatory profile (n = 8, two GCA, six non-GCA), by transcriptome analysis. We find 1,832 upregulated and 1,032 downregulated genes in the inflammatory profile group compared with the non-inflammatory profile group. Pathway analysis detected macrophage-related signatures in the inflammatory profile. Pathological examination shows many multinucleated giant cells in media. By immunohistological evaluation, various disease-related macrophages infiltrated the vessel wall in TABs of the inflammatory profile group. [Conclusions] These results imply that disease-related macrophages play a role in the pathogenesis of GCA.

W5-3

The diagnostic value of temporal artery ultrasound in cranial giant cell arteritis; A single-center retrospective study

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Conflict of interest: None

[Objective] We examined the diagnostic value of temporal artery ultrasound (TAU) in diagnosing cranial giant cell arteritis (GCA) in a Japanese center. [Methods] We retrospectively analyzed consecutive patients whose temporal arteries were evaluated with ultrasound for suspicion of cranial GCA between January 2011 and December 2021 in our hospital. The temporal artery wall thickness of 0.5 mm or more was defined as the positive TAU finding. Patients who were diagnosed with cranial GCA by treating physicians and received continuing treatment in the follow-up period were defined as cranial GCA patients. We examined the diagnostic value of TAU compared with temporal artery biopsy (TAB) and clinical diagnosis. [Results] Over the observation period, 204 TAUs were performed. 59 TABs were performed, and 32 cases were biopsy positive. 53 patients were diagnosed with cranial GCA. The sensitivity and specificitiy of TAU were 81% and 65% in comparison with TAB, 62% and 91% in comparison with clinical diagnosis. [Conclusions] TAU is considered to be useful in confirming the diagnosis of cranial GCA, however, careful consideration in conjunction with the result of temporal artery biopsy and other imaging modalities is needed in excluding cranial GCA when the result of TAU is negative.

W5-4

Proposal of a method for diagnosis as an optimization of Cranial type imaging diagnosis of giant cell arteritis for 56 cases who were enforced vascular echo: presentation of flowchart for diagnosis from Japan

Toshio Kawamoto, Michihiro Ogasawara, Yuko Muramoto, Mariko Harada, Eri Hayashi, Masakazu Matsushita, Ken Yamaji, Naoto Tamura
International Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Objective] Giant cell arteritis of Cranial type (c-GCA) can quickly lead to blindness and stroke, and a rapid and appropriate diagnostic method is required, and we aim to optimize diagnostic imaging. [Methods] We evaluated the effect of optimizing diagnostic imaging and methods for patients with suspected GCA who visited our hospital during 2019 to 2022. Vascular mapping was carried out using vascular ultrasonography for three-dimensional computed tomography angiography and other imaging methods as references. We also evaluated 31 cases after 2021 for detailed clinical features. [Results] We diagnosed seventeen cases of GCA among the 56 patients; the sensitivity was v-US: 82.3%, TAB: 78.6%, CTA: 71.4%, PETCT: 50.0%, MRA: 38.5%. Match rate of v-US was PETCT: 87.5%, CTA: 71.4%, TAB was v-US: 64.3%, CTA: 63.6%. In mimic 39 cases, 15 cases were PMR, 6 cases were LV-GCA, 5 cases were chronic headache, and others were collagen diseases. In 31 cases (10 cases of c-GCA, 21 cases of mimic), halo sign of v-US (p-value 0.01), jaw claudication (0.02) and both side of temporal headache (0.01). [Conclusions] We present from our results for flowchart about diagnosis of c-GCA from Japan, proposal of a method for diagnosis as an optimization of Cranial type imaging diagnosis of GCA.

W5-5

Diagnosis of elderly onset large vessel vasculitis (LVV)

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Division of Rheumatology, Department of Internal Medicine, Nagano Red Cross Hospital, Nagano, Japan

Conflict of interest: None

[Object] The aim of this study is to elucidate how to differentiate elderly onset LVV. [Methods] We retrospectively reviewed medical records of LVV patients (60 years old over) in our hospital from October 2015 to September 2022. [Results] 17 patients were enrolled in this study. 7 cases met both the classification criteria for giant cell arteritis (GCA) and the diagnostic criteria for Takayasu arteritis (TAK), 6 for GCA alone, and 4 for TAK alone. All cases meeting both criteria were finally diagnosed with GCA because of abnormal temporal artery biopsy, coexistence of polymyalgia rheumatica (PMR), or halo sign in temporal artery echocardiography. Initial symptoms were headache (11 cases), fever (5 cases) in GCA. In TAK initial symptoms were fever (3 cases), fatigue (2 cases), and none of headache. There were 6 GCA cases and 0 TAK cases with PMR. The distribution of vascular lesions was head and neck arteries in 11 cases with GCA and 1 case with TAK, and aorta in 7 cases with GCA and 4 cases with TAK. [Conclusion] There are cases in which the criteria for both GCA and TAK are met in elderly-onset LVV, making diagnosis more difficult. However, it is possible to make a differential diagnosis based on headache, PMR, temporal artery biopsy, and temporal artery echocardiography.

W5-6

Clinical features and outcomes of Japanese patients with giant cell arteritis: A comparison with Takayasu arteritis

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Conflict of interest: None

[Objective] Giant cell arteritis (GCA) and Takayasu arteritis (TA) are distinct types of large-vessel vasculitis (LVV); however, the clinical features of these diseases have some similarities. Limited data are available regarding Japanese patients with GCA and TA. The aim of the present study was to compare the clinical features and outcomes of Japanese patients with GCA and TA, as well as the effects of large vessel involvement (LVI). [Methods] We conducted a retrospective cohort study of 15 patients with GCA and 30 patients with TA at Fukushima Medical University Hospital. Signs and symptoms attributed to the disease, treatment, clinical outcomes, and mortality were recorded using a standardized database. [Results & Conclusions] There were no significant differences in survival or

the cumulative rates of cardiovascular events between the GCA and TA groups. However, relapse-free survival rates were significantly higher in patients with GCA than those in patients with TA. Among the 15 patients with GCA, 7 had a large vessel involvement (LV-GCA), which did not affect the survival or relapse rates. The rates of achieving prednisolone (PSL) tapering (PSL <7.5 mg/day) were significantly higher in patients with GCA, than those in patients with TA.

W6-1

MRI-detected muscle abnormalities in ANCA-associated vasculitis: Comparison with Inflammatory myopathy

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Conflict of interest: None

[Objective] MRI scan revealed high-intensity lesions in the muscle of patients with dermatomyositis/polymyositis. We experienced ANCA-associated vasculitis (AAV) patients with similar muscular abnormalities. We attempted to examine the frequencies of muscular abnormalities in AAV and to determine whether the muscular lesions in AAV were similar to those in DM/PM. [Methods] The participants were consecutive patients with AAV who were admitted to our hospital for initial induction therapy and received tight MRI scans before starting therapy. Controls were patients with DM/PM who received tight MRI scans before and after induction therapy. [Results] This study included 23 patients with AAV, with 11 males and 12 females, with a mean age of onset of 67.8 ± 11.0 years, 14 of MPA, 1 of GPA, and 8 of EGPA. Muscular abnormalities were detected in 18 of 23 patients (78%). Among ten patients with muscular abnormalities, the abnormalities disappeared in 5 cases (50%) and improved in 5 cases (50%) in 1 month. In contrast to AAV, immunosuppressive therapy did not improve muscular abnormalities in 7 of 7 patients with/PM, who received follow-up MRI scans one month later. [Conclusions] AAV had muscular abnormalities with a high frequency which differ from those in DM/PM.

W6-2

A case of eosinophilic granulomatosis with polyangiitis (EGPA) that was examined early in the onset but delayed the start of treatment

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Conflict of interest: None

[Introduction] Early diagnosis and treatment for EGPA are essential in both acute and long-term prognosis. In this case, I delayed the diagnosis and treatment despite being examined early after the onset of leg pain. [Case Presentation] A 27-year-old woman visited our hospital with leg pain worsening by sitting. There is no abnormality on visual examination. I observed Lasegue's sign, normal muscle strength, and right-side convex scoliosis. Therefore, I diagnosed a lumbar disc rupture. One week after, erythema and paralysis appeared on her right foot. I conducted a dermatological consultation and hospitalization. A blood test showed a significant increase in eosinophils; I found that she suffered from asthma and rhinitis. I immediately started Steroid pulse therapy with suspicion of EGPA and switched to oral medication afterward. [Clinical Significance] Peripheral neuropathy caused by EGPA is multiple mononeuritis, but the pattern varies, and 3% is the lumbar radiculopathy type. At the initial examination, I made a diagnosis of disc herniation without suspicion of EGPA. Although it was very similar to lumbar disorders, I thought that early diagnosis and treatment could have been possible if I had thoroughly interviewed her medical history and done a blood test at the first visit.

W6-3

Validation of ACR/EULAR 2022 classification criteria for ANCA-associated vasculitis, compared with the diagnostic criteria of Ministry of Health, Labour and Welfare

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Conflict of interest: Yes

[Objective] To compare the ACR/EULAR 2022 criteria with the diagnostic criteria of the Ministry of Health, Labour and Welfare (MHLW) for anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). [Methods] We used data from two nationwide cohort studies. The enrolled patients were classified as having eosinophilic granulomatosis with polyangiitis (EGPA), granulomatosis with polyangiitis (GPA), or microscopic polyangiitis (MPA) according to the ACR/EULAR 2022 criteria as a golden standard. [Results] Among the 477 patients, 51, 47, and 361 were classified as having EGPA, GPA, and MPA, respectively; 29 were unclassifiable. The sensitivity and specificity of the MHLW definite criteria were 66.7% and 100% for EGPA; 51.1% and 67.4% for GPA; and 37.1% and 92.2% for MPA, respectively. These measures of the MHLW probable criteria were 86.3% and 99.1% for EGPA; 100% and 16.7% for GPA; and 91.4%, 69.8% and 63.5% for MPA, respectively. After modifying each MHLW criteria, classification performance improved (94.0% and 97.1% for EGPA; 89.2% and 92.3% for MPA; 92.3% and 91.6% for GPA, respectively). [Conclusions] Minor modifications of the MHLW criteria may allow the classification to be consistent with the new ACR/EULAR criteria.

W6-4

Validation of the 2022 ACR/EULAR ANCA-associated vasculitis Classification Criteria in a Japanese Cohort Study; the Japan Collaborative registry of ANca-associated VASculitis (J-CANVAS)

Nakako Mabuchi[1], Takashi Kida[2], Yoshiaki Kobayashi[1], Shunichiro Hanai[1], Yoshiyuki Abe[2], Masatoshi Kadoya[2], Naoho Takizawa[2], Atsushi Nomura[2], Yuji Kukida[2], Yasuhiko Yamano[2], Takuya Yanagida[2], Koji Endo[2], Shintaro Hirata[2], Kiyoshi Matsui[2], Tohru Takeuchi[2], Kunihiro Ichinose[2], Masaru Kato[2], Ryo Yanai[2], Yusuke Matsuo[2], Yasuhiro Shimojima[2], Ryo Nishioka[2], Ryota Okazaki[2], Mayuko Moriyama[2], Ayuko Takatani[2], Yoshia Miyawaki[2], Toshiko Ito-Ihara[2], Takashi Kawaguchi[2], Nobuyuki Yajima[2], Yutaka Kawahito[2], Daiki Nakagomi[1,2]
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Conflict of interest: None

[Objective] ACR/EULAR developed novel classification criteria for ANCA-associated vasculitis (AAV) in 2022. This is the first study to validate these criteria in the Japanese population, featuring J-CANVAS, a cohort of AAV patients from multiple institutions and medical departments in Japan. [Methods] The study included 680 patients diagnosed with Microscopic Polyangiitis (MPA), Granulomatosis with polyangiitis (GPA), or Eosinophilic Granulomatosis with Polyangiitis (EGPA) based on the 2012 Revised International Chapel Hill Consensus Conference definition. We investigated the sensitivity/specificity, patients diagnosed with the other two disease subtypes served as the control group. [Results] 408 MPA, 146 GPA, and 126 EGPA patients were enrolled in J-CANVAS. The mean age was 74, 68, 61 years, the male-to-female ratio was 219,81,73 females, respectively. Sensitivity/specificity were as follows; MPA 96.1%/71.7%, GPA 51.4%/97.0%, EGPA 77.0%/98.0%. [Conclusions] The 2022 ACR/EULAR AAV Classification Criteria were established referring to the Diagnostic and Classification Criteria in Vasculitis Study (DCVAS). The sensitivity/specificity of this criteria was MPA 91%/94%, GPA 93%/94%, EGPA 85%/99%. However, the sensitivity of GPA, EGPA and the specificity of MPA was lower in a Japanese cohort.

W6-5

The usefulness of the 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for antineutrophil cytoplasmic antibodies-associated vasculitis in the diagnosis of granulomatosis with polyangiitis in Japan

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Conflict of interest: None

[Objective] The 2012 CHCC criteria and the 2007 EMA algorithm were generally used to diagnose GPA. Recently the 2022 ACR/EULAR classification criteria for AAV have been released. In this study, we aimed to investigate the advantages and disadvantages of the new classification criteria. [Methods] We retrospectively investigated 107 patients conventionally diagnosed with GPA at three medical institutions in Japan between 2000 and 2021. We analyzed the features of each organ lesion and their response to immunosuppressive therapy through the reclassification of conventionally-diagnosed GPA patients in Japan according to the new criteria. [Results] Sixty-seven patients were reclassified as GPA but not as MPA (Group A), 13 patients were reclassified as both GPA and MPA (Group B), and 26 patients were reclassified not as GPA but as MPA (Group C). In Group A, all patients were PR3-ANCA-positive, and patients with orbital mass were all included. In Group B, all patients were MPO-ANCA-positive, and 9 out of 13 patients had RPGN. In Group C, all patients were MPO-ANCA-positive. [Conclusions] The new classification criteria can be helpful in picking up GPA patients with poor functional prognosis but are likely to reclassify MPO-ANCA-positive patients as MPA.

W6-6

Comparison of the 2022 ACR/EULAR classification criteria and EMEA algorithm in Japanese patients with ANCA-associated vasculitis (AAV)

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Conflict of interest: None

[Objective] We clarify the characteristics of the 2022 ACR/EULAR classification criteria in Japanese patients with AAV. [Methods] Consecutive patients diagnosed with AAV at our department between 2012 and 2022 were classified according to the EMEA algorithm and the 2022 criteria. Their clinical characteristics were retrospectively compared. [Results] 114 patients were enrolled. The mean age was 67 y/o, and females were 61.4%. In the EMEA, 21 EGPA, 53 GPA, 20 MPA, and 20 unclassifiable. In the 2022 criteria, 25 EGPA, 19 GPA, 68 MPA, and 9 unclassifiable. All EGPA cases in the EMEA algorithm met the EGPA-2022 criteria. Of the EMEA-GPA, 39 classified as MPA-2022 were significantly older (P<0.01), had more p/MPO-ANCA (P<0.01) and interstitial pneumonia (P<0.01), but fewer pulmonary nodules or mass (P=0.02) than 11 classified as GPA-2022. Of the EMEA-MPA, 17 met the MPA-2022 criteria. Of the EMEA-unclassifiable, 11 classified as MPA-2022 were significantly older (P=0.01), had more MPO-ANCA (P<0.01) and interstitial pneumonia (P=0.04), but fewer ENT lesions (P=0.01) than others. Overall survival was significantly different in the 2022 criteria (p=0.014), but not in the EMEA algorithm (p=0.224). [Conclusion] The characteristics of the 2022 criteria in Japanese patients with AAV were clarified.

W7-1

Prediction of rheumatoid arthritis in healthy subjects from high-risk groups: Nagasaki Island Study

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Conflict of interest: None

[Objective] To evaluate the usefulness of the Clinically Suspect Arthralgia (CSA) score defined by the European Against Rheumatism (EULAR) in predicting rheumatoid arthritis (RA) progression in healthy subjects at high risk of RA. [Methods] The subjects were 112 patients from 2014 to 2021, and the observation period was 13-93 months. Subjects at high risk of developing RA were defined as having (1) anti-citrullinated peptide antibody (ACPA) positivity or (2) a family history of RA with arthralgia in the finger joints. RA was diagnosed according to the 2010 RA classification criteria. [Results] RA progression was observed in 16 patients (14%) at a median of 6 months after initial diagnosis. The CSA score was evaluable in 52 patients with a median value of 0, 60.0% of patients with a score >=3 and 14.9% of patients with a score <3 developed RA. Of the 49 ACPA-positive patients, 13 (26.5%) developed RA at a median of 13 months. The CSA score had a high specificity (95%) and negative predictive value (83%) for predicting RA progression. However, the sensitivity was low compared with the previously reported 70%. [Conclusions] The CSA score had low sensitivity but high specificity for RA progression. Because recruiting from the health checkup subjects, many of them were asymptomatic.

W7-2

Mid-term 6-year prognostic study of rheumatoid arthritis-related biomarker-positive participants in a population-based large cohort study

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Conflict of interest: None

[Objective] The positive predictive value (PPV) of anti-citrullinated protein antibodies (ACPA) for rheumatoid arthritis (RA) in three years ahead is reportedly low among the general population. In this study, RA-related biomarker positive non-RA participants were followed for 6-years to survey the incidence rate of RA and the joint destruction. [Methods] Of the 1569 participants with data of ACPA and rheumatoid factor (RF) in the third survey of the ROAD study, 1542 were followed in the fourth (3 years later) and fifth (6 years later) surveys. Medical and medication history were used to judge the onset of RA. The joint destruction was defined as the increase of modified total Sharp score ≧3 in hand radiographs. [Results] Among 28 ACPA-positive non-RA participants, 20 were able to be followed at 3-years and 16 at 6-years. PPVs for RA onset and joint destruction in three years were 15.0% and 15.0% in ACPA positive subjects, respectively, and 30.0% and 30.0% in ACPA high-titer positive subjects. There was no new case of RA onset or joint destruction in seven years. [Conclusions] ACPA high titer-positive in the general population have a high probability of developing RA and joint destruction within 3 years.

W7-3

Clinical course in rheumatoid arthritis after Immune Checkpoint Inhibitor Administration - The ANSWER cohort study -

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Conflict of interest: None

[Objective] To clarify the presence of worsening arthritis activity in patients with rheumatoid arthritis (RA) who received an immune checkpoint inhibitor (ICI) for malignancy. [Methods] We investigated the treatment and disease activity of RA patients who received ICI from the Kansai consortium for the well-being of rheumatic disease patients (ANSWER) cohort database for 12 months before and after the introduction of ICI. Descriptive statistics were performed. [Results] Sixteen RA cases were included in the analysis. The median age at ICI initiation and the median duration of RA were 72 years and 22 years, respectively, and the positive rates of ACPA and RF were 62% and 60%, respectively. Of the 11 patients whose disease activity could be analyzed before and after ICI induction, 3 had exacerbations, 1 continued MTX, and 9 started or increased corticosteroids at least 6 months before ICI induction. [Conclusions] RA patients receiving ICI had a small number of worsening arthritis. The reestablishment of a treatment strategy centered on steroid reduction in long-term survivors is an issue to be considered.

W7-4

Characteristics of difficult-to-treat rheumatoid arthritis: results from the multicenter observational cohort study, FRANK Registry

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Conflict of interest: None

[Objective] We report the characteristics of patients with difficult to treat rheumatoid arthritis (D2T RA) from the FRANK registry, a multicenter prospective observational cohort study started in 2018 at hospitals and clinics in the suburbs of Fukuoka. [Methods] A total of 3105 patients registered from March 2018 to August 2021 were included in this study. D2T RA was extracted according to the EULAR definition and compared with non-D2T RA. In addition, to adjust for baseline patient characteristics between the two groups, we applied propensity score matching (PS). [Results] Among 3038 patients with RA, 48 (1.6%) were D2T RA. The mean age was 62.8 years. Compared to the 96 cases of Non-D2T RA extracted by PS, there was a higher rate of PSL use (79.2%, 40.6%), lower use of csDMARDs (70.8%, 85.4%), and especially a higher rate of MTX discontinuation (31.0%, 11.8%). Jak inhibitors were also more commonly used in D2T RA (33.3%, 0.0%). The mHAQ score and EQ-5D score were significantly lower. In addition, patient satisfaction for ADL and global treatment were also significantly lower. [Conclusions] The frequency of D2T RA in the FRANK registry was 1.6%. Jak inhibitors were more commonly used in D2T RA, and their ADL, QOL patient satisfaction were significantly lower.

W7-5

Trends of disease activity in elderly patients with rheumatoid arthritis - the ANSWER cohort study -

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Conflict of interest: Yes

[Objective] Elderly patients with rheumatoid arthritis (RA) are currently increasing and they often fail to achieve T2T due to comorbidities such as cognitive disorder and renal dysfunction. To investigate whether disease activity (DA) in elderly RA patients is getting improved over time. [Methods] We retrospectively evaluated the DA of RA patients in each year between 2014 and 2021 using a Japanese multicenter observational registry. Patients were categorized into 3 groups (age of 18-64: group Y, 65-74: group I, over 75: group E). The Cochran-Armitage trend test was used to evaluate the annual change in the rate of patients in achieving remission (CR) or low disease activity (LDA). [Results] The total of patients was 34,754. Median (IQR) age was 65 (54-71) in 2014 and 68 (56-76) in 2021. The rate of group E in total was 16.5% in 2014 and 27.2% in 2021. The rate of b/tsDMARDs use increased (19.8% in 2014 and 35.8% in 2021) while that of glucocorticoid use decreased (44.6% in 2014 and 33.3% in 2021). The rate of patients achieving CR or LDA in group E increased from 62.2% in 2014 to 76.9% in 2021 ($p<0.01$). The improvement of DA over time was observed in both patients with or without b/tsDMARDs. [Conclusions] Disease activity in elderly RA patients improved over time.

W7-6

Epidemiological Analysis of the Medical Conditions of Articular Type Juvenile Idiopathic Arthritis and Takayasu's Arteritis using the National Database of Designated Incurable Diseases of Japan

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Conflict of interest: Yes

[Objective] To explore patients' unmet needs by evaluating the real world data of medical treatment for articular type juvenile idiopathic arthritis (aJIA) and Takayasu arthritis (TA). [Methods] We analyzed data from the national database of designated incurable diseases of Japan for aJIA and TA submitted from April 2018 to March 2020. [Results] A total of 216 patients of aJIA were included in the analysis. The female-to-male ratio was 6.7. The disease types were RF-positive polyarthritis (59%), RF-negative polyarthritis (21%), persistent oligoarthritis (12%), and extended oligoarthritis (8%), respectively. Eighty-six percent of all the patients had a history of biologic agents (bDMARDs), and 44% of RF-positive polyarthritis and 30% of RF-negative polyarthritis had a history of multiple bDMARDs. TA consisted of 3,290 patients for analysis. There were 198 new-onset patients with onset <1 year. The female-to-male ratio was 7.3. bDMARDs were used in 17% of the new patients, with subcutaneous tocilizumab injection (TCZsc) accounting for 84% of these patients. In all, bDMARDs were used in 24% of the patients, 71% of which were TCZsc. [Conclusions] The data analysis revealed that using high-cost drugs (e.g., bDMARDs) was necessary in many patients of aJIA and TA.

W8-1

Ixekizumab Improves Signs, Symptoms, and Quality of Life in Patients with Axial SpA Irrespective of Symptom Duration: Data from three Global Phase III Randomized Controlled Trials

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Conflict of interest: Yes

Objective: Assess treatment response to Ixekizumab (IXE) up to 52 weeks (Ws) by symptom duration (<5 years (yrs), ≧5 yrs) in patients (pts) with ankylosing spondylitis/radiographic axial spondyloarthritis (AS/r-axSpA; hereafter, AS) and non-radiographic axial spondyloarthritis (nr-axSpA). Methods: Pts with AS (COAST-V [NCT02696785]; -W [NCT 02696798]) or nr-axSpA (COAST-X [NCT02757352]) were randomised to receive 80 mg IXE every 2 Ws, or 4 Ws, or placebo (PBO: 16 Ws COAST-V/W; 52 Ws COAST-X). Assessments included ASAS40, ASDAS <2.1, and BASDAI. Outcomes were compared between pts with <5 yrs and ≧5 yrs symptom duration. Data was from pooled IXE pts. Results: In IXE pts with AS and <5 yrs symptom duration (n=33), ASAS40 response was achieved by 51.5% at W16 and 60.6% at W52, compared to 36.9% at W16 and 40.5% at W52 in pts with ≧5 yrs symptom duration (n=306). In IXE pts with nr-axSpA and <5 yrs symptom duration (n=73), ASAS40 response was achieved by 42.5% at W16 and 54.8% at W52, compared to 36.0% at W16 and 41.4% at W52 in pts with ≧5 yrs symptom duration (n=111). A similar pattern was observed for ASDAS <2.1 and BASDAI. Conclusions: Improved response with IXE treatment was observed in both subgroups (<5 and ≧5 yrs) based on symptom duration, with numerically higher responses in the <5 yrs subgroup.

W8-2

Efficacy and Safety of Upadacitinib in Patients With Active Ankylosing Spondylitis Refractory to Biologic Therapy: a Double-Blind, Randomized, Placebo-Controlled Phase 3 Trial With Japanese Subjects Sub-analysis

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Conflict of interest: Yes

[Objective] To assess the efficacy and safety of upadacitinib (UPA) in patients (pts) with active ankylosing spondylitis (AS) with an inadequate response (IR) to biologic disease-modifying antirheumatic drugs (bDMARDs). [Methods] SELECT-AXIS2 (NCT04169373) AS bDMARD-IR study is a randomized, double-blind, placebo (PBO)-controlled, phase 3 trial that enrolled pts with active AS who met modified New York criteria, and had an IR to one or two bDMARDs. [Results] All 420 randomized pts including 12 Japanese pts with active AS received assigned treatment (UPA 15 mg, n=211; PBO, n=209); 409 (97%) received study drug through week (wk) 14. Significantly more pts achieved the primary endpoint of ASAS40 response at wk 14 with UPA vs PBO (45% vs 18%; P<0.0001). The rate of Treatment emergent adverse events was similar between treatment groups through wk 14 (UPA, 41%; PBO, 37%). Efficacy and safety of Japanese pts were generally consistent with overall pts. ASAS40 at wk 14 was numerically higher with UPA (50%; 3/6) compared to PBO (17%; 1/6) in the Japanese subgroup. Herpes Zoster was observed in 2 Japanese pts with UPA. [Conclusions] UPA 15 mg once daily was significantly more effective than PBO over 14 wks of treatment in pts with bDMARDs-IR active AS and no new safety risks were identified.

W8-3

Efficacy and Safety of Upadacitinib in Patients With Active Non-Radiographic Axial Spondyloarthritis: a Double-Blind, Randomized, Placebo-Controlled Phase 3 Trial With Japanese Subjects Sub-analysis

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Conflict of interest: Yes

[Objective] To assess the efficacy and safety of upadacitinib (UPA) in patients (pts) with active non-radiographic axial spondyloarthritis (nr-axSpA). [Methods] SELECT-AXIS2 (NCT04169373) nr-axSpA study is a randomized, double-blind, placebo (PBO)-controlled, phase 3 trial that enrolled pts with a clinical diagnosis of nr-axSpA (who also fulfilled 2009 ASAS classification criteria for axSpA but did not meet modified New York criteria), who had active inflammation by MRI of sacroiliac joints or hsCRP. [Results] Of 314 pts including 11 Japanese subjects randomized, 313 received study drug (UPA 15 mg, n=156; PBO, n=157) and 295 (94%) received study drug through week (wk) 14. A significantly higher ASAS40 response rate at wk 14 was achieved with UPA vs PBO (45% vs 23%; P<0.0001). The rate of treatment emergent adverse event was similar between treatment groups (UPA, 48%; PBO, 46%). Efficacy and safety of Japanese pts were generally consistent with overall pts. ASAS40 at wk 14 was numerically higher with UPA (25%; 1/4) compared to PBO (14%; 1/7) in the Japanese subgroup. [Conclusions] UPA 15 mg once daily demonstrated significantly greater efficacy than PBO after 14 wks of treatment in pts with active nr-axSpA and no new risks were identified.

W8-4

Ixekizumab efficacy on spinal pain, disease activity and quality of life in patients with psoriatic arthritis presenting with symptoms suggestive of axial involvement: integrated analysis of two global phase 3 studies

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Conflict of interest: None

[Objective] To determine the efficacy of Ixekizumab (IXE) in reducing axial symptoms in patients with active psoriatic arthritis (PsA) presenting with symptoms suggestive of axial involvement. [Methods] This post-hoc analysis included data from patients with PsA (pooled SPIRIT-P1 and -P2 [NCT01695239 and NCT02349295]). Symptoms suggestive of axial involvement were defined as BASDAI Q2 (back pain) ≧4, and an average of BASDAI Q5 + Q6 (intensity and duration of morning stiffness in the spine) ≧4 at baseline. IXE efficacy assessment included change from baseline in BASDAI questions, total BASDAI, ASDAS, and SF-36 PCS, and BASDAI50 response rate at Week (W) 16, 24, and 52. [Results] A total of 450 patients (placebo [PBO], N=151; IXE every 4 weeks (Q4W), N=162; IXE Q2W, N=137) met the analysis criteria. At 16 W, both IXE treatment groups showed significant improvement compared to PBO on all assessment measures (all; p<.001); mean changes from baseline at 16 W in BASDAI Q2 and ASDAS for each treatment group were -1.2/-2.1/-2.3 and -0.4/-1.3/-1.2, respectively. These improvements were also observed at 24 W and sustained at 52 W. [Conclusions] IXE is effective in reducing axial symptoms and improving QoL in patients with active PsA presenting with symptoms suggestive of axial involvement.

W8-5

Upadacitinib Versus Adalimumab on Routine Assessment of Patient Index Data 3 (RAPID3) in Patients with Psoriatic Arthritis

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Conflict of interest: Yes

[Objective] To evaluate the impact of treatment with Upadacitinib (UPA) vs Adalimumab (ADA) on RAPID3 through 56 weeks in SELECT-PsA 1 [Methods] The Data from SELECT-PsA 1 trial, in which patients (pts) with PsA and an inadequate response or intolerance to ≧1 non-biologic DMARD received UPA 15 mg or 30 mg once daily, ADA 40 mg every other week (wk), or placebo (PBO; switched at wk 24 to either UPA 15 mg or 30 mg). This analysis included data from the UPA 15 mg, ADA, and PBO treatment arms. [Results] A total of 1,274 pts (PBO: n=421; UPA 15 mg: n=425; ADA: n=428) were included from SELECT-PsA 1. Pts receiving UPA showed a greater improvement from BL in RAPID3 vs ADA at all visits from wk 16 to wk 56, -9.5 vs -7.7 respectively at wk56. A higher proportion of pts treated with UPA achieved MCID in RAPID3 than those on ADA from wk 24 to wk 56. By wk 56, approximately half of pts on either therapy were in RAPID3 remission or LDA, with UPA showing a numerical improvement relative to ADA (30/21/31/18% of pts were in remission/LDA/MDA/HDA on UPA vs 28/17/30/25% on ADA). [Conclusions] UPA 15 mg treatment led to greater improvements over ADA in RAPID3 from wk 16 to 56. The majority of pts achieved MCID in RAPID3 after 12 wks of UPA or ADA, with higher proportions achieving MCID on UPA vs ADA by wk 24.

W8-6

Efficacy of ixekizumab in patients with active psoriatic arthritis, with and without concomitant methotrexate: two global Phase 3 study 3-year results

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Conflict of interest: Yes

[Objective] To evaluate the 3-year efficacy of ixekizumab (IXE) in patients with active psoriatic arthritis (PsA) based on concomitant methotrexate (MTX) use. [Methods] Patients with PsA who were biologic-naïve (SPIRIT-P1, NCT01695239) or had prior inadequate response/intolerance to tumor necrosis factor inhibitors (SPIRIT-P2, NCT02349295) were randomized to receive 80-mg IXE every 4 weeks after receiving 160-mg IXE at baseline. In this analysis, IXE efficacy was evaluated in 2 subgroups: (1) IXE monotherapy, (2) IXE and concomitant MTX. The assessment included ACR 20/50/70 responses and mTSS at Week (Wk) 52, 108, and 156. [Results] A total of 177 patients were included in the analysis: 89 patients in IXE monotherapy, 88 in IXE and MTX. Improvements in signs and symptoms of PsA were observed in both subgroups; ACR20/50/70 at Wk 156 were 59.1/46.2/30.7% and 67.0/47.4/28.4%, respectively. The cumulative probability plot for change from baseline in mTSS (SPIRIT-P1 only) showed that radiographic progression of structural joint damage was similar between two subgroups. At Wk 156, mean (SD) mTSS change from baseline were 1.1 (3.2) and 2.6 (9.3), respectively. [Conclusions] IXE showed sustained efficacy in treating patients with PsA up to 3 years regardless of the concomitant use of MTX.

W9-1

Analysis of the characteristics of rheumatoid arthritis patients with or without fractures

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Conflict of interest: None

[Objective] We investigated the characteristics of rheumatoid arthritis (RA) patients, depending on the presence or absence of fractures. [Methods] As of September 2022, 369 patients undergoing RA treatment were divided into 104 patients with fractures (F group) and 265 patients without fractures (NF group). We examined age, sex, disease duration, RA treatment, oral glucocorticoid rate, Steinbrocker stage/class, DAS28-ESR, bone mineral density (BMD) examination rate, %Young adult mean, and osteoporosis treatment rate/methods between the two groups. [Results] Only items with significant differences were listed. Age was significantly older in the F group. The disease duration was significantly longer. The rate of oral glucocorticoid rate was significantly higher. Both Steinbrocker stage and class were significantly higher, and the DAS28-ESR was significantly higher. BMD examination rate was significantly higher. The rate of treatment for osteoporosis was significantly higher. [Conclusions] RA patients undergoing treatment in our department with fractures were elderly, had a long disease period, were frequently taking oral glucocorticoid, had progressive joint destruction, had decreased ADL, and were actively undergoing osteoporosis treatment.

W9-2

Prevalence of and factors associated with sarcopenia in Japanese patients with rheumatoid arthritis: results from the IORRA cohort study

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Conflict of interest: None

[Objective] This study aimed to evaluate the prevalence of, and the factors associated with, sarcopenia in Japanese patients with rheumatoid

arthritis (RA). [Methods] Patients with RA enrolled in the Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort completed self-administered questionnaires, which included SARC-F. Sarcopenia was assessed by the SARC-F. Logistic regression analyses were used to evaluate associations between clinical variables and sarcopenia. [Results] Among 2,720 Japanese patients with RA (87.3% female, mean age 62.3 years) who participated this sarcopenia study, 385 (14.1%) patients were categorized as sarcopenia. In multivariable models, age (per 10 years, odds ratio [OR] 1.18, 95% confidence interval [CI] 1.01 to 1.38), body mass index (BMI) (OR 1.09, 95% CI 1.04 to 1.15), the European Quality of Life-5 Dimensions (per 0.1 points, OR 0.59, 95% CI 0.52 to 0.66), Japanese version of the Health Assessment Questionnaire (OR 14.7, 95% CI 10.2 to 21.2) were significantly ($P < 0.05$) associated with sarcopenia. [Conclusions] Our data suggest that more than a few Japanese patients with RA have sarcopenia. Older age, high BMI, low health related quality of life, and high disability appear to be associated with sarcopenia in Japanese patients with RA.

W9-3

Risk factor analysis of fractures in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To explore the risk factors for fragility fractures in rheumatoid arthritis (RA) patients. [Methods] From January 2010, through July 2020, 636 RA patients were included in this study. The patients were divided into two groups: the new incident fracture group (group A: 147 cases) and the no incident fracture group (group B: 489 cases) based on evidence or absence of new incident fractures. The demographics, and clinical characteristics, were analyzed. [Results] After age and sex matching, 147 patients were allocated to each group, respectively. Young adult mean (YAM) values of femur were 67.7/73.7% and those of lumbar spine were 81.0/86.0% in group A/B, both of which were significant ($p<0.01$, 0.01, respectively). In univariate analysis, evidence of osteoporosis intervention, especially denosumab use, and a history of steroid use were associated with fracture incidence ($p = 0.02$, 0.002, 0.03, respectively) significantly. In multivariate analysis, YAM value of femur (OR: 0.386), a history of steroid use (OR: 2.04), and osteoporosis intervention (OR: 0.413) were significantly associated with the incidence of fractures. [Conclusions] YAM value of femur, a history of steroid use, and osteoporosis intervention were significant fracture risk factors.

W9-4

Determination of criteria for initiation of pharmacotherapy for osteoporosis using FRAX® in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The primary osteoporosis (OP) guideline-based decision for initiation of medications (GL judgment) is often applied to RA patients in real clinical practice. We compared the GL judgment with the Fracture Risk Assessment Tool (FRAX) judgment. [Methods] A total of 103 RA patients with a mean age of 72.0 years were enrolled, in whom bone mineral density (BMD) and FRAX results were simultaneously obtained. For the FRAX judgment, patients who met either a hip fracture risk of ≧5.5% or a major osteoporotic fracture risk of ≧17.0% were judged to be requiring OP medications according to a previous study (J Bone Miner Metab. 40: 860-868). The difference between the GL and FRAX judgments was evaluated, and the accuracy of the GL judgment when the FRAX judgment was taken as the true prevalence of OP was also evaluated. [Results] Forty-nine patients (47.6%) and 60 patients (58.3%) required medications according to the GL and the FRAX judgment, respectively ($p<0.001$). The positive and negative predictive values and the diagnostic accuracy of the GL judgment were 0.959, 0.759, and 0.854, respectively. [Conclusions] The fracture risk of RA patients may be underestimated, suggesting the need to use FRAX results to determine the indication for OP medications.

W9-5

Low serum 25 (OH)D levels may influence that patients fall within 1 year after primary total knee arthroplasty

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Conflict of interest: None

[Objective] We conducted a cross-sectional survey of patients who fall within 1 year after TKA. [Methods] Patients with end-stage osteoarthritis of the knee who underwent primary TKA at our hospital for July 2020 to May 2021 and who gave written consent for this study were included. Preoperative and 1 year postoperative locomotive syndrome, presence of sarcopenia, presence of frail, functional assessment (JOA score, KSS, EQ-5D), quadriceps strength, knee range of motion, femoral YAM value, serum 25 (OH)D levels, and bone turnover markers (TRACP-5b, total P1NP) were measured and a comparison was made between the two groups based on the presence or absence of a history of falls within 1 year postoperative TKA. [Results] The subjects consisted of 65 patients with 65 knees, 8 with falls and 57 no falls. Preoperative serum 25 (OH)D levels were 11.7±4.7 ng/ml in fall group and 15.9±5.8 ng/ml in no fall group, which were significantly lower in fall group ($p=0.041$). The rate of preoperative severe sarcopenia was significantly higher in fall group ($p=0.014$), and the rate of pre-frail or frail at 1 year postoperatively was significantly higher in fall group ($p=0.03$). [Conclusions] We hypothesize that the effect of low serum 25 (OH)D levels may be related to fall within 1 year postoperative TKA.

W9-6

Measurement of 25 (OH)vitamin D and the effectiveness of nutritional guidance in patients with rheumatic diseases. Measurement of 25 (OH) vitamin D and the effectiveness of nutritional guidance in patients with rheumatic diseases

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Conflict of interest: Yes

[Objective] To analyze the shortage of 25 (OH) vitamin D (25VD; ng/ml) and the effectiveness of nutritional guidance in patients with rheumatic diseases. [Methods] We measured 25VD in 686 patients (M 161, F 525, 65.6±14.9y/o) and provided nutritional guidance to patients with deficiency (less than 20) and shortage (more than 20, less than 30). We initiated denosumab and precipitated calcium carbonate, cholecalciferol, magnesium carbonate (Ca/VD) in patients with osteoporosis (OP) diagnosed based on bone mineral density (BMD). [Results] There were 513 patients with RA, 38 patients with SSc, 33 patients with PMR, and others (n=102). Among patients without vitamin preparation (n=623), there were 414 patients with deficiency (66.5%, 13.0±4.4), 167 with shortages (26.8%, 24.2±2.9), and 42 with normal 25VD (6.7%, 34.1±3.6). In 353 patients with deficiency, with only nutritional guidance, 25VD significantly increased from 12.9±4 to 18.8±6.9 ($p<0.001$) after one year. 122 patients (34.6%) became shortages and 21 patients (5.9%) became normal. 44 out of 686 (7.1%) started denosumab and Ca/VD. [Conclusions] Many patients had 25VD deficiency or shortages. Measurement of BMD is a good screening tool of OP in these patients. Increment of 25VD by nutritional guidance without medication was achieved.

W10-1

Clinical presentation and treatment of giant cell arteritis with and without intracranial lesions

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Conflict of interest: None

[Objective] It has been suggested that the clinical presentation of giant cell arteritis (GCA) differs whether intracranial lesions were included or not. In this study, we investigated the clinical presentation and treatment of cranial GCA (C-GCA) and large vessel GCA (LV-GCA). [Methods] Thirty-eight patients treated for GCA at our hospital from April 2009 to September 2021 were included. [Results] Of the 38 patients, 28 were in the C-GCA group and 10 in the LV-GCA group; the mean age of the entire GCA group was 75.3 years, and 9/38 (23%) were male. The LV-GCA group was younger at diagnosis ($p=0.03$), and the time to diagnosis was longer in the LV-GCA group ($p=0.01$). The median initial dose of prednisolone was 30 mg in the C-GCA group and 20 mg in the LV-GCA group, with the LV-GCA group having a significantly lower initial dose ($p<0.01$) and a lower cumulative dose of prednisolone during the first year of treatment ($p=0.02$). There was no significant difference between the two groups in the use of concomitant immunosuppressive drugs within one year ($p=0.71$), and in the relapse-free rate at 60 weeks ($p=0.08$). [Conclusions] The results suggest that patients with LV-GCA may be able to start treatment with a lower dose of steroids than those with C-GCA.

W10-2

The relationship between early-relapse and glucocorticoid reduction in giant cell arteritis

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Conflict of interest: None

[Objective] Since patients with giant cell arteritis (GCA) are elderly, adequate reduction of glucocorticoid (GC) dose is necessary to avoid their adverse effects. The aim of study is to elucidate the relationship between early-relapse and glucocorticoid in GCA patients. [Methods] GCA patients visited our department until 2010 to 2022 were included. Patients were divided in two groups according the recent dose of prednisolone (higer GC group, PSL>5 mg/day; lower GC group, PSL≦5 mg/day). We retrospectively analyzed the differences of clinical characteristics between these two groups. Relapse is defined as intensification treatment with some inflammatory signs. [Results] The mean age of the GCA patients were 72.9 years old and female were 85%. Higher GC group had higher prevalence of polymyalgia rheumatica (PMR; 42% vs 0%, $p=0.04$), and shorter time to first relapse (6.5±3.1 months vs 12.5±4.6 months, $p=0.04$) than lower GC group. There were no differences in large-vessel type, CRP titer, induction dose of GC, or severe infection. [Conclusions] GCA patients with insufficient reduction had higher prevalence of PMR and shorter time to first relapse. To avoid early-relapse with using other immunosuppressants is important for adequate reduction of GC in maintenance phase.

W10-3

Continuation Rate and Extended Interval of Tocilizumab in Patients Treated with Tocilizumab at our Hospital for Large Vasculitis

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Conflict of interest: None

[Objective] Giant cell arteritis (GCA) and Takayasu's arteritis (TAK) are classified as large vessel vasculitis, and tocilizumab (TCZ) has recently been used for their treatment. administration was discontinued in some cases due to side effects. We reviewed the use of TCZ in cases of large vasculitis at our hospital. [Methods] As of September 2022, we investigated the continuation rate, administration interval, and relapse rate of TCZ in patients with large vessel vasculitis (GCA: 10 cases, TAK: 7 cases) who could be followed at our hospital and affiliated hospitals. [Results] The mean time since the first TCZ administration was 42.2 months for all patients, and TCZ was discontinued in 3 of 17 patients, 2 at the patient's request and 1 due to suspected hepatotoxicity. The dosing interval was every 1 week in 2 cases, every 2 weeks in 2 cases, every 3 weeks in 2 cases, every 4 weeks in 9 cases, every 5 weeks in 1 case, and every 8 weeks in 1 case. There were 4 cases of relapse: 2 cases of relapse after extending the dosing interval, and 2 cases of relapse after discontinuing TCZ at the patient's request.

W10-4

Efficacy and safety of tocilizumab in patients with giant cell arteritis

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Conflict of interest: None

[Objective] To investigate the efficacy and safety of tocilizumab (TCZ) in giant cell arteritis (GCA) [Methods] Among 8 patients treated with TCZ for GCA, Patient background, Persistency rate, Average GCs administration period until GCs-free, Duration of remission and relapse rate after achieving GCs-free and Adverse events were examined retrospectively. [Results] The age at start of TCZ was 78 years (68-87), all cases were female, time from initial treatment to TCZ administration was 2 months (0-60), 6 cases were at the time of induction therapy, and 2 cases at the time of relapse. Two cases of polymyalgia rheumatoid arthritis and of aortic regurgitation were present. The average GCs dose at the time of TCZ introduction was 35 mg/day (20-45). TCZ was continued in all cases. 7 out of 8 cases had passed more than 6 months after starting TCZ. Currently, 5 cases have achieved GCs-free, and the time to achieve GCs-free is 2 years (1.4-3.3). All cases that achieved GCs-free are still in remission, and the duration of remission was 3 years (0.1-5.2). No adverse events were observed during TCZ use. [Conclusions] It was suggested that administration of TCZ may safely maintain GCs-free remission for a long period. The appropriate time to achieve GCs-free needs to be continuously examined.

W10-5

The clinical course of the GiACTA protocol for the remission induction therapy of giant cell arteritis

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Conflict of interest: None

[Objective] To investigate the clinical course and prednisolone (PSL) dose at 26 weeks after starting induction therapy of Japanese patients with giant cell arteritis (GCA) who were treated according to the GiACTA protocol. [Methods] Thirteen patients with cranial GCA who were treated from April 2016 to October 2021 in our hospital were enrolled. We compared the patients who were treated with Tocilizumab according to the GiACTA protocol (G group, n=4) with the patients who were received conventional therapy (C group, n=9). The efficacy was evaluated using CRP, ESR, ultrasound, MRI, PSL dose, and the absence of symptoms. [Results] Twenty-six weeks after starting induction therapy, the PSL dose (G group; 1.75±1.71 mg/day, C group; 12.78±5.22 mg/day, $P=0.006$), the levels of CRP (G group; 0.012±0.012 mg/dL, C group; 0.463±1.022 mg/dL), and ESR (G group; 6.00±3.00 mm/hr, C group; 11.25±8.66 mm/hr) were lower in G group. None of the patients experienced recurrence in both groups. None of the patients in G group required additional immunosuppressive treatment or increasing PSL dose. One patient in G group showed the halo sign at the temporal artery in ultrasound. [Conclusions] The PSL reduction regimen in GiACTA protocol may be useful for induc-

tion treatment for GCA.

W10-6

Interval spacing of Tocilizumab for Japanese Giant Cell Arteritis

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Conflict of interest: None

[Objective] In GCA, TCZ supported early glucocorticoid tapering and prevented disease relapse, improving long-term prognosis. However, evidence of its withdrawal or interval spacing has been limited. The objective of this study was to reveal whether interval spacing of TCZ is a feasible plan or not in Japanese GCA patients. [Methods] In this retrospective, single-center study, patients diagnosed with GCA who fulfilled ACR in 1990 criteria, and treated with subcutaneous TCZ 162 mg every week, also proved large vessel vasculitis by either TAB or PET-CT or contrasted CT were included. [Results] 23 patients were analyzed in this study. 12 (52.2%) patients were diagnosed with cranial GCA patients. All cases had maintained remission under TCZ every week and 17 (73.9%) patients discontinued GC at data collection. Among 17 patients who discontinued GC, spacing of TCZ to every 2 weeks was performed in 12 (70.6%) patients, every 3 weeks was 6 (35.3%) patients, and every 4 weeks was 5 (29.4%) patients. There was no relapse until TCZ intervals were spaced every 4 weeks. [Conclusions] After achieving glucocorticoid-free, more than half of the patients were able to space TCZ interval without relapse. Spacing TCZ up to every 4 weeks seemed to be a feasible treatment plan for Japanese GCA patients.

W11-1

Co-infection of Campylobacter jejuni and non-typhoidal Salmonella in a patient with systemic lupus erythematosus

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Conflict of interest: None

[Case] A 22-year-old, female patient with systemic lupus erythematosus presented to the emergency department with headache, chills, vomiting, non-bloody watery stools, abdominal pain, and fever. History-taking revealed that she had eaten grilled chicken five days earlier. A stool Gram stain and stool culture were performed; the former revealed Gram-negative spiral rods, leading to the diagnosis of Campylobacter enteritis. As the patient was immunocompromised, azithromycin 500 mg was administered for three days. The abdominal pain and vomiting improved thereafter, and the fever gradually resolved. Later, a stool culture grew non-typhoidal Salmonella. Later, *Campylobcter jejuni* was detected in a blood culture performed on the day of admission. A second blood culture was performed, and an additional 14 days of azithromycin therapy was prescribed. The second blood culture remained negative, and there was no symptom flare after the azithromycin therapy. [Clinical Implications] Whenever bacterial enteritis is suspected in an immunocompromised patient, it is important to perform blood and stool cultures and, whenever possible, a stool Gram stain as well.

W11-2

Re-start biologics and risk of recurrent serious infection in patients with rheumatoid arthritis during bDMARDs therapy

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Conflict of interest: None

[Objective] After serious infection (SI) during bDMARD (Bio) therapy in patients with rheumatoid arthritis (RA), Bio is either restarted or discontinued. Herein, we investigated the relationship between restarted Bio and recurrent SI in RA patients who had SI previously during Biotherapy. [Methods] Forty-four RA patients hospitalized due to SI during Bio therapy in our hospital between 2018 and 2021 were included. Discontinuation was defined as a case in which other Bios could not be continued, and a change to another Bio was considered a continuation. In addition, we analyzed whether restarting Bio after SI caused a recurrent SI. [Results] The details were as follows: ABT (mean age, 77 years; 13 cases), TCZ (69.1 years, 17 cases), SAR (50 years, one case), GLM (74.5 years, seven cases), ETN (75 years, two cases), CZP (82 years, one case), and ADA (65.3 years, three cases). Bio-resumption after SI occurred in 33 cases and was discontinued in 11 cases. Among the 33 resumed cases, 10 had recurrent SI, while three of the 11 discontinued cases had recurrent SI, with no significant difference between the two groups (p=0.8487). [Conclusion] No significant difference in the incidence of recurrent SI was observed between the resumption and discontinuation of Bio after SI in patients with RA.

W11-3

Actual status of pneumocystis pneumonia in rheumatoid arthritis patients using Aichi Prefecture DPC data

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Conflict of interest: None

Background: Pneumocystis pneumonia (PCP) in RA progresses rapidly, and early diagnosis and treatment of PCP are reported to be essential for the prevention of severe disease. It is important to understand the actual status of PCP from the viewpoint of prevention and early diagnosis of RA-PCP. Objective: To understand the actual status of PCP in RA patients. Methods: Using Aichi Prefecture DPC data, we included 31571 patients with PCP (n=707) among those with RA included in the DPC disease title at admission from 2015 to 2022. We defined comorbidities based on ICD10 codes and examined risk factors by logistic regression analysis as explanatory variables. Results: The background of patients with PCP was male (38%), and the mean age at admission was 70±13 years. Significant differences were observed in age, male, CCI score, dementia, diabetes mellitus (DM), malignancy, and interstitial pneumonia (IP) and logistic regression analysis revealed significant differences (OR,95% confidence interval) in age (0.98, 0.98-0.99), dementia (0.46,0.28-0.77), DM (1.3, 1.09-1.55), malignancy (1.49, 1.26-1.75), and IP (3.7,3.15-4.33) were factors associated with the development of PCP. Conclusion: Age, dementia, DM, malignancy and IP were factors associated with the development of PCP.

W11-4

A 20-year study on the standardized incidence ratio (SIR) of tuberculosis (TB) in rheumatoid arthritis (RA) patients by NinJa cohort data, and clinical characteristics of 83 cases newly developed TB

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Conflict of interest: None

[Objective] In 2021, the incidence of TB was 9.2 per 1 million population, Japan was able to join the long-awaited “low-prevalence countries”. We examined the transition of TB in RA patients for 20 years, and examined the clinical characteristics of RA patients who newly developed TB. [Methods] We calculated the SIR of TB from the clinical data on National Database of Rheumatic Diseases in Japan (***NinJa***) prospectively from 55 facilities for 20 years. [Results] TB developed in 83 of 204,604

RA patients enrolled in 2002-21, and the SIR of TB among RA patients was 1.58 for men, 2.14 for women, and 1.58 for all patients (95%CI: 1.24-1.92). Looking at the changes in the SIR for TB every two years, it peaked at 3.73 in 2008-09 and declined to 0.97 in 2020-21. 83 patients (26 males, 57 females) who developed TB were aged 68.6 years old and had long-term RA duration of 11.6 years. 26 patients (31.3%) were receiving MTX, 14 patients (16.9%) were receiving biologic agents and 1 patient (1.2%) was receiving a JAK inhibitor. Extra-pulmonary TB was frequently seen in 18 cases (21.7%). One patient died of TB, and the others recovered. [Conclusions] Our prospective study reaffirmed that the SIR of TB in RA patients is also on the decline, although the incidence of TB is decreasing in Japan.

W11-5

A nationwide survey report on the use of "The HTLV-1-positive rheumatoid arthritis medical care handbook Q&A (2nd Revised Edition)" targeting educational institutions certificated by Japan College of Rheumatology

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Conflict of interest: None

[Objective] This nationwide survey was performed to examine the use of "The HTLV-1-positive rheumatoid arthritis (RA) medical care handbook Q&A (2nd Revised Edition)" in clinical practice and assess the validity of its contents. [Methods] 596 educational institutions with Japan College of Rheumatology (JCR) certificates received both the handbook's second revision and a questionnaire. The questionnaire was used to perform an epidemiological descriptive study. [Results] Of the 596 facilities, 256 responded (response rate, 34.4%). About 30% of the responded facilities had experienced treating HTLV-1-positive RA patients. Of the 205 facilities, 35% were aware of the existence of the medical care handbook for HTLV-1-positive RA. Although 90% of facilities assessed the contents of the 2nd revised edition as suitable, there were constructive opinions that description based on evidence is required. The most frequently seen problem that was difficult to explain were whether biologics or JAK inhibitors affect the emergence of HTLV-1-associated illnesses such adult T-cell leukemia and myelopathy. [Conclusion] Although the medical care handbook is not well known yet, it has become clear that it is being used at facilities with medical care experiences of HTLV-1-positive RA.

W11-6

The study of clinical characteristics of Rheumatoid arthritis (RA) patients diagnosed with non-tuberculous mycobacterial pulmonary disease in our hospital

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Conflict of interest: None

Background: Rheumatoid arthritis (RA) patients have a higher prevalence of non-tuberculous mycobacterial pulmonary disease (NTM-PD) than that of the general population. Increasing risk of NTM-PD and other infectious disease are believed to be due to the presence of central and peripheral airway lesions as the lung complication of RA or combination with immunomodulation by RA treatment. However, NTM-PD with bronchiectasis sometimes precede the onset of RA. Objective: To evaluate the difference of pathology between two groups, we compared the clinical features of NTM-PD preceded by the diagnosis of RA (RA-NTM) and RA preceded by the diagnosis of NTM-PD (NTM-RA). Result: Of the 55 RA patients diagnosed with NTM-PD, 14 (25.5%) were in NTM-RA. The age at diagnosis of RA in NTM-RA was significantly higher than RA-NTM ($p<0.001$). As the causative bacteria of NTM-PD, the ratio of bacteria other than MAC in NTM-RA was significantly lower and the ratio of *Mycobacterium intracellulare* in NTM-RA was significantly higher than that of RA-NTM. However, history of use of biologics and JAK inhibitors in RA-NTM was significantly higher than the NTM-RA. Conclusion: The presence of bronchiectasis with NTM before the onset of RA may affects the pathology of NTM-PD itself and the treatment course of RA.

W12-1

The long-term trajectory of anti-MDA5 antibody level and recurrence in patients with dermatomyositis: a single-center, retrospective study

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Conflict of interest: None

[Objective] To investigate the trajectory of anti-MDA5 antibody levels and its relationship with recurrence in patients with dermatomyositis (DM). [Methods] Nineteen patients with anti-MDA5 antibodies who visited our hospital from August 2014 to July 2022 and were followed for >12 months were eligible. Anti-MDA5 antibody levels at diagnosis and every 6 months until 72 months were collected from the database. We analyzed the association of longitudinal changes of anti-MDA5 antibody levels with recurrence of DM. [Results] Clinical diagnosis included DM in 6, amyopathic DM in 12, and interstitial pneumonia with autoimmune features in one. During a median follow-up period of 1605 days [IQR 952-2181], anti-MDA5 antibody turned negative in 15 patients (79%) at a median of 12 months [IQR 8-30] after treatment introduction. Reappearance of anti-MDA5 antibodies was observed in 3 patients and one of them experienced recurrence of interstitial lung disease (ILD), while recurrence was not observed in the remaining 12 patients with sustained absence of anti-MDA5 antibodies. Anti-MDA5 antibody levels remained positive in 4 patients, and ILD recurred in all but one. [Conclusions] Patients with continuous positivity or reappearance of anti-MDA5 antibodies are at high risk for recurrence.

W12-2

Long-term prognosis of patients with anti-MDA5 antibody positive dermatomyositis

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Conflict of interest: None

[Object] Although improvements of short-term survival are observed in anti-MDA5 autoantibody-positive dermatomyositis (anti-MDA5+DM), little information exists regarding the long-term events. [Methods] 36 patients with anti-MDA5+DM during 2014 to 2022 were retrospectively analyzed for the long-term prognosis and medications. [Results] Early deaths within six months were observed in eight patients (22.2%), and two patients died after six months due to unresponsiveness to induction therapy at eight months and relapse of interstitial lung disease at 18 months. Among 26 cases survived, two patients required home oxygen therapy. 22 patients who were followed in outpatient setting, relapse was not observed, and titer of anti-MDA5 became normal in median 10 months. The dose of prednisolone was 6.6 mg/day in average, IVCY was performed six times in median, and tacrolimus and tofacitinib was continued in 82% and 30%, respectively. Infections were frequent in elderly patients and patients receiving rituximab. Vertebral compression fracture and disuse syndrome were major adverse events. [Conclusions] Relapse in long-term was infrequent in anti-MDA5Ab+DM, and tailored treatments should be provided based on the risk of death and adverse events of medications.

W12-3

Long-term prognosis of anti-MDA5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objective] Anti-MDA5 antibody-positive dermatomyositis (MDA5-DM) has a poor prognosis due to rapidly progressive interstitial lung disease. Although the triple therapy (high-dose glucocorticoid, cyclophosphamide, and calcineurin inhibitor) and tofacitinib are effective, details of long-term prognosis are still unknown. [Methods] A total of 78 MDA5-DM patients were enrolled retrospectively. Clinical data regarding long-term prognosis were collected. [Results] The median age was 54 years old, and females were 45 cases. Seventy-six cases had lung involvement including 32 cases with rapid-progressive interstitial lung disease. Seventeen cases died during the observation period (14 at remission induction and three at relapse). Fifteen cases relapsed, and none of the patients who achieved normalization of anti-MDA5 antibody relapsed. Nine cases developed serious infections, and one case died due to infection. Seventeen cases achieved glucocorticoid-free remission, and seven withdrew all immunosuppressant therapy. [Conclusions] Long-term prognosis of MDA5-DM patients was generally good when they succeeded in remission induction at the onset. However, relapses and serious infections were sometimes seen. Normalization of anti-MDA5 antibody might be associated with a reduced risk of relapse.

W12-4

Characteristics of Anti-MDA5 Antibody-Positive Dermatomyositis complicated by skin ulcer

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Conflict of interest: None

[Objective] To investigate the clinical characteristics and prognosis of patients with anti-MDA5 antibody-positive dermatomyositis (DM) and amyopathic dermatomyositis (CADM) complicated by skin ulcers. [Methods] Twenty-four patients with anti-MDA5 antibody-positive DM and CADM experienced at our hospital from May 2005 to May 2022 were included. Patient background, treatment, and prognosis were compared between patients with skin ulcers (5 cases) and those without skin ulcers (19 cases). [Results] Patients with skin ulcers were predominantly male (60% vs 26%). Age, white blood cells, and levels of creatinine kinase, aldolase, LDH, CRP, and KL-6 were not different, but anti-MDA5 antibody levels were slightly higher in patients with skin ulcers (195 index (191, 1550) vs 175 index (148. 190). Arthritis was more frequent (80% vs 26%, p=0.047) and acute interstitial lung disease was somewhat less frequent (20% vs 37%) in patients with skin ulcers. Although survival was not significantly different, there were no early deaths (within 6 months) in patients with skin ulcers (0 vs 5). [Conclusions] The complication of skin ulcers may not be a poor prognostic factor in anti-MDA5 antibody-positive DM and CADM.

W12-5

Prognostic Factors in the cases with anti-MDA5 antibody positive clinically amyopathic dermatomyositis (CADM)

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Conflict of interest: None

[Objective] To reveal predictors of prognosis in the patients with anti-MDA5 antibodies positive CADM patients. [Methods] We identified 12 patients with anti-MDA5 antibody positive CADM who hospitalized between 2014 and 2022, and retrospectively evaluated 1) baseline characteristics and treatment outcomes, 2) the predictors of mortality, and 3) risk factors of recurrence. [Results] 1) Mean age was 56.2±9.7 years old. Gender was 4 men and 8 women. The mean amount of oxygen demand before treatment was 1.7±3.0 L/min. All of them were treated with glucocorticoid (GC), calcineurin inhibitor and cyclophosphamide. GC pulse or tofacitinib were administered in 9 and 4 patients, respectively, plasma exchange therapy was performed in 3 cases. There were 2 death cases with rapidly progressive interstitial lung disease (RP-ILD), 1 death case with infection, and 2 recurrence cases. 2) ALT was higher and more oxygen demand was needed before treatment in the death cases with RP-ILD than the other. ALT was also higher in comparison with the other seven cases developing RP-ILD. 3) The risk factor of recurrence were not identified. [Conclusions] ALT and oxygen demand at baseline may be predictors of prognosis in anti-MDA5 antibodies positive CADM patients.

W12-6

The efficacy of a triple combination of Baricitinib, Rituximab, and Tacrolimus in the treatment of Anti-MDA 5-Positive Dermatomyositis with predicted poor prognosis

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Conflict of interest: None

[Objective] Anti-MDA5-Positive Dermatomyositis (MDA5-DM) is often accompanied by rapidly progressive interstitial lung disease (ILD) and has poor prognosis. Recently, combined therapy with Tacrolimus (TAC) and Cyclophosphamide (CY) (TC therapy) has been reported to improve its prognosis, but some cases cannot be saved. Three cases with poor prognosis treated by combination of Baricitinib (BAR), Rituximab (RTX), and TAC (BRT therapy) were survived. [Methods] TC (n=2) and BRT (n=3): age (TC: 64±3, BRT: 56±4), ferritin (TC: 914±657, BRT: 1378±475), LDH (TC: 433±108, BRT: 561±246), anti-MDA5 (TC: 3750 ±235, BRT: 2935±2602). One on BRT already had rapidly progressive ILD + mediastinal emphysema. [Results] One on TC worsened during prednisolone reduction and died after 51 days, while all on BRT survived. There was no clear difference in laboratory findings between the two groups after initiation of therapy. [Conclusions] In BRT, BAR was used to inhibit IFNγ and GM-CSF against uncontrollable hyperactivity of macrophages, and RTX was used for depletion of B cells which works rapidly and last for longer. Although we could not find significant immediate response of BRT as compared to TC, our results suggest the possibility of saving the lives which could not be saved in the past.

W13-1

Assessment of salivary gland ultrasonography in stimulated and unstimulated whole salivary flow rate test in primary Sjögren's syndrome

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Conflict of interest: None

[Objective] SWS and USW tests are used as WSFR tests in the diagnosis and classification criteria for SS, but discrepancies may be observed in both tests. The aim of this study was to examine the relationship between both WSFR tests and the salivary gland disorders using SGUS. [Methods] Forty-nine pSS patients were studied. The WSFR test used by gum test for SWS and the spitting method for UWS. SGUS was measured by OMERACT SGUS score and ultrasound elastography (USE). [Results] The SWS and UWS were correlated (r=0.78), with positive rates of 81.6% and 57.1%, respectively. Both tests showed that the SGUS grade increased as the WSFR decreased, which was consistent with the results of PGUS in SWS and SMGUS in UWS. (SWS: SMGUS grade 0 vs 3, p=0.029, PGUS

grade 0 vs 3, p=0.027, grade 1 vs 2, p=0.044, grade1 vs 3, p=0.0036, USW: SMGUS grade0 vs 3, p=0.032, grade1 vs 3, p=0.0064, PGUS: grade0 vs 3, p=0.030). Decreased WSFR significantly decreased tissue elasticity in SMGUSE (SWS: Vs/E, p=0.0041/p=0.0037, USW: Vs/E, p=0.029/p=0.027), but no significant difference was observed in PGUSE. [Conclusions] SWS indicates damage to PG and USW indicates damage to SMG, suggesting that SMGUSE is more useful for elastography to observe inflammation and viscosity.

W13-2

Two years follow up of power doppler signals of salivary gland ultrasonography and correlation with disease activity in patients with Sjogren's Syndrome

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Conflict of interest: None

[Objective] The usefulness of power doppler signals (PD) of salivary gland ultrasonography in patients with Sjogren's syndrome (SS) is not established. Our purpose is to investigate the clinical usefulness of PD in daily medical care. [Methods] We studied 98 patients who were diagnosed SS from 2019 to 2022. We used scoring system of OMERACT, and studied relations with PD, greyscale (GS) and several clinical markers, and with changes of GS, PD and disease activity in 1,2 years later. Treatment was at an attending physician's discretion. [Results] Fifty-nine patients were primary SS. Fifty-nine and 31 patients were investigated one and two years later. Anti-SS-A antibody was associated with GS score of parotid glands (PG) and fibrosis, anti-SS-B with GS, PD of PG and fibrosis of submandibular glands (SG), and anti-centromere with GS, fibrosis in SG. Compared with GS, changes of PD were significant in PG and SG, and PD in PG decreased one year later. Initial PD was associated with GS 1 year later, and changes of 2 years of PD in SG correlated with changes of ESSPRI. [Conclusions] Anti-SS-B Ab was associated with PD. The changes of PD were significant and might predict the changes of the structure of salivary glands. Together with GS, PD could be useful for monitoring disease activity.

W13-3

Comparison of parotid gland and submandibular gland findings in salivary gland ultrasonography

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Conflict of interest: None

[Objective] We performed salivary gland ultrasonography in patients with suspected Sjögren's syndrome (SS) and compared the findings of the parotid and submandibular glands. [Methods] The grade of parotid gland findings in 139 suspected SS cases who underwent salivary gland ultrasound was classified into G0 to G4 according to the report by Ariji et al. Submandibular gland findings were classified as G0 corresponding to G0 of the parotid gland, G1 corresponding to G1+2 of the parotid gland, and G2 corresponding to G3+4 of the parotid gland. [Results] G0 was 29% in the submandibular gland and 48% in the parotid gland, which was significantly lower in the submandibular gland than in the parotid gland (p=0.0016). Increased blood flow detected by pulsed Doppler was found in 12% of parotid G1+2+3+4 and 21% of submandibular G1+2 (p=0.099). All cases with G0 submandibular glands also had G0 parotid glands. In the parotid gland G0 cases, the submandibular gland was G0 in 59%, G1 in 31%, and G2 in 10%. [Conclusions] This study suggests that salivary gland ultrasound findings are more pronounced in the submandibular gland than in the parotid gland. In SS, morphological changes appeared and progressed earlier in the submandibular gland than in the parotid gland.

W13-4

Diagnostic utility of salivary gland scintigraphy in Sjögren's syndrome with normal salivary secretion

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Conflict of interest: Yes

[Objective] Sjögren's syndrome (SS) may respond well to immunosuppressive treatment in the early stages when salivary secretion is preserved. We will discuss salivary gland scintigraphy findings to determine whether to perform a lip biopsy in patients with normal salivary secretion and to diagnose SS at an early stage. [Methods] Patients who underwent salivary gland scintigraphy, lip biopsy, and gum test at our institution were included. We divided patients into those with a positive gum test and examined the maximum accumulation rate (MAR) and maximum excretion rate (MSR) of salivary gland scintigraphy and the results of lip biopsy. [Results] The lip biopsy positivity rate was higher in the following patterns of salivary gland scintigraphy: 1) parotid MSR, submandibular gland MAR, and MSR, 2) parotid MSR and submandibular gland MSR, and 3) only submandibular gland MSR was decreased, and the rate was 50, 44, and 54.5%, respectively. The cutoffs calculated with ROC analysis for salivary and submandibular gland MAR, MSR and positive lip biopsy were used, the positive lip biopsy rate increased. [Conclusions] Patterns of salivary gland scintigraphy findings and cutoffs useful in determining whether to do lip biopsy in suspected SS patients with normal salivary gland secretion.

W13-5

Histological and immunological features of anti-centromere antibody positive patients with dryness

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Conflict of interest: None

[Objective] Anti-centromere antibody (ACA)+ Sjögren's syndrome (SS) is considered as a distinct clinical subgroup in SS. The purpose was to clarify immunological and histological features of ACA+ patients with dryness. [Methods] Patients with dryness who visited our department were enrolled. Clinical information was collected and statistically analyzed. [Results] 308 patients who had undergone labial salivary gland biopsy before SS diagnosis were enrolled. They were divided into four groups by serum ACA and anti-Ro/SS-A antibody (Ro) status as follows: 20 had ACA only (ACA), 201 had Ro only (Ro), 15 had both ACA and Ro (double-positive), and 72 had neither ACA nor Ro. A Focus Score (FS) ≧1 was observed in 80% with ACA, 73% with Ro, and 89% with double-positive. There was no relationship between the time course from the awareness of dryness to labial gland biopsy and a FS. Compared with Ro, ACA had a significantly lower proportion of fulfilling the classification criteria. In cases of SS diagnosis with ACA, histological change progressed compared to Ro. [Conclusions] There was no histological difference between patients had dryness with ACA and Ro. FS≧1 is required in patients without Ro for the diagnosis of SS. Therefore, histological change progressed more in ACA alone than in Ro.

W13-6

Altered number of CD8 positive regulatory T cells (CD8+Treg) and inhibition of the pathogenesis by induction of CD8+Treg differentiation in patients with primary Sjögren's syndrome (pSS)

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Conflict of interest: None

[Objective] To clarify pathogenic roles and therapeutic potential of $CD8^+$Treg in pSS. [Methods] 1) The population of peripheral $CD8^+$ and $CD4^+$Treg were compared by FCM between pSS patients and age gender-matched healthy controls (HC) (each N=10). 2) In pSS, the association between the population of peripheral $CD8^+$ and $CD4^+$Treg and clinical features were examined. 3) We examined the effects of CDK8/19 inhibitor (CDKi) against the induction of $CD8^+Foxp3^+$T cells differentiation from peripheral memory $CD8^+$T cells derived from HC by IL-2 and TGF-b in vitro. 4) The expression of functional molecules, suppressive ability for proliferation of responder T cells, and IL-10 production in the cells induced by method 3) were compared with those in memory $CD8^+$T cells. [Results] 1) $CD8^+$Treg population was significantly lower in pSS than in HC, while $CD4^+$Treg population was comparable. 2) In pSS, there was no significant association between the population of $CD8^+$ and $CD4^+$Treg and the clinical features. 3) The induction of $CD8^+Foxp3^+$T cells was significantly enhanced by CDKi. 4) The expression of CD25, GITR, CTLA4, and suppressive ability for proliferation were significantly enhanced, and IL-10 production was tended to increase. [Conclusion] CDKi might restore $CD8^+$Treg which had suppressive function in pSS.

W14-1

A prospective cohort study of the association between shared decision-making and trust in physicians in systemic lupus erythematosus: the TRUMP2-SLE study

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Conflict of interest: None

[Objective] To investigate the relationship between SLE patients' involvement with shared decision-making (SDM) and their trust in physicians through a multicenter prospective cohort study. [Methods] For SLE patients who visit outpatient clinics of five facilities, we collected data on SDM-Q-9, the score of SDM, and the Trust in Physician scale (TIPS), the index of reliability with the physician, through a self-administered questionnaire, and analyzed their relationship. [Results] We analyzed the data from 300 SLE patients (age 45.5 ± 14.2 years, 88% female). When patients were divided into two groups, those with baseline SDM-Q-9 of 75 or more (high SDM group; 159 cases, median 89 [IQR 80-96]) and those with SDM-Q-9 less than 75 (low SDM group; 141 cases, median 60 [53-69]), the high SDM group had a significantly higher TIPS at one year than the low SDM group (73 [66-82] vs. 66 [61-71], $p < 0.0001$). A multiple regression analysis with age, sex, disease duration, disease activity, annual income, final education, marital status, and TIPS at enrollment as covariates revealed a 0.88 (95% CI 0.24-1.52, $p = 0.007$) increase of 1-year TIPS by a 10-point rise in baseline SDM-Q-9. [Conclusions] The SDM contributes to building trust in physicians for SLE patients.

W14-2

Shared decision making and internet use for gathering health information in patients with systemic lupus erythematosus: a multicenter cross-sectional study

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Conflict of interest: None

[Objective] Shared decision-making (SDM) is one of the overarching principles in the management of systemic lupus erythematosus (SLE). We aimed to investigate how online information gathering behavior affect SDM in SLE. [Methods] In this cross-sectional study conducted at five academic centers, 464 patients with SLE were analyzed. The main exposures were the time of Internet use and patient's first preference for health information source. The outcome was degree of SDM measured via SDM-Q-9 (range: 0-100 pt). A general linear model adjusted for age, gender, education, income, marital status, history of cancer, disease duration, and SLEDAI was fit. Predicted mean scores on the SDM-Q-9 were calculated by levels of the exposures. [Results] SDM-Q-9 were lower among those who did not use the Internet than those who used it for ≧2 hrs (66.9 vs. 75.7 pt, difference: -8.8 pt [95%CI -16.9 to -0.6]). There was no difference in SDM-Q-9 between those who chose physician and those who chose the Internet as their first access. Those who chose other media had lower SDM-Q-9 than those who chose physician (74.9 vs. 67.4 pt, difference: -7.6 pt [95% CI -13.2 to -1.9]). [Conclusions] The present study suggests that degree of SDM is positively associated with online information-gathering behavior.

W14-3

Association between sleep-disordered breathing risks and depression in systemic lupus erythematosus patients: a cross-sectional study from TRUMP2-SLE study

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Conflict of interest: None

[Objective] Depression is a frequent problem in patients with systemic lupus erythematosus (SLE). Glucocorticoid (GC) treatment can lead to obesity; consequently, it can develop sleep-disordered breathing (SDB) such as sleep apnea syndrome (SAS). In SLE patients, the prevalence of SAS and the impact of SDB on depression are not known; therefore, we estimated the prevalence of SAS and the impact of SDB on depression. [Methods] 464 patients were enrolled. Patient Health Questionnaire-9 (PHQ-9) was used to evaluate depression (PHQ-9 score ≧110) as the outcome. The risk of SDB was assessed by the Berlin questionnaire (BQ). Logistic regression analysis was performed using age, sex, BMI, smoking history, alcohol consumption, diabetes, dyslipidemia, HT, and GC dose as adjustment variables. [Results] The mean age and BMI were 48, and 22.1, respectively. 76 patients were suspected of depression. 64 patients were suspected to have SAS. 1-, 2-, or 3- positive BQ risk categories were associated with depression (OR 3.3, 95%CI 1.8-6.3; OR 7.8, 95%CI 3.2-18.6; OR 6.6, 95%CI 1.1-39.6, respectively). [Conclusions] In SLE patients, suspected case SAS is not rare; having a risk category of SDB was associated with depression. The presence of SDB should be confirmed in SLE patients who have depression.

W14-4

Changes in Clinical Symptoms and Diagnosis of Anti-ARS Antibodies Positive Cases at the Initial Diagnosis

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Conflict of interest: None

[Objective] To reveal the clinical characteristics of patients with idiopathic inflammatory myopathy (IIM) positive for anti-ARS Ab (anti-aminoacyl transfer RNA synthetase antibodies), especially the changes in symptoms over the clinical course and diagnosis. [Methods] This was retrospective analysis of 126 IIM patients who had visited our hospital between 1998 and 2022 with anti-ARS Abs detected immunoprecipitation assays. [Results] Anti-ARS Ab positive IIM patients (n=98) included anti-Jo-1 (n=36), anti-EJ (n=31), anti-PL-7 (n=11), anti-PL-12 (n=12), anti-KS (n=4) and anti-OJ (n=3). Interstitial lung disease was detected in 96 (98%), 29% cases lacked cutaneous and muscular symptoms. The prevalence of myositis in anti-PL-7 Ab positive cases was 36% at the initial diagnosis, but myositis symptoms appeared in more cases than in other anti-ARS Ab positive cases within 3 years of onset of disease. 78% of cases were eventually diagnosed as polymyositis or dermatomyositis. [Conclusions] Patients with anti-ARS Ab positive IIMs have a high rate of interstitial lung disease from the initial diagnosis, and although PL-7 Ab positive cases lack muscle symptoms at initial diagnosis, many develop myositis during the course of the disease.

W14-5

Descriptive epidemiological study of polymyalgia rheumatica by age group using routinely collected health data (Cross-sectional study)

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Conflict of interest: Yes

[Objective] To evaluate the clinical features of polymyalgia rheumatica (PMR) in Japan by age group. [Methods] Using the RWD database (DB, approximately 23 million patients (pts)), pts who visited a department of rheumatology for PMR (ICD-10: M35.3) at least once or other departments at least twice (PMR pts) in 2020 were analysed by age group (≧50 and ≧65 years old (y)). The data included age, sex, comorbidities and prescribed medications. [Results] 2,170 PMR pts were recorded in the DB in 2020 (mean age, 75.3 y), and 2,052 pts and 1,869 pts were aged ≧50 and ≧65 y. The proportions of pts with osteoporosis (OP), hypertension (HT), diabetes mellitus (DM) and malignancy (MA) were 59.1%, 43.1%, 40.2% and 9.8% in ≧50 y and 59.1%, 44.4%, 41.0% and 10.0% in ≧65 y. The proportion of pts with MA in the prostate, gastrointestinal and lung were 4.7%, 3.2% and 1.0% in ≧50 y and 5.2%, 3.2% and 1.1% in >65 y. The proportions of pts who were prescribed glucocorticoids, medications for OP, HT and DM were 57.9%, 44.5%, 37.4% and 18.5% in ≧50 y and 59.4%, 45.7%, 39.1% and 19.6% in ≧65 y. [Conclusions] There were no major differences in the demographics, comorbidities or prescribed medications between age groups of the PMR pts and considering comorbidities for the treatment of PMR is desired.

W14-6

Glucocorticoid therapy and glucocorticoid-related adverse events in patients with polymyalgia rheumatica in Japan - A cohort study using routinely collected health data

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Conflict of interest: Yes

Objective: To evaluate glucocorticoid (GC) therapy and GC-related adverse events (GC-AE) in patients (pts) with polymyalgia rheumatica (PMR). Methods: The RWD database (approximately 23 million pts) was used. Inclusion criteria were pts with newly assigned PMR (ICD-10, M35.3) at 2010-2019, ≧2 GC prescriptions (Rx) within 180 days from the first assignment, GC dose ≧5 mg/d on D0 (the first Rx date), age ≧50y and CRP ≧1.0 mg/dL etc. The pts with autoimmune disease, Rx of immunosuppressant, GC dose ≧7.5 mg/d, RF (+), ACPA (+) etc. before D0 were excluded. Results: 373 PMR pts (mean age 77.3y) were analysed. The median initial GC dose was 15.0 mg/d, which gradually decreased to 3.5 mg/d at W52. The median cumulative (Cum) GC dose at W52 was 2455.0 mg. The Cum incidence rates of GC-AE up to W52 were 49.0%, 30.2%, 14.9%, 12.2%, 11.3%, 2.9% and 4.3% for osteoporosis, diabetes, hypertension, peptic ulcer, dyslipidemia, glaucoma and serious infection. The median CRP on D0 was 6.4 mg/dL, which fluctuated (0.1-0.3 mg/dL) W4-52. The proportion of pts with CRP higher than 0.3 mg/dL (pre-defined higher limit of normal) at W52 was 39.0%. Conclusions: The incidence of GC-AE was associated with the increased in Cum GC dose for the treatment of PMR. A treatment strategy that allows GC-sparing need to be considered.

W15-1

The results of Total Elbow Arthroplasty for patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] TheThe aim of this study is to evaluate the result of Total Elbow Arthroplasty for patients with Rheumatoid Arthritis. A total of 5 cases has revision in 17 cases. By multivariate analysis, the likelihood of being revision by poor cement technique. [Methods] To examined the results of total elbow replacement for patients with Rheumatoid Arthritis in Fukui Red Cross Hospital from 2005 through 2022. There were 6 male and 11 female with a mean age of 64.0±7.5 years. Complication were recoded and the predictor of revisions were calculated by multivariate analysis. [Results] A total of 5 cases has revision in 17 cases. By multivariate analysis, the likelihood of being revision by poor cement technique. [Conclusions] In this study, Revisions may be caused by poor cement technique

that It thought to be failure of long results of total elbow replacement.

W15-2

Long-term results of wide synovectomy of the elbow as a joint preserving surgery in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The incidence of elbow joint destruction is reported to be 20-65% of the patients with rheumatoid arthritis (RA). Total elbow arthroplasty is usually recommended for the joints of radiographically advanced stages (Larsen grades 3-5), however, we performed wide synovectomy even for rheumatoid elbow with advanced stages. [Methods] Twenty-three rheumatoid elbows were involved in this study. The changes of Larsen grade before and after surgery, and the changes of biological agents after surgery were retrospectively investigated. [Results] The averaged age at the time of surgery was 56.3 years. Fifteen elbows (65.2%) remained at the same Larsen grade as before surgery. In 8 cases which showed the progression in Larsen grade, 6 cases (75.0%) were needed to change biological agents after the surgery, on the other hand, in 15 cases which showed no progression, only 4 cases (26.7%) were needed to change biological agents. [Conclusions] Wide synovectomy for the rheumatoid elbows showed a good long-term outcome in terms of radiological evaluation. The results of this study suggest that wide synovectomy as joint preserving surgery may be adapted to even destroyed rheumatoid elbow joints if the disease activity is well controlled by the modern drug therapy.

W15-3

Total Wrist Arthrodesis using WFR® (Wrist Fusion Rod) for Rheumatoid Wrist

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Conflict of interest: None

[Objective] To investigate the results of total wrist arthrodesis using the WFR® and to investigate the patients who would benefit from this procedure. [Methods] Thirty-nine patients underwent total wrist arthrodesis using the Wrist Fusion Rod (WFR®) and Darrach procedure at the Niigata Rheumatic Center. The mean age was 66.2 years, the mean disease duration was 18.4 years, and the mean follow-up period was 76.6 months. There were 38 patients with RA and one patient with SLE. The clinical and radiological assessments were performed preoperatively and at the last follow-up. Using the satisfaction questionnaire sheet, the patient reported outcome was measured. [Results] At the last follow-up, disease activity, grip strength, forearm rotation, and radiographic alignment were significantly improved, and PtGA was significantly improved in the PRO. In the satisfaction questionnaire, pain, appearance, and overall satisfaction were high. The patient with an advanced ulnar carpal shift was highly satisfied with the operation. Complications occurred in 8 hands, and hardware was removed in 4 hands. [Conclusions] The total wrist arthrodesis using WFR® appeared to be useful.

W15-4

Relationship between finger range of motion and fracture rate at 6 months postoperatively in AVANTA finger arthroplasty

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Conflict of interest: None

[Purpose] We previously reported at this meeting that AVANTA is more susceptible to bending and fracture than Swanson. Although the independent risk factor for AVANTA failure is the bending angle, it is unclear how much bending is required to cause implant fracture. The purpose of this study was to investigate the cutoff value of the flexion angle for this failure. [Methods] We evaluated the hand range of motion of 279 MCP joint fingers in 72 patients before surgery and at 6 months postoperatively. They underwent MCP joint arthroplasty using AVANTA and postoperative rehabilitation at our hospital between June 2005 and May 2019, [Results] The mean flexion angle of the fracture group was 65.9 degrees, and that of the intact group was 56.9 degrees, with the fracture group having significantly more flexion ($P<0.05$). ROC analysis of AVANTA flexion angle and fracture showed a cutoff value of 61 degrees (AUC: 0.67) [Discussion] The results of the ROC analysis showed that the cutoff value for fracture was 61 degrees (AUC: 0.67). During flexion range of motion training of MCP in postoperative rehabilitation, the flexion angle should be carefully considered, and we informed for patients the risk of fracture implant depending on the flexion angle.

W15-5

Total management for rheumatoid hand in the era of well-controlled inflammation

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Conflict of interest: None

[Objective] In RA, it became possible to control the inflammation. On the other hand, rheumatoid hand will worsen over time, so it is necessary to perform accurate evaluation and functional reconstruction at the appropriate time. We examined the evaluation and the timing of surgery based on the course of treatment for rheumatoid hands that underwent joint-preserving surgery. [Methods] Joint-preserving surgery was performed for 14 thumbs with Type I deformity, who were unable to actively flex the IP joint. In 39 fingers of ulnar deviation with extensor tendon dislocation, soft tissue reconstruction was performed prioritizing joint preservation. Pain, limited range of motion, functional assessment, and recurrence were investigated. [Results] The average postoperative follow-up period for thumb deformity and ulnar deviation were 55 and 49 months. All deformities were corrected, range of motion and function was significantly improved. [Conclusion] Rheumatoid hand cannot be evaluated only by composite measure such as DAS28 and SDAI, and it is not possible to determine the optimal timing of surgery. By conducting an accurate assessment of the current situation and selecting the optimal surgical timing, it is possible to treat rheumatoid hand by preserving the joints.

W15-6

Surgical repair of extensor tendon ruptures in the rheumatoid wrist under the selective sensory nerve block and monitored anesthesia care

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Conflict of interest: None

[Objective] This paper explains the combined use of MAC and the selective sensory nerve block under us to induce intraoperative awareness to decide the tension of tendon and reports on its effectiveness. [Methods] The subjects are 8 hands with RA which underwent the reconstruction of subcutaneous extensor tendon rupture in our department between 2020 and 2021. For all cases, we released tourniquet after S-K procedure. About ten minutes later, patients were instructed to spontaneously move fingers so that the operator can check the ROM. Geldmacher criteria for outcome assessment was used for the motion range of MP joint at survey, while HAND20 and Quick-DASH were used in clinical evaluation. [Results] Appropriate tension of tendon suture and early training resulted in no cases with limited inflection at survey, with five cases marking "good" and two cases "fair" in the Geldmacher criteria for outcome assessment. While the values at operation at HAND20 65.3 and Quick-DASH 59.2 improved

to 28.8, 25.3 at survey respectively, no significant differences were observed. [Conclusions] Combined use of MAC and selective sensory nerve block in reconstruction of subcutaneous extensor tendon rupture due to RA seems to be effective in enabling decision on the tension of tendon suture.

W16-1

Is the patient-reported outcome measures for hips with rheumatoid arthritis inferior after total hip arthroplasty than those for osteoarthritic hips?

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Conflict of interest: None

[Objective] To compare patient-reported outcome measures (PROMs) after total hip arthroplasty (THA) between hips with rheumatoid arthritis (RA) and osteoarthritis (OA). [Methods] Twenty-one patients with 25 RA hips and 246 patients with 306 OA hips were included. Postoperative satisfaction for THA (100-point visual analog scale, VAS satisfaction), Oxford hip score, Forgotten Joint Score-12, and UCLA activity scale were evaluated. [Results] The mean age at surgery was 60 years in the RA group and 61 years in the OA group, and the mean postoperative follow-up was 5.7 years in the RA group and 5.8 years in the OA group. No significant differences were found between the two groups in postoperative VAS satisfaction (90 ± 13 vs 90 ± 15, respectively), Oxford Hip Score (43 ± 11 vs. 42 ± 8, respectively), Forgotten Joint Score-12 (48 ± 27 vs. 52 ± 26, respectively), and UCLA activity scale (4.8 ± 1.6, 4.7 ± 1.6, respectively). [Conclusions] THA for RA hips generally demonstrated good PROMs without significant differences compared with OA hips in any scores. Control of disease activity with disease-modifying anti-rheumatic drugs, appropriate surgical techniques, and postoperative care may lead to favorable outcomes in RA hips as in OA hips after THA.

W16-2

the influence of low muscle mass estimated by BIA in female patients with osteoarthritis undergoing total hip arthroplasty

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Conflict of interest: None

[Objective] Arthroplasty generally give good results for osteoarthritis (OA) but the results are some differences in individual cases. We investigated whether preoperative muscle mass and gait speed, are associated with postoperative outcomes in female patients with total hip arthroplasty (THA) (36 cases). [Methods] Cases were divided into a low muscle mass group (L-M group) and a normal group (N-M group), and a low gait speed group (L-G group) and a normal group (N-G group). [Results] Height, weight, and Geriatric Nutritional Risk Index (GNRI) were lower in the L-M group, but there was no difference in the preoperative JOA score, the number of days required to achieve 10 m cane walking, and the JOA score half a year later. Compared to the N-G group, the L-G group had higher age, hospitalization days, and the number of days required to acquire 10 m postoperative cane walking, and had lower, preoperative and 6 months postoperative JOA scores. [Conclusions] Although the low muscle mass group may have worse condition, there was no significant difference in short-term postoperative results. On the other hand, the low gait speed group had a longer hospital stay, and although the JOA score improved, it was significantly lower even half a year later, suggesting a significant impact.

W16-3

Walking ability after hemiarthroplasty for femoral neck fractures with rheumatoid patients

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Conflict of interest: None

[Objective] we report the walking ability of rheumatoid arthritis patients (RA patients) after hemiarthroplasty for femoral neck fractures compared with non-rheumatoid arthritis patients (non-RA patients). [Methods] The subjects were 36 femoral neck fractures in 36 patients with RA who underwent hemiarthroplasty at our hospital for 10 years from April 2010 to March 2020. There were 6 males and 30 females, with an average age at the time of surgery of 64 years. On the other hand, the control group consisted of 200 femoral neck fractures in non-RA patients who underwent hemiarthroplasty at our hospital during the above period. We compared the walking ability of the RA group and the non-RA group at 6 months after surgery. [Results] In the RA group, 74% were able to walk independently and 26% were not, and in the non-RA group 52%were able to walk independently and 48% were not. Postoperative walking ability was significantly ($P<0.05$) better in the RA group. [Conclusions] The walking ability of RA patients after hemiarthroplasty for femoral neck fracture was better than that of non-RA patients.

W16-4

Patient-reported outcomes in patients with rheumatoid arthritis after knee and hip total arthroplasty

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Conflict of interest: None

[Objective] To clarify the impact of total hip/knee arthroplasty on patient-reported outcomes in patients with rheumatoid arthritis. [Methods] 60 patients who underwent THA/TKA were included. Modified Health Assessment Questionnaire (mHAQ), patients' global and pain visual analogue scale (VAS) were examined just before surgery and at median 19 months follow up. [Results] mHAQ, patients' global and pain VAS decreased with statistic significance by -0.22, -21, and -18, respectively. Among mHAQ items, the score of walking, activity, and dressing were improved significantly (p value <0.01, 0.03, and 0.03, respectively. [Conclusions] Patient-reported outcomes after THA/TKA in patients with rheumatoid arthritis improved.

W16-5

High tibial osteotomy can afford good clinical outcome in rheumatoid arthritis patients treated with biologic disease-modifying anti-rheumatic drugs

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Conflict of interest: None

High tibial osteotomy (HTO) has been generally contraindicated in patients with rheumatoid arthritis (RA) traditionally, because synovial inflammation may exacerbate joint damage after surgery. Recently, the natural course of joint destruction in RA has dramatically changed with new treatment strategies and introduction of biologic disease-modifying anti-rheumatic drugs (bDMARDs). We report three RA cases who underwent HTO, whose disease activities were well controlled by bDMARDs. They showed sufficient clinical results evaluated by objective and subjective assessment. We believe that HTO can be a joint preservation surgery even for RA patients when selected with combination of bDMARD.

W16-6

Review of the rheumatoid knees that could avoid TKA

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Conflict of interest: None

[Introduction] We investigated the characteristics of cases in which TKA could be avoided by aggressive drug therapy. [Subjects and Methods] Patients with rheumatoid arthritis who wished to undergo TKA for severe knee joint pain or whose doctors considered TKA were included in this study. We compared the non-TKA group (13 patients, 21 knees) who could avoid TKA by starting or changing biologics/JAK inhibitors with

the TKA group (94 patients, 126 knees) who could not avoid TKA. Preintervention data including age, sex, disease duration, medications, CRP, pain VAS, DAS28, and Larsen grade were examined. Medication changes and post-intervention data were also investigated. [Results] The age and duration of disease were 65.2 years and 2.5 years in the non-TKA group, and 69.5 years and 9.8 years in the TKA group. Biologics/JAK inhibitor use were higher in the non-TKA group. In the non-TKA group, biologics and JAK inhibitors were added in 7 cases and changed in 6 cases, and after the intervention CRP, pain VAS, and DAS28-CRP improved to 0.2, 30, and 2.5, respectively. [Discussion] There are many cases in which TKA can be avoided by starting or changing biologics/JAK inhibitors, and aggressive drug therapy should be considered first in elderly cases with a short disease duration.

W17-1

Nursing care of apheresis therapy for psoriatic arthritis ~ Nursing interventions for granulocyte adsorption therapy (GMA/GCAP) ~

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Conflict of interest: None

[Objective] Granulocyte and monocyte adsorptive apheresis (GMA/GCAP) was expanded in 2019 as an option for the treatment of psoriatic arthritis (PsA). From a survey of patients with GMA/GCAP, the purpose of this study is to determine what nursing interventions are needed to improve Patient Reported Outcome (PRO). [Methods] PsA patients with GMA/GCAP at our center from February 2021 to September 2022 were included (N=41). We examined the relationship between patients' psychology during and after the GMA/GCAP and the interventions of health care professionals. [Results] The average BASDAI at the time of GMA/GCAP introduction was approximately 4.49 (SD 2.08) and was resistant to several biological DMARDs. 39/41 patients underwent the procedure 10 times. Regarding "Impression of GMA/GCAP during the treatment" and "Impression of GMA/GCAP at the end of the treatment", 57.9% of the patients felt better than the treatment. 84.2% of the respondents felt secure about "Attendant by a nurse or other health care provider". The ΔBASDAI and "morning stiffness" was significantly improved. [Conclusions] Nurses' efforts to listen to complaints and alleviate pain, and their nursing interventions and innovations that were close to the patient, contributed to the improvement of ΔBASDAI as a patient PRO.

W17-2

A Study on Foot Care Interventions for Psoriatic Arthritis

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Conflict of interest: None

[Objective] Although the importance of foot care is a well-known fact, it is unclear whether there is a difference in frequency and symptoms of patients with foot care, between rheumatoid arthritis (RA) and psoriatic arthritis (PsA) which have pathological difference. [Methods] We enrolled 166 patients, including RA (N=123) and PsA (N=43) who got foot care, at our hospital from Feb 2021 to April. We evaluated and scored patients' symptoms by foot care record sheet and analyzed the results. [Results] Compare to RA and PsA patients, the mean duration of the disorder is 5.9 and 14 years and average number of foot care are 10.8 and 9.7 times. There are no significant difference between the two different disease patients in coldness (p=0.1709), pain (p=0.593), valgus (p=0.1630), callus (p=0.4712), tinea pedis (p=0.1252) and onychomycosis (p=0.0860). [Conclusions] Regardless of the difference of disease duration and pathological difference between RA and PsA, PsA patients also had foot problems as same as RA patients. We considered that the results of this study reminded us the importance of foot care for PsA patients, especially skin and nail symptoms.

W17-3

Shared Decision Making (SDM) in the treatment of rheumatoid arthritis - Rheumatoid care nurse intervention

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Conflict of interest: None

Early diagnosis and T2T are essential for rheumatoid arthritis treatment, but the patient's understanding is very important. Shared Decision Making (SDM) is an interactive decision-making method that requires three conditions: patient's willingness to participate, treatment staff's willingness, and completeness of information materials called decision aids. In our department, rheumatoid arthritis care nurses use joint ultrasound POCUS to help explain the pathology of rheumatoid arthritis and treatment strategies. In SDM this time, he examined whether POCUS played a role using a questionnaire to patients. Results: We found that POCUS was useful for SDM. Conclusion: POCUS is considered useful for SDM.

W17-4

Survey on the Challenges of Telephone Consultations by Nurses in Rheumatology Care

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Conflict of interest: None

Purpose: This study aimed to clarify the challenges of telephone consultations by nurses. Methods: The study design was a qualitative descriptive study using a focus group interview. The participants were nurses engaged in rheumatology care. Results: Two groups of seven nurses each participated. The median age, nursing experience, and rheumatology care experience were 50 years old, 27 and 16 years, respectively. The results showed that the challenges faced by nurses were grouped into five categories: (1) psychological state of nurses receiving calls, (2) knowledge of consultation contents, (3) consultation system, (4) information sharing, and (5) education. Firstly, nurses felt some anxiety when receiving calls. The consultations covered a wide range of topics besides rheumatology, with participants citing a lack of knowledge as a challenge. Insufficient support system was also an issue. Information was not shared properly (e.g., doctor's descriptions in the medical record were insufficient). Furthermore, a lack of proper education was also identified. Conclusion: Telephone consultations are initially received by nurses usually. This survey revealed a wide range of challenges for nurses. Patient-accessible telephone consultation is important for patient care and needs to be addressed.

W17-5

Survey of Registered Pharmacists of the Japan Rheumatism Foundation -Part 1 ~A nationwide questionnaire survey on the current status of registered pharmacists and issues for drug-pharmacy collaboration~

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Conflict of interest: None

[Objective] The Japan Rheumatism Foundation registered pharmacist (registered pharmacist) system was established in 2015, and more than 500 pharmacists provide patient guidance for rheumatic diseases. However, hospital pharmacists and pharmacy pharmacists do not work together, so it is difficult to understand what each of them needs. To solve this problem, we launched the Japan Rheumatology Pharmacists' Study Group (JRAPP) in November 2021 and surveyed the current situation and needs.

[Methods] From January to March 2022, we randomly selected one registered pharmacist from each facility, and mailed questionnaires to 214 hospital pharmacists and 134 pharmacy pharmacists. [Results] 84 hospital pharmacists and 48 pharmacy pharmacists responded. The main reason (77%) for qualification acquisition was "to be involved in rheumatic diseases". Many pharmacists chose "increased opportunities for self-improvement" as a merit (70%), and difficulty to use and maintain as a demerit. Eighty percent of them obtained knowledge from external scientific meetings. [Conclusions] Many registered pharmacists make use of workshops and lectures and maintain their qualifications for team medicine to support patients. We want to consider methods of educational activities that can improve the quality.

W17-6

Survey of Registered Pharmacists of the Japan Rheumatism Foundation -Part 2 -Analysis of the current situation and issues for collaboration through a nationwide questionnaire survey-

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Conflict of interest: None

[Objective] Cooperation between hospitals and insurance pharmacist is important, but the activities of each are difficult to grasp. Therefore, in order to clarify issues for medicine-pharmacy collaboration, we surveyed the activities of registered pharmacists of the Japan Rheumatism Foundation ("registered pharmacists"). [Methods] January to March 2022, 347 registered pharmacists were surveyed. [Results] The response rate was 39% (84 hospital and 48 pharmacy). Hospital pharmacists provided 43% of outpatients with medication guidance, while pharmacy pharmacists provided guidance and monitoring of adverse drug reactions (73%) and checking medication adherence (77%) at every visit. The level of satisfaction with drug-drug collaboration was low, at 5% for hospital pharmacists and 21% for pharmacy pharmacists, with many respondents stating that the reasons for this were not only the "lack of pharmacists" and the "lack of a system", but also the "lack of collaboration tools". [Conclusions] This survey revealed the actual activities of registered pharmacists. The cooperation between pharmacists and pharmacies is still insufficient. In the future, we would like to increase opportunities to exchange information and strengthen collaboration.

W18-1

A Study of Satisfaction with Treatment and Life of Rheumatoid Arthritis Patients-A Clinical Examination of Unmet Medical Needs as a Factor in Decreased Satisfaction-

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Conflict of interest: None

[Introduction] This study investigated and analyzed factors associated with RA patients' satisfaction with treatment and life. [Methods] Seventy-five outpatients (55.4±16.0 years old) with RA were surveyed about factors influencing treatment satisfaction and life satisfaction. Patient characteristics (age, gender, disease duration, Steinbrocker Class/Stage), disease activity (SDAI, CDAI, DAS28 CRP/ESR), and daily life functioning factors (HAQ) were evaluated for statistical analysis. [Results] Satisfaction with treatment and life was influenced by disease activity, but not by HAQ. To improve satisfaction, 65% of the patients reported pain management, 20% of the patients reported fulfillment of roles other than ADLs and employment/leisure activities, and 70% of the patients reported fulfillment of pharmacotherapy. Even among patients who achieved remission, there were patients with low satisfaction with treatment and life, highlighting the difficulty in dealing with these patients. [Discussion] This study showed that achieving remission alone is not sufficient to increase satisfaction with treatment and life. It is important to deal with residual pain and patients' daily life and social activities in order to improve treatment satisfaction and quality of life of RA patients.

W18-2

The physical activity of Rheumatoid Arthritis patients evaluated by the IPAQ

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Conflict of interest: None

[Objective] Physical activity (PA) of Rhymatoid Arthritis (RA) patients was assessed by the International Physical Activity Questionnaire short version (IPAQ) and searched for related factors. [Methods] Patients participated FRANK registry in Kyushu Medical Center were asked to complete the self-administered questionnaires including IPAQ in 2019 and 2020. Number of patients completed questionnaires were 799 in 2019, 807 in 2020, and patients with significantly different metabolic equivalent of task-minutes per week (METs) between the two years were excluded in the analysis. Total of 321 patients were assessed by the analysis. Mean age was 63.6 and mean disease duration was 15.4 years. [Results] In univariate analysis, there were significantly different with Steinbrocker class, EQ5D, have hobbies, like exercise, previous orthopaedic surgery, using care insurance, m-HAQ, Fatigue Severity Score (FSS), UCLA activity score. In multivariate analysis, there were significantly different with m-HAQ and previous orthopaedic surgery, especially spine surgery. [Conclusions] It was reported that PA in RA patients was lower than that in healthy controls. In this study, PA in RA patients was significantly low with previous orthopaedic surgery, especially spine surgery.

W18-3

Time trends of rheumatoid arthritis patients' characteristics and risk factors associated with balance and falling

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Conflict of interest: None

[Introduction] In a study of RA patients conducted at our hospital 16 years ago, the rate of falls was 25.8% and the risk factor was oral dose of steroids. [Objective] We investigate the backgrounds and risks for falling in modern RA patients and examine the changes from the previous report. [Methods] RA female patients who visited our hospital from January to July 2022 and could walk independently were included. Patient background, disease activity, HAQ-DI, and motor function assessment were analyzed. [Results] 126 patients were included; Fall group (n=31, 24.6%), age was 70.8±10.5 y.o. and non-fall group (n=95, 75.4%), age was 68.3± 9.4 y.o.. The differences between the two groups (fall vs. non-fall group) were as follows: steroid dosage (0.74 vs. 0.34 mg/day, p=0.01), HAQ-DI (0.53 vs. 1.66, p=0.03), grip strength (16.9 vs. 19.0 kg, p=0.02), and total time standing on one leg (12.0 vs. 36.6s, p=0.04). The mean age of the non-fall group is about 6 years older than in the previous group, although the rate of falls is almost the same for both of them. [Conclusions] The mean age of RA patients has been increasing, but the risk for falling is still oral steroid use today. The results suggest reducing the oral dose of steroids, in addition to improving activity may contribute to reducing the risk of falls.

W18-4

Exercise Can Prevent Kidney Function Deficit in Elderly Rheumatoid Arthritis PatientsA 5-year follow-up study

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Conflict of interest: None

[Objective] Kidney function deficit with age, especially in the elderly and RA patients. The purpose of this study was to investigate whether exercise can reduce the decline in eGFR (cy) in RA patients over a 5-year period. [Methods] The subjects were 240 RA patients from 2016 to 2021. Exercise was defined as exercise lasting at least 5 years and performed at least 3 days per week for at least 30 minutes at a time. Age, duration of disease, eGFR (cy), DAS28, HAQ, and MTX use were investigated. eGFR, DAS28 crp, and HAQ score were defined as the change between 2016 and 2021. The patients were divided into two groups, those aged 65 years and older and those aged 64 years and younger, and were examined according to whether they exercised according to age. The Mann-Whitney test and the χ-square test were used to examine statistics for the groups with and without an exercise habit for ages 65 and older and 64 and younger. [Results] The difference between the initial and final ΔeGFR was -2.9 mL/min/1.73 m^2 in the group with exercise habits and -7.8 in the group without exercise in patients aged 65 years and older. [Conclusions] Our study suggest that exercise in elderly RA patients may prevent the decline in eGFR at 5 years.

W18-5

The influence of the fitness of the female patients with rheumatoid arthritis for the functional remission

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Conflict of interest: None

[Objective] We conducted the Body-weight Exercise of Lower and Upper extremity (BELU) program to clarify the effect of the body-weight exercise for the female patients with rheumatoid arthritis. We described the fitness of the female patients wit RA and the factor to influence the functional remission (HAQ ≦ 0.5) at the beginning of the BELU program. [Methods] We recruited the participants in the regulatory visit. The physical and occupational therapists measured muscle strength, joint range of motion and walking speed. [Results] Fifty two female patients were included. The mean age was 67.8 ± 12.2 years old. The mean DAS28-ESR was 2.83 ± 0.93. The mean HAQ score was 0.67 ± 0.6 and 27 patients (51.9%) reached the functional remission. The mean walking speed was 1.05 ± 0.2 m/sec. Fifty (96%) patients were right handed and the mean grip strength was 18.7 ± 6.5. The patients reached the functional remission had stronger muscles-strength, wider joint range of motion and faster walking speed. The multi-variant analysis revealed the higher hand grip strength and walking speed lead to the functional remission. [Conclusions] The patients without the functional remission had weaker and narrow joint range of motion. They need the exercise to strengthen the hand grip and walking ability.

W18-6

Report on the influence of auto injectors and grip strength

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Conflict of interest: None

[Objective] Auto-injector (AI) operation for biological agent self-injection can be difficult due to the patient's upper limb function and the shape of the device. We report on the effect of grip strength on satisfaction with AI operation. [Methods] The subjects were 44 patients with RA who were hospitalized for treatment at the hospital and were eligible for AI. Patient background (age, years of disease), hand function factors (grip strength, HANDS20), and daily life function factors (FIM, HAQ) were evaluated. Patients were divided into three groups based on a grip strength of 130 mmHg: bilateral high group, unilateral high group, and bilateral low group. [Results] The results showed that there was a difference between etanercept and sarilumab in the satisfaction with each AI in the low bilateral group (P<0.05). The difference between the three groups was significant for etanercept (P<0.05). [Discussion] In the present study, the satisfaction with AI operation was higher when grip strength on one side was 130 mmHg or higher, suggesting a relationship between grip strength and AI operation. On the other hand, some AIs are less susceptible to the effects of grip weakness, and it is desirable to develop AIs that are less susceptible to upper limb dysfunction such as grip weakness.

W19-1

Predictors for clinical effectiveness of baricitinib (Bari) in Patients (pts) with Rheumatoid Arthritis (RA): All-case Post Marketing Surveillance Study (PMSS)

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Conflict of interest: Yes

[Objective] In an ongoing PMSS, we examined the predictors for effectiveness of Bari; which was approved in Jul 2017, for RA pts who have inadequate response to other treatments. [Methods] 3780 pts whose CDAI score was available at some points were included; of the 4724 effectiveness analysis set. Using CDAI score at wk24 as an endpoint, logistic regression analysis was performed. The predictors were age, sex, disease duration (0-2/2-5/5-10/10-20/≧20yrs), initial Bari dose, number of past biologic (Bio) use, CDAI score at baseline (BL), concomitant use of MTX at BL and concomitant use of steroids at BL. Missing values were imputed by the multiple imputation. [Results] In the overall analysis set, mean age/disease duration were 64/12yrs, and a female proportion was 80%. The odds ratio (OR 95% CI) of effectiveness analysis set by multivariate analysis was high for concomitant MTX use: 1.1 (1.0-1.2) and low for steroid use: 0.8 (0.7-0.8). The OR of disease duration decreased as the duration became longer: 0.9 (0.8-1.0). Bio naïve as a reference, ORs of past Bio use were 1: 1.2 (1.0-1.4), 2: 1.0 (0.8-1.2), and ≧3: 0.6 (0.5-0.7). [Conclusions] BL concomitant medications, disease duration, and the history of Bio use may be predictors for effectiveness of Bari by CDAI score.

W19-2

Efficacy and safety of reduced-dose use of the renally excretory JAK inhibitor baricitinib according to renal function

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Conflict of interest: None

[Objective] Baricitinib (Bari), a Janus kinase (JAK) inhibitor, is about 70% renally excreted, and is given at half-dose in patients with moderate renal impairment (eGFR>=30 to <60 ml/min/1.73 m2). We will clarify

whether the reduced dose of Bari in patients with renal impairment is different in efficacy and safety compared with the normal dose in patients with normal renal function. [Methods] Based on data from NinJa2017-2019, 169 patients who newly started Bari, were divided into 4 groups (GroupA: eGFR>=60, Bari4 mg, GroupB: eGFR>=60, Bari2 mg, GroupC: eGFR>=30 to<60, Bari4 mg, GroupD: eGFR>=30 to<60, Bari2 mg), and compared the data of the previous year and the following year. [Results] There was a difference in mean age (GroupA: 61±13 years vs. GroupD: 72.7±8.73 years, P<0.05). ACR20/50/70 achievement rates were (18% vs. 13%, P=0.88) / (12% vs. 13%, P=1) / (2.4% vs. 0%, P=1), and improvement by DAS28 were (good: 18% vs. 20%, moderate: 16% vs. 13%, no: 64% vs. 66%, P=0.93), respectively, showed no significant difference in efficacy. Herpes zoster was observed in (3.8% vs. 9.5%, P=0.26). There were no deaths, in either group. [Conclusions] The reduced dose of Bari in patients with moderate renal impairmentlower did not show any clear difference in efficacy and safety.

W19-3

Efficacy of baricitinib for rheumatoid arthritis patients

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Conflict of interest: None

[Objective] To examine the use and efficacy of baricitinib (BAR) for rheumatoid arthritis (RA). [Methods] We conducted a retrospective study of RA patients who were introduced to BAR at our hospital from 2018 to 2021 and who were followed for at least 6 months. The presence or absence of b/tsDMARDs and the combined use of csDMARDs before and after BAR use, and the continuation rate of BAR were investigated from medical records. [Results] Twenty-four cases (4 mg/day, n=12; 2 mg/day, n=12; female, n=21; male, n=3) were included. The mean age was 62.5±15.4 years. The mean follow-up period was 761.3±339.5 days. The concomitant medications included PSL (n=14; 58.3%) at a mean dose of 4.9±2.1 mg/day, MTX (n=10; 41.7%) at a mean dose of 7.0±2.3 mg/week, and immunosuppressive agents (tacrolimus and mizoribine; n=12; 50%). The number of b/tsDMARDs used before BAR use was 0/1/2/3/4 (drugs)=3/5/8/5/3 (cases). The mean age of the 2 mg group (n=12) was significantly older than that of the 4 mg group (n=12) and their disease activity was significantly reduced. The continuation rate at the time of observation was 0.58 (14/24 cases), and seven cases discontinued treatment within one year. [Conclusions] The use of BAR (2 mg/day), which was administered in half of the elderly patients, was effective.

W19-4

Evaluation of efficacy and safety in long-term administration of JAK1/2 inhibitor baricitinib

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Conflict of interest: Yes

[Objective] We evaluated the efficacy and safety of the JAK1/2 inhibitor baricitinib. [Methods] 191 patients started treatment with baricitinib. [Results] In 191 patients (163 females), the average number of treatment weeks was 77.7 weeks (median 70.0 weeks, maximum 207.7 weeks). Treatment continuation rate was 79.4% at 26 weeks and 72.5% at 52 weeks, and there was no significant difference between the phase II initiation group and the phase III initiation group (Log-rank p=0.3710). CDAI improvement rate was 85.0% at 26 weeks and 95.5% at 52 weeks. There was no significant difference in CDAI improvement rate between phase II and phase III start groups. There was no significant difference in CDAI improvement rate or treatment continuation rate depending on the number of b/tsDMARDs pretreated in the phase III initiation group. Of the 31 cases who discontinued treatment due to side effects, 1 case of MACE (acute myocardial infarction) and 7 cases of malignant tumor (6 cases of solid cancer, 1 case of lymphoma). The morbidity was 0.71/100 person-years for MACE and 2.47/100 person-years for malignant tumors. [Conclusions] Baricitinib shows early and sustained efficacy regardless of treatment phase.

W19-5

Therapeutic effect of baricitinib for RA patients in real-world clinical practice

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Okuda Orthopedic Clinic

Conflict of interest: None

[Purpose] At our hospital, which is an orthopedic clinic, we investigated the continuation status and therapeutic effects of rheumatoid arthritis (RA) patients using baricitinib (BAR) [Subjects and Methods] The subjects were 42 patients who had been using BAR at our hospital since March 2019 and had passed for more than 1 year after the start of administration. Mean age was 66.7 years, and 24 bionaive cases were included. There were 15 cases of change from bioformulation There were 3 cases of change from other JAK inhibitors (TOF). [Results] Twenty-six patients continued treatment one year after the start of administration (continuation rate: 61.9%). Herpes zoster was observed in 3 patients as an adverse event, but there were no other serious adverse events. Bio-naive cases persisted in 19 of 24 cases. Of the 15 cases in which BAR was changed from biologics, 7 cases were not effective and 3 cases returned to the previous treatment. The change from TOF to BAR was continued in 2 out of 3 cases. In 26 cases who were able to continue administration for 1 year, the change in DAS28-CRP average value was 3.57 before administration and improved to 2.22 after 1 year. [Discussion] The use of BAR is useful for RA patients who are difficult to control with MTX.

W19-6

Inhibitory effects on joint destruction by Peficitinib in patients with rheumaatoid arthritis

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Conflict of interest: None

[Objective] Peficitinib is a well-known Jak inhibitor to inhibit Jak 1,2,3 and Tyk2 and has been reported to inhibit joint destruction in Japanese RA patients with inadequate response to methotrexate (MTX). We demonstrated the inhibitory activity of peficitinib in joint damage in clinical practice. [Methods] 26 RA patients were analyzed disease activity index 28 joint counts (DAS28) with ESR or CRP, patient VAS, pain VAS, physician VAS for clinical disease activity and modified total Sharp score (mTSS) for radiographic data. Patient's demographic data were as follows: sex: 5 male and 21 female; age (mean): 70.4 years; disease onset: 186 months; MTX dose: 8 mg/week (41%), biogics: 50%. [Results] DAS28-ESR, DAS28-CRP, patient VAS, pain VAS, physician VAS at baseline, 3 months, 6 months were respectively 4.7, 3.7, 3.5; 4.1, 3.7, 3.2; 49.6, 40.6, 42.1; 52, 48.4, 45; 38, 27.4, 23.5. The mTSS/y was reduced from 3.91 to 0.3 (0.15 for bone erosion score, 0.15 for joint space narrowing score). Joint destruction was not recognized for clinically non responders. Rapid radiographic progression was observed in one patient. [Conclusions] Joint destruction effect by peficitinib were observed in clinical practice.

W20-1

Real-world comparative study of JAK inhibitors efficacy for the treatment with rheumatoid arthritis patients: the ANSWER cohort study

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Conflict of interest: None

Objective: The aim of this study is to compare the efficacy of JAK inhibitors for treatment with rheumatoid arthritis using the ANSWER cohort database. **Method:** The 622 patients who were treated with Tofacitinib (TOF), Baricitinib (BAR), Peficitinib (PEF), or Upadacitinib (UPA) were selected from the ANSWER cohort database. The patient's background was matched using propensity score-based inverse probability of treatment weighting (IPTW) among 4 treatment groups. The values of CDAI at 6 months after drug initiation were compared among 4 groups. Furter, the predictive factor for TOF and BAR efficacy was analyzed by logistic regression analysis. **Results:** The mean values of CDAI at 6 months after drug initiation were 8.7 (TOF), 8.7 (BAR), 10.6 (PEF), and 9.0 (UPA), respectively. There was no significant difference of CDAI among 4 treatment groups. Baseline CRP titer (OR 0.76, p=0.045) and baseline CDAI (OR 1.09, p<0.001) were identified as the predictive factor for the efficacy of TOF. PSLdose (OR 1.18, p=0.035), CDAI (OR 1.07, p<0.001), and a number of previous bDMARDs (OR 1.36, p=0.004) were identified as the predictive factor for drug efficacy of BAR. **Conclusion:** The efficacies of TOF, BAR, PEF, and UPA were not significantly different for the treatment of RA patients.

W20-2

Comparison of effectiveness and safety of baricitinib versus abatacept in patients with rheumatoid arthritis in a real-world setting

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Conflict of interest: Yes

[Objective] To compare the effectiveness and safety of baricitinib versus abatacept in patients with rheumatoid arthritis in a real-world setting. [Methods] This study was performed based on data from a multicenter registry, and included 220 and 513 patients treated with baricitinib and abatacept, respectively, who were observed for longer than 52 weeks. Propensity score matching was performed to address potential treatment-selection bias. [Results] A total of 85 matched pairs of patients were identified. Log-rank test revealed no significant differences in the cumulative discontinuation rate due to insufficient response and adverse events between the baricitinib and abatacept groups. No significant difference in the DAS28-CRP score was observed between the two groups at baseline. The DAS28-CRP score at 4, 12, 24, and 52 weeks was significantly lower in the baricitinib group compared to the abatacept group. Compared to the abatacept group, the baricitinib group had significantly higher rate of remission according to DAS28-CRP at 52 weeks (34% vs. 59%, P=0.002). [Conclusions] This 1-year observational study indicates that baricitinib has higher effectiveness and comparable safety compared to abatacept.

W20-3

The effectiveness of barcitinib versus peficitinib in patients with rheumatoid arthritis in real clinical practice

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Conflict of interest: None

Object The aim of this study was to compare the effectiveness of baricitinib (BAR) and peficitinib (PEF) for rheumatoid arthritis (RA). Methods: 249 RA patients with BAR treatment and 66 patients with PEF treatment for at least 24 weeks were included. We compared the change of SDAI and the rate of discontinuation between BAR and PEF treatment. Results: Comparing baseline characteristics, the patients in PEF group were a significantly higher age, lower eGFR, lower rate of previous treatment of bDMARDs or JAK inhibitor, lower rate of concomitant methotrexate, and higher titer of SDAI. Mean SDAI was significantly decreased in both groups (BAR: 17.2 to 8.1/ PEF: 22.1 to 11.5). Although the mean SDAI at 24 weeks was significantly higher in PER group than BAR group, the rate of decline of SDAI was not significantly different between the two groups (Bar: -30.8%/PEF: -33.3%). There were no significant differences in retention rates between the two groups. We identify the associated factor for the achievement of low disease activity at 24 weeks. A lower proportion of class 3/4 and a lower titer of SDAI was identified in BAR group and a lower titer of SDAI was identified in PEF group. Conclusion: There was no significant difference in the rate of improvement of disease activity and retention rate.

W20-4

Retention ratio and efficacy of JAK inhibitors with or without MTX in patients with RA

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Conflict of interest: None

[Objective] The use of non-TNF inhibitors or JAK inhibitors (JAK) should be used when methotrexate (MTX) is not used, but there is concern that the effect may be slightly weak without MTX. We investigated real-world data with and without MTX in rheumatoid arthritis (RA) patients started JAK. [Methods] 211 RA patients who started JAK was included. The patients were devided into a group of 87 patients without MTX (non-MTX group) and a group of 124 patients with MTX (MTX-used group) at the start of JAK. We investigated the retention rate and efficacy for 24 weeks. [Results] The non-MTX group was older, had worse renal function, and had a higher rate of steroid use, but there was no difference in disease duration of RA compared to the MTX-used group. No significant difference was observed between the two groups in the retention rate at 24 weeks and the improvement of disease activity during 24 weeks. In MMP-3, improvement was poor in the MTX non-used group, and a significanly different between the two groups after 12 weeks. [Conclusion] The retention ratio and effectiveness of JAK with and without MTX was almost same. However, it is possible that the suppression of synovitis might be insufficient without MTX.

W20-5

Practice of RA treatment according to EULAR Recommendation 2019 in our hospital

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Conflict of interest: Yes

Purpose: B/tsDMARDs for RA have brought great benefits to RA patients. In practice, treatment has been conducted in accordance with various recommendations and guidelines, and we report the current status of b/tsDMARDs treatment at our hospital in accordance with EULAR Recommendation 2019. Methods: We analyzed 1265 treatments in 514 patients initiated at our hospital. Results: Number of patients using b/tsDMARDs: 514, of which TNF inhibitors: 36.8%, non-TNF inhibitors: 51.8%, and JAK inhibitors: 11.4%. CDAI remission rate at 1 year was 36.5%. 31% of the patients were able to continue on the first drug during the observation period. The continuation rate was Jaki>non-TNFi>TNFi including adverse events. Remission was discontinued in 14.2% of the cases with 46.5% of all cases relapsing. The second drug was switched to a drug with a different mechanism of action in 72.5% of the patients. Among b/tsDMARDs, JAK inhibitors were superior in both efficacy and persistence rate after the third drug, but there were more discontinuations due to adverse events. Conclusion: Achieving the goal of RA treatment with the first drug is extremely important, and the superiority of JAK inhibitors as treatment after the third drug was demonstrated.

W20-6

Efficacy and Safety of JAK Inhibitors in the Phase II of the JCR Treatment Guideline 2020 for RA

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of JAK inhibitors (JAKi) in RA patients who were biologics/JAKi naive and csDMARDs (including MTX) -inadequate responders (IR). [Methods] Sixty-five biologics/JAKi-naïve csDMARDs-IR RA who had received JAKi in our hospital were enrolled. DAS28 at start and at 12, 24 and 52 weeks and retention rate at 52 weeks were evaluated retrospectively by LOCF method from the medical records. [Results] Background of the 65 patients was as follows: mean age 62.7 years, disease duration 9.2 years, stage 4 ratio 43.7%, and 25 (38%) were treated with tofacitinib, 29 (45%) with baricitinib, 6 (9%) with peficitinib, 2 (3%) with upadacitinib, and 3 (5%) with filgotinib. DAS28 had decreased significantly from 4.9 at baseline to 3.3 at week 4, 3.0 at week 12, 2.9 at week 24, and 2.7 at week 52. The retention rate at 52 weeks was 86.2% (56 patients), and the reasons for discontinuation were inefficacy and economic reasons in 3 patients each, adverse events in 2 (lung cancer and interstitial pneumonia), and surgery in 1. Herpes zoster developed in 3 patients during the observation period. [Conclusions] In this study, JAK inhibitors in Phase II for csDMARD-IR RA were effective and well tolerated in most patients.

W21-1

Clinical significance of anti-SS-A antibodies and rheumatoid factor in systemic lupus erythematosus

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Conflict of interest: None

[Objective] In patients with systemic lupus erythematosus (SLE), anti-SS-A antibody or rheumatoid factor (RF) positive cases are often identified. However, their clinical significance, especially in relation to Sjögren's syndrome is not well understood. [Methods] Of 155 patients with SLE who had visited our department, 113 patients in whom anti-SS-A antibody (FEIA) and RF were measured were analyzed retrospectively. [Results] The clinical background was age 47.1 years, 87.6% female, and duration of disease 171.6 months. The number of RF-positive patients was higher in SS-A antibody-positive patients (33.3%: 22/66) compared to that in anti-SS-A antibody-negative patients (10.6%; 5/47) (χ square test, $p = 0.0053$). Sjögren's syndrome (SS) was diagnosed in 12 of 66 anti-SS-A antibody-positive patients (18.2%), while there was no patients diagnosed as SS in anti-SS-A antibody-negative patients. The ratio of patients diagnosed as secondary SS in anti-SS-A antibody-positive RF-positive patients (31.8%; 7/22) was significantly higher than that in anti-SS-A antibody-positive RF-negative patients (11.4%; 5/44) (χ-square test, $p=0.042$). [Conclusions] In patients with SLE, the assessment of both RF and anti-SS-A antibodies can be helpful for the diagnosis of secondary SS.

W21-2

A study on the difference in clinical manifestations between positive for anti-Sm and anti-U1RNP antibodies in patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] We compared the clinical manifestations between patients with systemic lupus erythematosus (SLE) positive for anti-Sm and anti-U1RNP antibodies because there are few reports comparing them in Japan. [Methods] SLE patients visiting our hospital were classified into four groups; positive for both antibodies (Sm+RNP+), only positive for anti-Sm (Sm+RNP-), only positive for anti-U1RNP (Sm-RNP+), and negative for both (Sm-RNP-). Their clinical features were compared using the chi-square test and Fisher's exact test. [Results] Of 599 SLE patients, Sm+RNP+ group (n=244, 41%), Sm+RNP- group (n=39, 7%), Sm-RNP+ group (n=95, 16%), and Sm-RNP- group (n=221, 37%) were classified. The anti-Sm antibody-positive group (Sm+RNP+, Sm+RNP-) was more frequently positive for anti-SS-A (n=191, 72%, $p<0.01$) and had leukopenia (n=246, 89%, $p<0.01$). Arthritis was more common in Sm+RNP+ group (n=209, 87%, $p<0.01$). Sm-RNP+ group had lower frequencies of thrombocytopenia (n=21, 23%, $p<0.01$) and proteinuria (n=25, 26%, $p<0.01$). [Conclusions] Our result suggested the differences in clinical features of Japanese SLE patients between positive for anti-Sm and anti-U1RNP antibodies. However, further investigation is required, including the relationship between anti-Sm and anti-SS-A antibodies.

W21-3

Anti-lipoprotein lipase antibody-associated autoimmune hypertriglyceridaemia in a patient with systemic lupus erythematosus

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Conflict of interest: None

A 20-year-old man with hypertriglyceridaemia and thrombocytopenia presented with photosensitivity, headaches, and polyarthralgia. Physical examination revealed erythema of the neck and shoulders. Laboratory examination revealed triglyceride, high-density lipoprotein, and low-density lipoprotein cholesterol levels of 2387 mg/dL, 17 mg/dL, and 39 mg/dL, respectively. The platelet count decreased to 4.6×104 /μL. Serological tests showed that the levels of anti-ds-DNA antibody, platelet-associated IgG, and anticardiolipin-β2-glycoprotein I antibody were all elevated. CH50, C3, and C4 were all decreased. He was diagnosed with systemic lupus erythematosus with autoimmune thrombocytopenia. Prednisolone (30 mg/day) was initiated, and his symptoms and serological data subsequently improved. Steroid treatment also improved platelet and triglyceride levels. When the sera of 30 systemic lupus erythematosus patients visiting our hospital were similarly tested, anti-LPL antibodies were detected in 4 (13.3%). Arteriosclerosis is known to be a problem in patients with systemic lupus erythematosus. It was suggested that the anti-LPL antibody was positive at a relatively high rate, and further suggested that steroid treatment may improve anti-LPL antibody and thereby improve lipid metabolism.

W21-4

Alternation of IL-6 and Anti-NMDA Receptor Subunit GluN2 Antibody (anti-GluN2) in Cerebrospinal Fluid (CSF) in a Patient with Systemic Lupus Erythematosus (SLE) who Developed Mood Disorder after Belimumab Introduction and spontaneously Improved with Discontinuation

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Conflict of interest: None

[Patient] A 29-year-old female [Present illness] She was diagnosed as SLE due to fever, general fatigue, polyarthritis, hypocomplementemia, the positivity of ANA and anti-dsDNA antibody (anti-dsDNA). HCQ monotherapy was initiated which improved her manifestations. As 14 months after HCQ introduction, arthritis was exacerbated with anti-dsDNA elevation, PSL 5 mg/day and MTX were added, quickly improving her arthritis. However, since her arthritis flared up again when tapering PSL up to 3 mg/day, we added belimumab. Three months after BEL introduction, she became to develop morbid anxiety evaluated by a psychiatrist. Brain MRI and electroencephalography were normal, but CSF findings were abnormal with protein elevation, IL-6 15.4pg/mL, anti-neuronal cell antibody (anti-N) 0.66 U/mL and anti-GluN2 0.12 U/mL. Therefore, we discontinued BEL in consideration of both adverse event by BEL as well as NPSLE development. Two months later, her anxiety almost disappeared with decreasing IL-6 7.0, anti-N 0.36 and anti-GluN2 0.02. As far, no psychiatric manifestation has been developed. [Clinical Significance] As one of the mechanisms in developing psychiatric manifestations after BEL introduction, paradoxical elevation of autoantibodies against neurons in the central nervous system may be involved.

W21-5

Survey of lipid management based on the risk factors of atherosclerotic diseases in patients with systemic lupus erythematosus -Does an evidence-practice gap (EPG) exist? -

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Conflict of interest: None

[Objective] In SLE patients, dyslipidemia treatment should follow recommendation used in the general population. However, the status of lipid management for SLE patients in Japan is still unknown. Here, we investigated the current status in accordance with the guideline in Japan. [Methods] 335 SLE patients attending Kyoto University Hospital were classified as 1) secondary prevention subjects (history of coronary artery disease or atherothrombotic stroke), 2) primary prevention subjects with high-risk conditions (peripheral artery disease, chronic kidney disease, diabetes) and 3) without them. In 3), for those aged 40 to 79, the Hisayama-cho study score was calculated. We checked if or not serum LDL-C is within the control target value according to each risk classification. [Results] The number (proportion) of the subjects was 1) 18 (5.3%), 2) 94 (28%) and 3) 223 (66.5%). Among 3), 105 patients had lipid management goals for low to medium risk classified by the Hisayama-cho study score (defined as 4)). The achievement proportion of control target values for serum LDL-C was 1) 77.7%, 2) 55.5% and 4) 94.3%. [Conclusions] As for SLE patients in Japan, lipid management in primary prevention subjects with high-risk conditions is insufficient, and thorough lipid control is considered necessary.

W21-6

Factors associated with vitamin D deficiency in patients with systemic lupus erythematosus and rheumatoid arthritis

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Conflict of interest: None

Objective: To clarify factors associated with vitamin D deficiency in patients with SLE and RA. Methods: This single-center retrospective study registered patients with SLE or RA whose serum 25 (OH)D levels were measured between September 2020 and August 2022. The seasons at the time of 25 (OH)D measurement were defined as winter from December to February, spring from March to May, summer from June to August and autumn from September to November. Results: A total of 57 patients (26 with SLE, 31 with RA) were included, with a median age of 45 years and a female ratio of 89.2%. Levels of 25 (OH)D were below the normal range (25 (OH)D <30 ng/mL) in all 57 participants. Among them, 44 patients (77.2%) met the definition of vitamin D deficiency (25 (OH)D <20 ng/mL) and 9 (15.8%) met that of severe deficiency (<10 ng/mL). In patients with SLE, 11 calcineurin inhibitor (CNI) users had numerically lower 25 (OH)D levels (median 12.6 vs. 15.8 ng/mL, p=0.11). Severe vitamin D deficiency was frequent in winter in RA patients, but not in SLE patients. Conclusions: CNI use was numerically associated with vitamin D deficiency. In SLE, 25 (OH)D levels were not affected by seasonality unlike RA, possibly due to sun protection.

W22-1

The evaluation of Late-onset SLE in our institution

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Conflict of interest: None

[Object] To elucidate the Characteristics of Late-onset SLE. [Methods] Forty three SLE patients satisfied the SLICC or 2019ACR/EULAR were included from June 2014 to March 2022. The comparative analysis between late-onset (age≧50) and early-onset (age<50) was performed retrospectively about clinical and immunological characteristics including the adaptation of treatments. [Results] Baseline of all SLE patient characteristics (n=43) were as follows; Age: 52.8±8.8y.o. (Male: 30 Female: 13). Late-onset group (n=26: 60.5%): Age: 75.3±9.4y.o. (Male: 16 Female: 10). Disease duration 1035±921.0 days. SLEDAI 11.77±7.0. The differences between late-onset and early-onset, hypertension: 50.0 vs 5.9 (*p=0.03*).

RF positive: 66.7% vs18.2% (*p=0.006*). APS positivity: 41.67% vs 75.0% (*p=0.04*). Immuno-suppressant agents: 26.9% vs 55.8% (*p=0.04*), antimalarial drug: 65.4% vs 94.1% (*p=0.03*). The Mortality rate was not significant different between groups. [Conclusions] In Late-onset SLE, Hypertension and RF positivity were significantly higher, but APS positivity, Immunosuppressant and antimalarial agents were lower than those of early onset SLE. Mortality did not differ between groups.

W22-2

Clinical characteristics of elderly onset (E-O) systemic lupus erythematosus (SLE) at our hospital

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Conflict of interest: None

[Objective] To clarify clinical characteristics of E-O SLE. [Methods] We examined patients with newly onset SLE, who admitted to our hospital between Jan 2012 and Sep 2022. We regarded patients who developed SLE at ≧50 years old as E-O, while patients at <50 years old as young aged onset (Y-O). 1) background, 2) clinical symptoms, 3) laboratory data, 4) involved organs, and 5) induction therapies were compared between E-O and Y-O groups, retrospectively. [Results] 1) 27 E-O (64.2±8.6 years old, 11 males/16 females) and 49 Y-O (32.1±1.0, 4/45) patients were identified. Male were dominant in E-O group. 2) Fever (33.3 vs 63.3%), malar rash (7.4 vs 44.9%), and Raynaud phenomenon (7.4 vs 28.6%) were less common in E-O group. 3) The titers of anti-DNA antibody (62.3±71.7 vs 112.3±107.4 IU/ml) and positive rates of anti-RNP antibody (22.2 vs 59.2%) were lower in E-O group. 4) The frequency of interstitial lung disease (ILD) (25.9 vs 6.1%) was higher in E-O group. 5) Immunosuppressants (51.9 vs 75.5%) were less used in E-O group. [Conclusions] E-O SLE had lower titers of anti-DNA antibody and positive rates of anti-RNP antibody. Male dominance with lower frequencies of fever, malar rash, Raynaud phenomenon and higher ILD were their characteristics.

W22-3

Clinical features of elderly-onset systemic lupus erythematosus in our hospital

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) is affected in young women, and elderly-onset SLE is uncommon. In this study, we clarified the clinical features of elderly-onset SLE patients. [Methods] Patients with SLE diagnosed at our hospital between 2005 and 2022 were classified into two groups: early-onset SLE (<65 years) and elderly-onset SLE (≧65 years). Their backgrounds were compared retrospectively. [Results] Twelve patients were classified as elderly-onset SLE and 84 as early-onset SLE. The elderly-onset patients had less frequently skin rash (65.5% vs. 16.7%, p=0.002), arthritis (73.8% vs. 33.3%, p=0.008) and positive anti-RNP antibodies (42.9% vs. 8.3%, p=0.018). Serositis (19.0% vs. 58.3%, p=0.007) and lupus enteritis (1.2% vs. 16.7%, p=0.040) were more frequently in elderly-onset. Median initial prednisolone dose and prescribed immunosuppressant agent showed no significant differences. Treatment-related complications were more frequently in elderly patients (56.3% vs. 100%, p=0.005), especially fractures (12.7% vs. 54.5%, p=0.004) and diabetes (14.1% vs. 54.5%, p=0.006), while the incidence of herpes zoster wasn't significantly. [Conclusions] Patients with elderly-onset SLE had higher frequency of treatment-related complications, especially diabetes and fractures.

W22-4

Prevalence of Osteonecrosis and Risk Factors of Surgery in Patients with SLE at Our Hospital

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Conflict of interest: None

[Objective] Osteonecrosis (ON) is a serious complication of systemic lupus erythematosus (SLE) that sometimes requires surgery. The present study aimed to investigate the prevalence of ON and the risk factors of hip arthroplasty in patients with SLE. [Methods] 571 SLE patients enrolled in our database (MiRAi) in March 2021 were investigated. Those patients were divided into a low-dose prednisolone group (<initial prednisolone 10 mg/day) and a high-dose group (initial prednisolone ≧10 mg/day). Descriptive statistics were used to analyze the risk factors of the prevalence of osteonecrosis of the femoral head (ONFH) in patients with surgery. The risk factors included CNS lupus, lupus nephritis, steroid pulse, cyclosporine, rituximab, and antiphospholipid antibodies. [Results] Fifty-five patients (9.6%) had ON; of these, all cases had ONFH, 43 (78.2%) had ONFH alone, and 12 (21.8%) had ON of the knee joint area and humerus. The chi-square test showed that it was significantly higher in the high-dose group (P=0.006). Of the 51 patients with ONFH, 37 had received hip surgery. These patients did not show any significant risk factors. [Conclusions] Prevalence of osteonecrosis was 9.6% in the present study and initial prednisolone ≧10 mg/day was a risk factor of osteonecrosis in SLE patients.

W22-5

Flares after SARS-CoV-2 mRNA vaccination in patients with systemic lupus erythematosus are associated with disease activity before vaccination

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Conflict of interest: None

[Objectives] To elucidate the neutralizing antibody and flare rates after the SARS-CoV-2 mRNA vaccination and the associated factors in patients with systemic lupus erythematosus (SLE). [Methods] We enrolled the uninfected patients received second dose of vaccine (BNT162b2 or mRNA-1273) between June and October 2021. The neutralizing antibodies and flares defined by the SELENA-SLEDAI Flare Index were measured in peripheral blood four weeks after the second dose of vaccine. [Results] Ninety SLE patients were enrolled. Nineteen (21.1%) were negative for neutralizing antibodies and were associated with older age, anemia, mycophenolate mofetil (MMF) use before the first dose of vaccine (p=0.030, p=0.014, and p=0.029). SLEDAI mildly increased significantly after vaccination (p=0.016, median change 0 [IQR: 0-1]). Thirteen (14.4%) and 4 (4.4%) patients experienced flares and severe flares, respectively. High titers of SLEDAI, anti-dsDNA antibodies, rash, and azathioprine use were associated with flares (p=0.046, p=0.034, p=0.037 and p=0.048). Types of vaccines and neutralizing antibody titer were not associated with flares. [Conclusions] Older age, anemia, and MMF use are associated with negative neutralizing antibodies. High disease activity before vaccination is a risk factor for flares.

W22-6

The discrepancy between attitudes toward infection control practices and vaccination preferences of patients with systemic lupus erythematosus in the COVID era

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Conflict of interest: None

[Objective] To investigate infection control practices and vaccine preferences except for the coronavirus vaccine among systemic lupus erythematosus (SLE) patients in the COVID-19 era. [Methods] We conducted a questionnaire on infection control practices (masks and hand hygiene) and vaccine preferences (influenza, pneumococcus, and herpes zoster) among SLE patients attending Kyoto University from Dec 2021 to Sep 2022. [Results] Of the 335 patients, 92.2% used unwoven masks, and more than 99% wore masks in public places and at medical institutions. The hand hygiene frequency was high (95% after returning home, 80% before meals). In contrast, vaccine preferences were low (influenza: 44%, pneumococcal: 24%, and herpes zoster: 15%). The COVID-19 epidemic was the reason for vaccine preference in 20% of 143 patients who requested vaccination. The vaccine preference was not associated with a history of COVID-19 infection (odds ratio (OR): 0.7, 95% confidence interval (CI): 0.2-2.4, p=0.61). Influenza vaccine preference was significantly associated with higher SLEDAI (OR: 1.2, 95%CI: 1.0-1.3, p=0.02). [Conclusions] SLE patients had high awareness of infection control practices while less willing to be vaccinated. The history of COVID-19 infection may not contribute to vaccine preferences.

W23-1

Three cases of elderly onset large vessel vasculitis without evidence supporting temporal arteritis, in which positron emission tomography/computed tomography was useful for diagnosis

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Conflict of interest: None

Case 1: A 68-year-old woman presented with left-sided chest discomfort, which began around November 20XX-1. Positron emission tomography/CT performed in May revealed accumulation in the ascending aorta to the aortic arch and the main arteries of the neck. **Case 2**: A 55-year-old man who had been experiencing evening fevers (38°C) since August 20XX and weight loss (3 kg) in one month showed increased accumulation in the lower abdominal aorta, iliac artery, and upper and lower limb vessels on PET-CT. **Case 3:** A 73-year-old woman who had been experiencing low-grade fever (37°C) since 20XX-11, underwent PET-CT in March X to examine her aorta, which revealed increased concentrations in the neck, subclavian, axillary, thoracoabdominal, and femoral arteries. **Clinical course:** The patients were treated with prednisolone 30 to 40 mg/day, and their symptoms improved. Patients described in Cases 1 and 2 were treated with tocilizumab, and steroids were tapered. **Clinical Significance**: Large vessel involvement associated with temporal arteritis was suspected in all three cases. Because there are cases of large vessel vasculitis in elderly patients with unexplained fever, close examination of vascular lesions using PET/CT may be useful when a clear cause cannot be identified.

W23-2

A Case of Giant Cell Arteritis Presenting as Medial Longitudinal Fasciculus Syndrome

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Conflict of interest: None

[Case] A 76-year-old female presented with acute diplopia and a one-month history of headache, bilateral neck pain and claudication of the upper limbs. Physical examination was significant for impaired adduction of the left eye and bilateral vertical nystagmus. MRI showed acute cerebral infarction of the left pontine tegmentum and medial longitudinal fasciculus syndrome (MLFS) was suspected. Further exams revealed no source of embolism and she was started on low dose aspirin. Elevated levels of C-reactive protein were noted and CT showed concentric wall thickening of the aorta and its branches. Ultrasonography was positive for halo and compression sign and temporal artery biopsy was consistent with giant cell arteritis (GCA). Ophthalmoscopy showed no ischemic changes. The patient was started on corticosteroids with the addition of weekly subcutaneous tocilizumab. [Clinical Significance] Our case of GCA presenting as MLFS is important in considering the symptomatology and pathophysiology of stroke in GCA. GCA is known to cause inflammatory response centered around the internal elastic lamina and initially thought not to cause intracranial vasculitis because of this characteristic. However, some studies suggest that inflammation-induced angiogenic activity may cause stroke in GCA.

W23-3

A case of giant cell arteritis with oculomotor nerve palsy: causal lesion implicated on the oculomotor nerve as a high-intensity area on contrast-enhanced magnetic resonance imaging

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Conflict of interest: None

[Case] An 82-year-old woman presented with a headache for 2 months. Eleven days earlier, she had left ptosis and diplopia. Physical examination revealed distention of both superficial temporal arteries (STA) and left oculomotor nerve palsy (ONP). Ultrasonography showed a “halo sign” and “compression sign” in both STA. Plain magnetic resonance imaging (MRI) and angiography (MRA) showed no abnormalities. A clinical diagnosis of giant cell arteritis (GCA) with intracranial lesions was made. She underwent methylprednisolone pulse therapy followed by tocilizumab and high-dose-prednisolone (40 mg/day). Temporal artery biopsy showed mononuclear cell infiltration, granulomatous inflammation with giant cells, and fragmentation of the internal elastic membrane, consistent with GCA. Contrast-enhanced MRI (CEMRI) showed a high intensity at the left oculomotor nerve. The headache resolved quickly, but the left ONP improved partially. She is now on tocilizumab and low-dose steroids. [Clinical Significance] Diplopia in GCA is caused by ischemia in the brainstem, cranial nerves, and ocular muscles. The main cause is ONP. While reported prognoses are mixed, several cases with high intensity of oculomotor nerve in CEMRI have fixed diplopia. To estimate the prognosis, CEMRI may be considered.

W23-4

A case of improvement of periauricular shadowing after high-dose steroid therapy for hearing impairment in Takayasu’s arteritis

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Conflict of interest: None

Hearing loss is a rare complication of Takayasu arteritis, and we have experienced a case of Takayasu arteritis with hearing loss whose image finding in the middle ear had improved after high-dose steroid therapy. The patient, a woman in her 40s, was diagnosed with Takayasu arteritis 12 years before and had been treated with prednisolone (PSL) and methotrexate (MTX). In March of X, she complained of hearing loss, and the dose of MTX was increased to 10 mg/week, but, in April of X, she became almost deaf and was hospitalized for fear of exacerbation of Takayasu arteritis. Increasing the dose of PSL to 60 mg improved her hearing and the imaging abnormality in the middle ear, so the dose of PSL was gradually reduced

to 35 mg and she was discharged. The mechanism of hearing loss in Takayasu arteritis is assumed to be an autoimmune reaction in the inner ear labyrinth and obstruction of nutrient vessels of the inner ear, but the details of the mechanism remain unclear. This improvement of periauricular shadows would be an important finding in considering the mechanism of hearing loss in Takayasu arteritis, thus we report this case with the review of the literature.

W23-5

A case of refractory giant cell arteritis in remission with intravenous cyclophosphamide therapy

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Conflict of interest: None

(Case) 74 years old female. (Chief complaint) Dysphagia (Progress) X-1st year, lameness of the jaw appeared. A few days later, headache appeared and persisted,, rotational vertigo at rest appeared, which was examined closely and a diagnosis of right parietal cerebral infarction was made. X year, vision loss and rotational vertigo appeared. Acute cerebral infarction was observed in the left posterior inferior cerebellar artery and posterior cerebral artery. Cerebral angiography showed severe stenosis with irregular caliber in multiple locations in bilateral vertebral arteries, which was markedly worsened compared to December X-1. He also complained of pain around the shallow temporal artery and continued to have a positive inflammatory reaction. A biopsy of the shallow temporal artery was performed, and a diagnosis of GCA was made. Subsequent treatment with steroid pulse therapy and post-treatment with PSL, TCZ did not improve the thickening of the bilateral vertebral artery walls. Despite a total of four steroid pulse therapies, the occlusion progressed gradually, and in March of X year, emergency balloon dilation surgery was performed. Since remission was not achieved with steroid pulse therapy and TCZ, the patient was switched to intravenous cyclophosphamide (IVCY).

W23-6

Outcome of 150 patients with Polymyalgia Rheumatica

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Conflict of interest: None

[Object] The diagnosis of PMR requires the exclusion of various diseases presenting with arthritis in the elderly and unknown fever. To invest the outcome of PMR patients diagnosed with 2012 EULAR / ACR PMR classification criteria. [Methods] We have followed up 150 patients diagnosed with 2012 EULAR/ACR criteria of PMR for 5 years. [Results] 68 males and 82 females, aged 73.6±10.9 years were diagnosed with PMR. Five years after diagnosis, 32 were treated for PMR, 30 were treated with prednisolone 2.7±1.9 mg, eight with MTX. 93 were cured. Complications included fractures in ten patients and cerebral hemorrhage in two. A total of 25 patients, including 9 solid cancers, 3 spondyloarthritis and hematologic disease, 2 rheumatoid arthritis and vasculitis, and 1 patient with gout, Graves' disease, Still's disease, interstitial pneumonia, and unclassifiable arthritis, had a different diagnosis of PMR and discontinued PMR treatment. During this period, 14 people died, 9 of whom were cancer. [Conclusions] 16.7% were diagnosed with other diseases and treatment was discontinued. These results suggest that it is important to screen for cancer. Twenty percent of PMR cases received long-term glucocorticoids, and complications became a problem.

W24-1

Clinical manifestations of eosinophilic granulomatosis with polyangiitis (EGPA) and mepolizumab has steroid sparing effect in EGPA: a retrospective study

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Conflict of interest: None

Objective: Mepolizumab (MPZ) has been reported to reduce prednisolone (PSL) dose in eosinophilic granulomatosis with polyangiitis (EGPA). We investigated clinical manifestations of EGPA and outcomes of the treatments with MPZ. Methods: Thirty patients with EGPA were enrolled from 2010~2022. We analyzed the findings and treatment details at onset of EGPA, and the progress of 26 patients who could be followed up for > 1 year. Results: The age at diagnosis of EGPA was 60 (42-73) years [median (quartile)], and 3 (2-11) years had passed since onset of asthma. MPO-ANCA was positive for 10 (33.3%) patients, had more hematuria (p=0.04) and higher BVAS (p=0.02). Twenty-six patients were followed for 4.1 (1.3-7.5) years, 12 cases (46.2%) received MPZ. PSL dose at MPZ initiation was 11 (10-15) mg/day and the cumulative duration of MPZ use was 14 (9-21) months. In the MPZ group, PSL could be reduced by 4 (0.6-6) mg/day, eosinophil counts were lower (p=0.003), and no relapse requiring PSL dose-up was observed. The VDI at last observation was 1.5 (1-2.3), bronchial asthma was the most common (50%), and 8 patients (66.7%) with MPZ also required asthma treatment. Conclusions: Although there were no cases with relapse requiring PSL dose-up under MPZ treatment, many of them required treatment for asthma.

W24-2

Effect of evaluation of reduction in glucocorticoid toxicity for maintenance therapy by mepolizumab of eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] We evaluate effect of reduction in glucocorticoid (GC) toxicity (GTI) after 12 months of Mepolizumab (MPZ) treatment using a GC toxicity index (GTI) in patients with eosinophilic granulomatosis with polyangiitis (EGPA). [Method] Patients, diagnosed with EGPA and treated at Toho University Sakura or Omori Medical Center between January 2016 and June 2022, were included if they met all of the following criteria: prednisolone ≦ 20 mg/day, BAS < 10 and MPZ was administered after 6 months or more from the onset of EGPA. GC toxicity was evaluated by the GTI. [Results] At the time of MPZ therapy initiation, mean age of the 16 patients with EGPA was 57.1 years and the disease duration were 66.1 months, mean eosinophil count was 576/μL, the daily mean GC dose was 7.1 mg/day. 2 patients were ANCA-positive, and 14 patients used immunosuppressants. The BVAS score decreased from 2.6 before MPZ administration to 2.0 after 12 months ($p = 0.06$). GTI was also decreased from 29.5 ± 38.8 points to 5.31 ± 22.9 ($p = 0.0003$). Serious adverse events requiring hospitalization during the observation period were 3 patients. [Conclusion] The present study suggests that MPZ for the treatment of EGPA during maintenance therapy reduces GC toxicity.

W24-3

Effect of Mepolizumab administration in patients with eosinophilic polyangiitis granulomatosis (the 2nd report)

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Conflict of interest: None

[Objective] To investigate the effect of mepolizumab against the patients with eosinophilic polyangiitis granulomatosis as the 2nd report. [Methods] We enrolled 21 (47.7%) patients who had started mepolizumab (MEP) out of 44 (2.48%) patients who met the Japanese EGPA diagnostic

criteria; in our hospital, 1773 patients visited combined 2 spring terms (from April to June) of 2021 and 2022. The average age was 62.7 year-old, the average disease duration was 7.7 years, the male to female ratio was 23:21. We analyzed statistically the effect of MEP for the patients with EGPA as comparing between the presence of MEP (21 cases: 47.7%) and absence of MEP (23 cases: 52.3%), with Fisher's exact test. [Results] In the MEP-users, 5 out of 21 patients (21.4%) achieved steroid-free treatment, but 1 patient (4.8%) relapsed after achieving steroid-free treatment. On the other hand, 2 out of 23 patients (8.7%) achieved steroid-free treatment in the non- MEP-users, but 1 patient (4.4%) relapsed after achieving steroid-free treatment. Including cases of recurrence after achieving steroid-free treatment, there was no significant difference in achieving steroid-free treatment with MEP (p=0.18). [Conclusions] Mepolizumab can withdraw eosinophilic polyangiitis granulomatosis patients from steroids.

W24-4

Long-term outcomes of remission induction therapy with mepolizumab in patients with eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] Mepolizumab is effective for refractory eosinophilic granulomatosis with polyangiitis (EGPA), but the reports of efficacies of mepolizumab in remission induction are still limited. We investigated the long-term outcomes of EGPA patients with and without mepolizumab therapy. [Methods] Among 29 EGPA patients, we enrolled 13 patients following-up for more than 2 years in this single center study. The patients who started mepolizumab 2 months or more after the initiation of treatment and lack of data due to hospital transfers were excluded. Cumulative glucocorticoid (GC) dosages, eosinophil counts and the Birmingham vasculitis activity score (BVAS) at the point of 2 years after the start of treatment were evaluated. [Results] Five patients with mepolizumab in remission induction were compared with 8 mepolizumab-unused patients. Although cumulative GC dosages in 0 to 1 year, eosinophil counts, and BVAS were equivalent, the cumulative GC dosages in 1 to 2 year were less in mepolizumab-treated patients (median, 1651.0 mg and 2227.5 mg, $p < 0.05$). Safety concerns with mepolizumab including infection and malignancy had not been observed in 2 years. [Conclusions] Mepolizumab is effective to reduce cumulative corticosteroid exposure without increasing vasculitic activities in EGPA.

W24-5

Effect of Mepolizumab in Eosinophilic Granulomatosis withPolyangiitis (EGPA)

Takeshi Shoda[1], Hideyuki Shiba[1], Youhei Fujiki[2], Yumiko Wada[1], Takao Kiboshi[1], Takayasu Suzuka[1], Kenichiro Hata[1], Takuya Kotani[1], Tohru Takeuchi[1]
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Conflict of interest: None

[Objective] Evaluate the effect of Mepolizumab (MEPO) in EGPA. [Methods] Consecutive cases of EGPA treated in our department and Yodogawa Christian Hospital between 2002 and 2022 were included. The clinical data, treatment, and course of EGPA were investigated, and the use of mepolizumab was evaluated. [Results] 64 pts were available for EGPA, with age of onset of 62 years. ANCA was positive in 22 pts (34%). The lesions affected 19% of central nerves, 36% of lung, 25% of heart, 16% of digestive organs, and 16% of kidney. Remission induction therapy consisted of PSL pulse in 29 pts (45%), IVCY in 29 pts (45%), RTX in 5 pts (8%), IVIG in 31 patients (48%), AZA in 28 patients (44%), MTX in 4 patients (6%), MEPO in 6 patients (10%), and maintenance therapy in 30 patients (47%) on AZA, 6 patients (9%) on MTX, and 25 patients (39%) on MEPO. Of the 25 patients with mepolizumab, ANCA positivity was 10 (40%), and many of them used it in the course of severe disease. The median pre-treatment PSL was 13 mg and the median post-treatment PSL was 6 mg. There were no EGPA relapses or adverse events in patients treated with mepolizumab. [Conclusions] Mepolizumab treatment of EGPA was effective in reducing steroid use and was well tolerated in patients with severe injuries.

W24-6

Interim Analysis of Post-marketing Surveillance Study of Mepolizumab (Mepo) in Patients with EGPA

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Conflict of interest: Yes

[Objective] To collect the safety data of Mepo for EGPA. [Methods] All EGPA patients treated with Mepo after May 2018 were included. The observation period was 96 wks. The incidence rate (IR, per 100 person years) of adverse events (AEs) was evaluated. [Results] As of 31/7/2022, 609 cases were included for safety analysis (609, 435, and 283 at Wks. 12, 48, and 96). The patient characteristics were 58.6% female, 62 yrs. of age, EGPA duration of 2.2 yrs., and observation period of 365 days (all median). The total person-years was 764.2. The IR of AEs was 76.82. The most common AEs (number of events) were asthma (56), condition aggravated (including worsening complication; 26), EGPA (24), and nasopharyngitis (22). Regarding AEs of special concerns, i.e. hypersensitivity, infection and malignant tumour, the IR were 4.45, 15.97 and 0.26, respectively. The IR of serious AEs were 0.79, 6.28 [pneumonia bacterial (11), pneumonia (10), respiratory tract infection (5), pyelonephritis (3), etc.] and 0.26 [prostate cancer (1), breast cancer male (1)], respectively, and the AEs resulting in death were circulatory collapse and aspiration pneumonia (1 each). [Conclusions] No new concerns have been detected up to the present in comparison with the known safety profile of Mepo. (Funding: GSK, 208505).

W25-1

A refractory case with TAFRO syndrome who was effectively treated with rituximab

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Conflict of interest: None

The case was 66-year-old male, visited a hematologist for a further examination of thrombocytopenia. The biopsy was performed since multiple lymphadenopathy was found by CT scan and showed no evidence of malignancy. Based on the elevation of the level serum IgG4, he was considered to have IgG4-related disease (IgG4-RD) and idiopathic thrombocytopenic purpura. Afterwards, since ascites was also started, which was thought to be derived from IgG4-RD peritonitis, 30 mg/day of prednisolone (PSL) was initiated. However, it was refractory to the dose reduction and he was referred to our hospital. After the admission, he was diagnosed as TAFRO syndrome based on the criteria, having ascites, thrombocytopenia, lymphadenopathy, high serum CRP level, and progressive renal dysfunction. PSL was increased up to 1 mg/kg/day and combined with pulse

therapy, which was ineffective. Then, rituximab (RTX) was introduced and ascites and platelet count were gradually improved. Although tocilizumab (TCZ) or cyclosporine (CyA) have been generally reported as a second-line treatment, recent report showed the effectiveness of RTX based on the elongation of the time from the initiation to the switch to the next therapy or death, compared with TCZ or CyA, This case was quite rare based on the literature search.

W25-2

Successful Treatment with Cyclophosphamide in Refractory iMCD-TAFRO

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Conflict of interest: None

[Case 1] A 37-year-old man presented with a one-month history of fever, nausea, abdominal pain, and diarrhea in addition to anasarca on exam. Laboratory tests showed thrombocytopenia and renal failure while imaging studies revealed mild axillary lymphadenopathy for which subsequent lymph node biopsy showed Castleman's disease-like changes compatible with iMCD-TAFRO. Initial treatment with methylprednisolone pulse therapy and tocilizumab failed to resolve his symptoms; therefore, intravenous cyclophosphamide was instead given with improvement of his symptoms. [Case 2] A 66-year-old man presented with a one-month history of oliguria, dyspnea, and anasarca. Laboratory tests showed thrombocytopenia, hematuria, and proteinuria while imaging studies revealed mild systemic lymphadenopathy for which lymph node biopsy showed Castleman's disease-like changes compatible with iMCD-TAFRO. After treatment with methylprednisolone pulse therapy and tocilizumab, his pleural effusion increased, so intravenous cyclophosphamide was given instead with improvement of his symptoms. [Conclusions] The optimal treatment for iMCD-TAFRO has not been established. These cases suggest that cyclophosphamide may be effective for refractory iMCD-TAFRO.

W25-3

Two cases of TAFRO syndrome complicated with posterior reversible encephalopathy syndrome (PRES)

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Conflict of interest: None

Case 1: A 42-year-old male was diagnosed with TAFRO (thrombocytopenia, anasarca, fever, reticulin fibrosis and organomegaly) syndrome at two months before the first appointment to our hospial. Despite ameliorated above symptoms with glucocorticoids, he suddenly developed high blood pressure, seizure and left hemiparalysis. The diagnosis of PRES was made based on the findings on brain MRI: multiple white matter lesions in cerebrum and brainstem. Case 2: A 52-year-old female presented conscious disturbance. The diagnosis of PRES was made according to the finding of high blood pressure and white matter lesions in bilateral posterior lobes detected by MRI. Enhanced CT revealed the image suggestive of adrenal infarction. Subsequently, she developed fever, anasarca, thrombocytopenia and renal dysfunction. After she was transferred to our hospital, reticulin fibrosis was identified in her bone marrow. Finally, she was diagnosed with TAFRO syndrome. Discussions: TAFRO syndrome possibly develop organ microangiopathies in the acute phase. The clinical courses of our patients imply that adrenal infarction due to TAFRO syndrome led to abrupt release of catecholamines, resulting in PRES.

W25-4

Severe TAFRO syndrome: a case-series and literature review

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Conflict of interest: None

[Objective] The aim of this study is to clarify clinical characteristics of severe TAFRO syndrome. [Methods] We retrospectively explored clinical records of 5 cases of TAFRO syndrome in our department. [Results] The mean age of 5 cases (all male) was 61.6 years. Lymph node biopsies showed plasma cell type (2 cases), hypervascular type (1) and hyaline-vascular type (1). All cases were performed combination therapies of steroids and immunosuppressive agents such as cyclosporin A (CsA): 4 cases, tocilizumab (TCZ): 4, and rituximab (RTX): 3. 2 cases were classified as Grade 4 (Severe) and three cases as Grade 5 (Very severe). Thrombocytopenia and anasarca were not improved in 2 cases, followed by death. All 3 survivors received immunosuppressive agents within 2 weeks after initiating steroid therapies and required dialysis temporarily. Among them, it took mean 33.6 days for CRP to be normalized after the start of steroid therapies, while 86.3 days for platelet count to return to normal (> 100,000 /μL). [Conclusions] Early administration of immunosuppressants added to steroids could be a novel approach for patients with severe TAFRO syndrome. It may take more than a few weeks or even months for platelet count to increase greater than 100,000 /μL after normalization of CRP levels.

W25-5

Report on the relationship between time from onset to therapeutic intervention and prognosis in TAFRO syndrome

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Conflict of interest: None

[Objective] TAFRO syndrome is a new disease characterized by thrombocytopenia, anasarca, fever, reticulin fibrosis, and organ enlargement. The purpose of this study was to report the relationship between the time from onset to therapeutic intervention and prognosis in our patients and to inform clinical practice. [Methods] Five patients diagnosed with TAFRO syndrome at our hospital between April 2020 and October 2022 were included. [Results] The patient who started treatment within 2 weeks achieved remission with steroids alone. The patient who took 1 month to start treatment achieved remission with tocilizumab and rituximab. The patient who took two months to start treatment achieved remission with a combination of steroids, cyclosporine, and tocilizumab. Of the two patients who died, one started treatment in one month but did not achieve remission with steroids, cyclosporine, and tacrolimus. The other patient, originally a rheumatoid arthritis patient, was treated with prednisone and tocilizumab, but died of gastrointestinal bleeding despite an increase in prednisone dose and a change in the tocilizumab regimen. [Conclusions] The patient with the shortest therapeutic intervention at our institution achieved remission with a single steroid and had a good prognosis.

W25-6

Clinical features of Castleman's disease in our department

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Conflict of interest: None

[Objective] Castleman's disease (CD) is a rare, benign polyclonal lymphoproliferative disease. In order to elucidate the clinicopathological features of CD. [Methods] Background, laboratory data, histopathological findings, treatment, and prognosis were retrospectively analyzed in 17 cases of CD (8 males, 9 females). [Results] Onset of CD was 51.9±14.6 y/o, disease duration from onset of CD was 4.2±5.6 y. Ten cases (58.8%) required histological evaluation repeatedly (2.60±0.52 times), and all cases were plasma cell type. The affected organs were lymph nodes (15 cases), lungs (6 cases), and skin (6 cases). The laboratory findings were as follows: IgG 4652±1800 mg/dL, CRP 6.22±4.10 mg/dl, Hb 10.2±1.6 g/dL, Alb 2.8±0.7 g/dL, LDH 82±36 U/mL, sIL-2R 1252±402 U/L, and CHAP Score 5.75±3.28. Anti-DNA antibodies were present in 8 instances, and

RF was present in 4 cases. Tocilizumab (TCZ) was given to 15 patients. Serum IL-6 was measured in 6 cases before and after administration of TCZ. The IL-6 level was 23.1±23.0 pg/mL before administration, and 664.2±431.3 pg/mL just before the second administration, showing a marked IL-6 increase by TCZ administration. [Conclusions] CD is a rare lymphoproliferative disease difficult to make early diagnosis. Further study is warranted.

W26-1

MALT lymphoma with rapid progression of tracheal stenosis suspected relapsing polychondritis

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Conflict of interest: None

A 69-year-old woman developed cough and hoarseness 5 months before admission. Serum IgM and soluble IL-2 receptor levels were elevated and no atypical cells in bone marrow biopsy. Chest CT showed bilateral bronchial wall thickening, infiltrative shadows, and axillary and mediastinal lymphadenopathy. The bilateral lacrimal gland gets swelled and PSL 30 mg was started without histological examination. When the dose was reduced to 5 mg, bilateral eyelid swelling reappeared. A few days before admission, hoarseness and respiratory distress appeared. Nasopharyngeal laryngoscope showed protruded lesions arising from the posterior pharyngeal wall. After tracheotomy for progressive subglottic stenosis, she was referred to our department because relapsing polychondritis (RP) was suspected. Steroid pulse therapy was started and eyelid swelling and respiratory distress improved rapidly. Thereafter a lacrimal gland biopsy showed clusters of atypical lymphocytes, and immunostaining of tracheal and lacrimal gland tissue revealed the lambda-positive plasma cells, leading to the diagnosis of MALT lymphoma. In tracheal lesions of RP, the membranous portion is not involved and early biopsy is necessary to distinguish lymphoma. We reviewed the literature on MALT lymphoma with tracheal lesions.

W26-2

A case of TAFRO syndrome developed lymphoproliferative disorder (LPD)

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Conflict of interest: None

A 50-year-old man presented with leg edema persisting for 2 months. Laboratory findings revealed high levels of WBC, CRP and D-dimer, however contrast CT and ultrasound examination of legs revealed no abnormal findings. After 1 month, he presented with appetite loss, abdominal fullness, and dyspnea. Laboratory tests showed acute renal injury and he was admitted to our hospital for further examination. He showed anasarca, thrombocytopenia, reticulin fibrosis, high inflammation, and acute renal insufficiency, and was diagnosed as TAFRO syndrome. We initiated PSL, CyA, and TCZ with additional treatments of hemodialysis, CART, and platelet transfusion, and his symptom improved after we observed improvement of CRP, ALP, sIL-2R, PCT, VEGF, IL-6. After leaving hospital, we maintained with PSL, CyA, and TCZ. But, he developed lymph node swelling and edema of the right arm and elevated LDH. Considering his disease progression despite CyA and TCZ cessation, he underwent surgical biopsy of lymph node. The histology was consistent with DLBCL. We diagnosed LPD and started R-CHOP. After his LPD improved by R-CHOP, we treated with rituximab for TAFRO syndrome. We describe the treatment and the hematological findings of TAFRO syndrome, and the management of TAFRO syndrome after LPD was occurred.

W26-3

A case of tenosynovitis and fascitis suspicious of invasion of peripheral T-cell lymphoma

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Conflict of interest: None

[Case] A 67-year-old woman with a history of peripheral T-cell lymphoma (PTCL), presented with a 3-week history of pain, swelling, and numbness in both arms and legs. Physical examination revealed pitting edema of both limbs and redness on the extensor surfaces of the forearms. Musculoskeletal ultrasonography revealed thickening of the extensor tendons of both hands and synovial effusion around the tendon sheaths, with power doppler signals from the extensor tendons to the forearm fascia. Contrast-enhanced magnetic resonance imaging of the left hand showed a contrast effect around the tendon sheaths. We considered tenosynovitis and fasciitis, and performed biopsy of the fascia of the posterior forearm. We administered prednisolone 20 mg/day and she was discharged on the 12th day without pain and edema. Histological findings showed perineural and perivascular inflammatory cell infiltrates predominantly composed of lymphocytes, with no eosinophil. Immunostaining showed a suspicious invasion of PTCL. Subsequently, generalized subcutaneous nodules appeared. Based on the results of skin biopsy, a diagnosis of recurrent PTCL was made. A case of tenosynovitis and fasciitis invading malignant lymphoma is rare. Histological findings are important to distinguish malignant disease.

W26-4

A case of fascial metastasis of gastric cancer with swelling of both lower limbs at the time of recurrence, which was differentiated from fasciitis-panniculitis syndrome by biopsy

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Conflict of interest: None

[Case] A 76-year-old, female patient had undergone a total gastrectomy for poorly differentiated adenocarcinoma two years ago. Two months before her current admission, low back pain developed, and one month before admission, swelling in the bilateral lower limbs gradually developed. Contrast-enhanced CT revealed retroperitoneal recurrence of the adenocarcinoma. PET-CT revealed myofascial edema and FDG accumulation in the thighs and left spinal erector muscles, raising suspicion of fasciitis. She was admitted for a thorough examination of the swelling after starting TS-1 chemotherapy for the retroperitoneal recurrence. A percutaneous biopsy of the left spinal erector fascia led to the diagnosis of metastatic adenocarcinoma having the same characteristics as gastric cancer. A biopsy of the lower extremities was avoided due to subcutaneous edema, but based on the PET-CT findings, fascial metastasis was tentatively diagnosed. She was discharged after initiating palliative care. Distinguishing between cancer-associated fasciitis-panniculitis and skeletal muscle metastasis in patients with cancer with fasciitis-like symptoms is important. Skeletal muscle metastasis of gastric cancer is extremely rare, but a biopsy is recommended because the treatment of malignant tumors may change.

W26-5

A case of anti-rhabdomyosarcoma antibody-positive irAE myositis after avelumab treatment for renal pelvis cancer

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Conflict of interest: None

[Case] An 88-year-old woman was diagnosed with right renal pelvis cancer (cT4N0M0) in October X-1. 6 courses of GCarbo (gemcitabine + carboplatin) therapy were started in January X, and Avelumab was started on May 24, X. She became aware of fatigue and limb weakness around June 1, and on June 14, she was referred to our department because of CK 4636 U/L. MRI showed high-signal areas in the bilateral thigh muscles. There was no ptosis or diplopia. Myocardial deviatoric enzymes were mildly elevated, but there were no abnormalities on electrocardiogram, echocardiogram, or cardiac MRI. Myositis-related antibodies were negative, but positive anti-rhabdomyosarcoma antibodies (anti-Titin and anti-Kv1.4 antibodies) were observed. The diagnosis of immune-related adverse event (irAE) myositis caused by immune checkpoint inhibitor (ICI) was made, and mPSL pulse therapy was administered after discontinuation of Avelumab, starting with PSL 40 mg (1 mg/kg/BW) as post-therapy. The patient showed rapid improvement after the start of treatment. [Discussion] Anti-rhabdomyosarcoma antibodies are frequently detected in thymoma-associated myasthenia gravis complicated by myositis, and cases have been reported in irAE myositis.

W26-6

Pembrolizumab-induced inflammatory arthritis is characterized by high proportion of mononuclear cells in synovial fluid

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Conflict of interest: None

[Objective] To evaluate the clinical features of pembrolizumab (PEMBRO)-induced arthritis and the leukocyte fraction, TNFα, IL-6 expression in synovial fluid (SF). [Methods] We investigated the patients with PEMBRO-induced arthritis from 2019 to 2021. Leukocyte fractions and concentration of TNFα, and IL-6 in SF were measured. We compared those with RA patients. [Results] SFs were collected from 3 patients with RA-like (2 lung adenocarcinoma, 1 lymph node metastasis from ureteral cancer) and 1 patient with PsA-like (lung squamous cell carcinoma). Median age was 63 (53-79) years, and all patients were male. MTX was administered as initial treatment, and following TAC was added for all patients, arthritis improved. In two patients, PEMBRO was interrupted after developing arthritis. At 12 months later, one of them was treated with MTX-&TAC, and his cancer kept CR. In the other 3 patients, the DMARDs was stopped because of changing the treatment for cancer. Leukocyte in SF was 4650 (1600-10600)/μL, and when compared with 4 male RA patients, mononuclear cells ratio and TNFα were significantly higher than those in RA. There was no difference in IL-6. [Conclusion] These data show that PEMBRO-induced arthritis is characterized by high proportion of mononuclear cells and high TNFα levels in SF.

W27-1

Performance of diagnostic and classification criteria in 50 cases of suspected IgG4-related disease

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Conflict of interest: None

[Objective] The 2019 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria and the 2020 revised comprehensive diagnostic (RCD) criteria are used for diagnosis of IgG4-related disease (IgG4-RD). We evaluated the performance of both criteria and the differences between IgG4-RD and mimickers. [Methods] This was a retrospective, single-center study in 50 cases with suspected IgG4-RD. IgG4-RD was finally diagnosed by Rheumatologists. We compared clinical characteristics and laboratory data at diagnosis between IgG4-RD patients (n = 42) and mimickers (n = 8). [Results] There were 21 cases in Definite group, 1 case in Probable group and 20 cases in Possible group with IgG4-RD meeting the 2020 RCD criteria, with a sensitivity of 100% and specificity of 50.0% for diagnosis of IgG4-RD. The 2019 ACR/EULAR classification criteria had a sensitivity of 88.1% and a specificity of 87.5%. IgG4-RD showed no difference compared to non-IgG4-RD, except for a significantly higher number of affected organs (p=0.002). [Conclusions] The 2019 ACR/EULAR classification criteria had a higher specificity of diagnosis, and the 2020 RCD criteria had a higher sensitivity of diagnosis. IgG4-RD had a significantly higher number of affected organs than non-IgG4-RD.

W27-2

Clinical characteristics and diagnostic problems in IgG4-related disease

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Conflict of interest: None

[Objective] IgG4-related disease (IgG4-RD) is an immune-mediated disorder that displays single or multiple organ involvement with IgG4 plasma cell infiltration and fibrotic change. In this study, we assessed clinical characteristics and diagnostic problems in IgG4-RD. [Methods] Clinical records for 43 patients under suspicion of IgG4-RD in our institute were retrospectively reviewed. [Results] In 33 patients diagnosed as IgG4-RD at a median age of 67 years, males accounted for 55%. The most affected lesions involved ophthalmic sites and submandibular glands. Interestingly, 63% of the IgG4-RD patients showed image findings of sinusitis. Almost all IgG4-RD patients were treated with oral prednisolone (PSL) at a dose of 0.48 mg/kg, whereas only 15% required immunosuppressants. Although eight IgG4-RD patients with swollen salivary glands underwent labial biopsy, only 25% exhibited pathological findings consistent with IgG4-RD. In non-IgG4-RD including Castleman disease, MALT lymphoma or idiopathic retroperitoneal fibrosis, 70% of patients showed more than 135 mg/dl in serum IgG4 concentration. [Conclusions] A biopsy of the affected lesions but not lip should be considered for diagnostic accuracy. It is important to exclude non-IgG4-RD which can display clinical features like IgG4-RD.

W27-3

Clinical features of IgG4-related diseases using cluster analysis based on involved organs

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Conflict of interest: None

[Objective] To explore differences in the clinical characteristics of patients (pts) with IgG4-related disease (IgG4RD) according to the organs involved. [Methods] We investigated the laboratory findings, organ involvement, and clinical course of IgG4RD pts who visited our division between January 2015 and September 2022. Pts were classified into four groups based on the involved organs (group A, hepatobiliary; group B, retroperitoneal fibrosis and aortitis; group C, head and neck; group D, systemic (lacrimal gland and salivary gland lesions + lung, retroperitoneal fibrosis, and renal)). [Results] A total of 42 pts were included. The numbers of pts in each group were: A, 3; B, 6; C, 11; and D, 22. The mean IgG4 levels (mg/dL) at diagnosis in A, B, C, and D were 732 (255-1540), 309 (131-660), 477 (161-597), and 1337 (98-4580). The IgG4 levels were significantly higher in D (p=0.025). 67% of pts in A, 100% in B, 36% in C, and 68% in D were treated. The mean starting doses of PSL (mg/day) were 37.5, 35.8, 20.0, and 37.0, and the mean maintenance doses of PSL (mg/day) were 5.5, 5.3, 3.3, and 6.2. The intervention rate was significantly lower in C (p=0.03). Two pts died. [Conclusions] The systemic type had higher IgG4 levels, and the head and neck type had a lower intervention rate.

W27-4

Current Status and Issues in Diagnosis and Treatment of Patients with IgG4-Related Diseases at Our Institution

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Conflict of interest: None

[Objective] We analyze the current status of diagnosis and treatment of patients with IgG4-RD. [Methods] Patients with IgG4-RD at our institution were evaluated for diagnosis (2020 revised comprehensive diagnostic criteria for IgG4-RD), affected organs, FDG-PET, biopsy, treatment and its outcome. [Results] 87 cases were diagnosed based on the 2020 revised comprehensive diagnostic criteria for IgG4-RD (definite; 43, probable; 8, possible; 35). In 79 cases, FDG-PET was performed. The salivary glands were the most frequently involved organ, followed by the lacrimal glands, lymph nodes, retroperitoneum, and kidneys. Biopsy was performed in 69 cases, mostly in the submandibular gland and superficial lymph nodes, with a diagnostic rate of 71.9%. The diagnosis rate for the submandibular gland biopsy was high at 93.3%, while that for minor salivary gland was low at 46.7%. Most of the cases followed up without therapy were cases with only submandibular or lacrimal gland lesions. 56 were treated, all with GC and improving, but 11 relapsed. GC at relapse averaged 7.1±2.4 mg. 22 received concomitant immunosuppressive drugs, most of them with azathioprine. [Conclusions] Submandibular gland biopsy had a good diagnostic rate. We compare relapsed cases with non-relapsed cases with GC dose reduction.

W27-5

Clinical characteristics associated with relapse in patients with IgG4-related disease in our department

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Conflict of interest: None

[Objective] We evaluate relapse predictors in IgG4-related disease (IgG4-RD). [Methods] We enrolled IgG4-RD patients visiting our department between April 2021 and September 2022, and evaluated responder index (RI) at diagnosis, 1, 2, 3, 6, 9, and 12 months. Relapse was defined as appearance of new lesions or worsening of existing lesions reflecting activity, regardless of increase in serum IgG4 level. [Results] Thirty-one IgG4-RD patients (17 women, 14 men) were enrolled. Median age was 60 (52-72) years, and serum IgG4 level was 603 (241-924) mg/dL at diagnosis. Twelve patients received prednisolone (PSL) 0.6 mg/kg/day. During 12 (10-12) months, RI decreased from 11 to 4, and relapse occurred in a patient (8%). Four patients received PSL 0.2-0.3 mg/kg/day. During 12 (11-12) months, RI tended to decrease from 9 to 6, and relapse in 3 patients (75%). Fifteen patients were followed without treatment. During 3 (1-12) months, RI decreased from 9 to 7, and relapse in 5 patients (33%). Relapse rate was different among three groups (p=0.033), and serum IgG4 level at diagnosis was associated with relapse in no-treatment group (p=0.025). [Conclusions] Relapse rate was different among treatment groups, and serum IgG4 level at diagnosis was associated with relapse in no-treatment group.

W27-6

Study on the medium-term prognosis of IgG4-related diseases

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Conflict of interest: None

[Objective] To investigate the course of treatment, relapse rate, and complications of IgG4-related disease (IgG4-RD), and to clarify the medium-term prognosis. [Methods] Patients with IgG4-RD at our hospital and Kagawa University were included in the study. IgG4-RD was diagnosed based on the 2020 revised comprehensive diagnostic criteria for IgG4-related diseases. Patients with IgG4-RD who had been followed for more than 3 years were analyzed for characteristics, affected organs, laboratory and imaging findings, relapse rate, and prognosis. [Results] Of the 82 cases selected as IgG4-RD, 64 could be followed up. 36 were observed for more than 3 years; 4 of the 36 patients had malignant tumour. Four patients died during the study. All 22 patients treated were started on glucocorticoids (GC) alone, but 15 were additionally treated with immunosuppressive drugs. All 22 treated patients improved but 12 relapsed; the mean dose of 3 mg/day in patients maintained on GC alone. Four of the relapses occurred in a different organ than at the onset. Relapses after concomitant immunosuppressive drugs occurred in 27% of patients. [Conclusions] Although GC treatment was effective for IgG4-RD, the high relapse rate made GC discontinuation difficult. There was also a high complication rate of malignancy.

W28-1

Does autoimmune pancreatitis exacerbate retroperitoneal organ damage in patients with IgG4-related disease?

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Conflict of interest: None

[Objective] IgG4-related diseases are a group of diseases of unknown cause that present with synchronous or metachronous swelling, nodules, and hypertrophic lesions in various organs throughout the body. AIP is a representative IgG4-related disease. We investigated whether the presence or absence of pancreatitis strongly affects retroperitoneal organs other than the pancreas. [Methods] 44 outpatients diagnosed with IgG4-related disease at our hospital were divided into AIP group and non-AIP group. The presence or absence of Vascular lesions (periarteritis/retroperitoneal fibrosis, aneurysm), renal lesions (hydronephrosis, tubulointerstitial nephritis) were examined by US, CT, PET/Ga, and renal histopathology. [Results] There were 22 patients in AIP group (18 males, 4 females, median 66), and 22 in non-AIP group (15 males, 7 females, median 62). Vascular lesions occurred in 9 (39.1%) in AIP group and 6 (27.2%) in non-AIP group. Renal lesions occurred in 6 (26.1%) in AIP group and 5 (22.7%) in non-AIP group. Serum creatinine and urinalysis abnormalities (urinary protein, occult blood, β2-MG, NAG) did not differ significantly between the two groups. [Conclusions] Vascular lesions and renal lesions were observed to the same extent in both AIP and non-AIP groups.

W28-2

Cholecystitis in patients with immunoglobulin G4-related diseases

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Conflict of interest: None

[Background] IgG4-relate cholecystitis (IgG4-CC) is a rare manifestation in IgG4-related disease (IgG4-RD) and is rarely presented as isolated cholecystitis. [Objective] To describe the clinicopathological features of IgG4-CC [Methods] 253 patients fulfilling ACR/EULAR 2019 IgG4-RD classification criteria on March 2022, were included. Patients with cholecystectomy specimens were selected further, and clinicopathological features were reviewed retrospectively. IgG4-CC was defined as cholecystitis with lymphoplasmacytic infiltration, fibrosis, IgG4-positive cell >10/HPF and $IgG4^+/IgG^+$ >0.4. [Results] 12 patients fulfilled the inclusion criteria. The median age at the cholecystectomy was 71. Eight cases were IgG4-CC. Two cases were the antecedent onset of IgG4-RD. There was a case complicated with gallbladder cancer. Among 6 patients with IgG4-CC after the diagnosis of IgG4-RD, four cases had further active organ

involvement of IgG4-RD with IgG4-CC. One patient was complicated with autoimmune pancreatitis. Histopathology revealed deep mucus inflammation could be an indicator of IgG4-CC. [Conclusions] Isolate IgG4-CC can often occur as the antecedent onset of IgG4-RD. Cholecystitis with deep mucus inflammation with dense lymphoplasmacytic infiltration with fibrosis can indicate IgG4-CC.

W28-3

MRIT2-weighted image low signal is useful in predicting the degree of fibrosis in IgG4-related tubulointerstitial nephritis

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Conflict of interest: None

[Objective] To investigate the relationship between MRI findings and renal histopathology in IgG4-related kidney disease (IgG4-RKD). [Methods] Of 46 patients with IgG4-RD diagnosed at our hospital, 19 patients (median age 76 years, 18 males) with IgG4-RKD diagnosed by renal biopsy and undergoing MRI at the same time were included. In renal histopathology, the extent of tubulointerstitial inflammatory cell infiltration (0: < 10%, 1: 10-25%, 2: 26-50%, 3: > 50%) and the degree of fibrosis (0: < 5%, 1: 6-25%, 2: 26-50%, 3: > 50%) were scored and evaluated MRI for presence of T2WI low signal, DWI high MRI was used to evaluate the presence of low T2WI signal and high DWI signal. [Results] Of the 19 patients, 11 (58%) had T2WI low-signal lesions. The T2WI low-signal lesion+ group had a significantly higher fibrosis score than the - group (T2WI low-signal+: 2.4±0.8 vs. 1.1±0.6: $p<0.05$). The DWI high signal + group had a higher inflammatory cell infiltration score than the - group, but it was not significant. (DWI high signal + group (DWI high signal+: 1.9 ±1.1 vs 1.8±1.0: $p=0.72$) [Conclusions] In IgG4-RKD, T2WI low signal is useful in predicting tubulointerstitial fibrosis. Diffusion-weighted images can also detect lesions with high sensitivity.

W28-4

A study of 10 cases of hydronephrosis due to IgG4-related retroperitoneal fibrosis

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Conflict of interest: None

[Objective] IgG4-related retroperitoneal fibrosis sometimes extends to the periureteral area and presents with hydronephrosis. We review the characteristics and clinical course of 10 cases of IgG4-related retroperitoneal fibrosis. [Methods] We evaluated the pre-treatment clinical findings, treatment details, and relapse of 10 patients diagnosed with IgG4-related retroperitoneal fibrosis with hydronephrosis at our department between April 2011 and October 2022. [Results] Age at diagnosis ranged from 63 to 86 years (median 70 years). Eight patients were male. Two patients had bilateral hydronephrosis and eight had unilateral. Eight patients underwent ureteral stenting or nephrostomy for hydronephrosis. All patients were treated with prednisolone (PSL) at an initial dose of 30-40 mg/day, except one. All patients had lesion reduction, and ureteral stents and nephrostomies were removed in 7 patients, with an implantation period ranging from 2 to 60 weeks (median 19 weeks). PSL was reduced in all patients, but all 3 patients who were reduced to less than 5 mg of PSL had relapse. [Conclusions] In the present study, relapse was observed when the dose was reduced to less than 5 mg of PSL, and further study of maintenance therapy is needed.

W28-5

Study of organ damage in patients with IgG4-related disease with marked hypocomplementemia

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Conflict of interest: None

(Background) IgG4-related diseases are systemic diseases with IgG4 plasma cells infiltration and characteristic fibrous lesions in pathology. Some cases show marked hypocomplementemia, which has been associated with disease activity, but this is not clear. **(Objective)** The purpose of this study was to investigate the clinical background of patients with marked hypocomplementemia among IgG4-related diseases. **(Methods)** Among 44 patients with high IgG4 levels of >135 mg/dL diagnosed with IgG4-related diseases, 10 patients with hypocomplementemia, especially C4 <10 mg/dL, were examined for organ involvement at the time of diagnosis. **(Results)** Hypocomplementemia patients: 8 men, 2 women. (mean age 74.2 years.) Lymphadenopathy 9 (20%), pulmonary involvement 7 (16%), renal involvement 7 (16%), perivasculitis or retroperitoneal fibrosis 7 (16%), autoimmune pancreatitis 3 (7%). Serologic findings: mean IgG4 level 1784 mg/dL, mean IgG4/IgG 0.40, and mean soluble IL-2 receptor level 1658 U/ml. **(Conclusion)** In IgG4-related diseases with marked hypocomplementemia, renal, periaortitis/retroperitoneal fibrosis, and pulmonary lesions tend to be observed in addition to lymphadenopathy. The clinical and imaging studies should be performed to evaluate systemic organ involvement at the time of diagnosis.

W28-6

An adolescent case of IgG4-related disease with atypical presentation

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Conflict of interest: None

A 20-year-old Japanese man visited our hospital for hypergammaglobulinemia. When he was 19, he presented with dorsal edema and purpura in bilateral legs. Blood tests showed high IgG and IgE titers, and he was referred to our department. He had swelling submandibular glands, and ultrasonography showed reticular hypoechoic findings. Additional blood tests confirmed IgG4 elevation and hypocomplementemia. Enhanced CT showed enlargement of lacrimal and submandibular glands and multiple hypodense lesions in the kidneys. Renal pathology revealed a well-demarcated diffuse tubulointerstitial lesion with mild fibrosis and lymphoplasmacytic infiltrate, and the ratio of IgG4/CD138 >40%. A salivary gland pathology showed that the ratio of IgG4/IgG was 50%. We diagnosed IgG4-related disease (IgG4RD), and prednisolone 35 mg/day was initiated. After two weeks, the salivary glands were shrunk. After two months, radiological abnormalities disappeared in the kidneys. Although his pathology included atypical findings such as tubulitis and neutrophil infiltration, he was considered to have IgG4RD because we excluded mimickers, including malignancy. Adolescent cases of IgG4RD should be gathered and analyzed to elucidate its characteristics in the future.

W29-1

The anti-U1 ribonucleoprotein antibody has a mild but apparent impact on interstitial lung disease in patients with scleroderma

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Conflict of interest: None

[Objective] To determine the impact of anti-topoisomerase 1 antibody (ATA) and anti-U1 ribonucleoprotein antibody (anti-RNP Ab) on systemic sclerosis (SSc) related interstitial lung disease (ILD). [Methods] Patients with SSc who visited our hospital between December 2020 to December 2021 were consecutively registered. The ILD score and traction bronchiectasis (TBE) score were evaluated using method by Walsh with minor modification. Patients were classified into three groups; 1); ATA+/anti-RNP Ab-, 2); ATA-/anti-RNP Ab+, 3) ATA-/anti-RNP Ab-. Severity of ILD at registration was compared (cross-sectional analysis). Patients available for the past computed tomography (CT) were included and compared for “progressive ILD” (longitudinal analysis). Cochran-Armitage trend test was used for statistics. [Results] Among 47 patients (group 1, 2, 3; n=6, 7, 34), the frequency of “extensive ILD” (ILD score≧20%) was 83.3,

28.5 and 5.8% in group 1, 2 and 3 ($p<0.01$). Among 25 patients available for the past CT (group 1, 2, 3; n=5, 6, 14), the frequency of "progressive ILD" (ΔILD≧5%) was 80.0, 50.0 and 14.3% in group 1, 2 and 3 ($p<0.01$). [Conclusions] The presence of anti-RNP antibody has a mild but apparent impact on the presence and severity of ILD as well as progression of ILD.

W29-2

Seasonal variation of serum KL-6 levels in patients with systemic sclerosis having interstitial lung disease

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Conflict of interest: None

[Objective] Serum KL-6 is used as a serological marker for interstitial lung disease (ILD), and that may fluctuate regardless of its severity. Based on our clinical experience, we hypothesized that serum KL-6 levels would be affected by the season, and we assessed that using data from patients with systemic sclerosis with ILD (SSc-ILD). [Methods] We defined summer (S) as July to September, and winter (W) as December to January. The diagnosis of ILD was confirmed by HRCT. Among SSc-ILD patients, those who had data of serum KL-6 levels in 2015 W, 2015S, and 2016 W were included. Patients with comorbidities that could affect serum KL-6 levels were excluded. Differences in serum KL-6 levels between S and W were analyzed. [Results] A total of 60 SSc-ILD patients were enrolled. 53 (88%) patients were female, the median age was 60.8 years, respectively. Serum KL-6 levels were significantly higher in the W compared with those in the S (2015 S vs 2015 W: 585 IU/L vs 648 IU/L, $p < 0.0001$; 2015 S vs 2016 W: 585 IU/L vs 690 IU/L, $p < 0.0001$). However, there was no difference between 2015 W and 2016 W. Similar results were obtained in 53 patients with the unchanged ILD area during the observational period. [Conclusions] In patients with SSc-ILD, serum KL-6 levels may fluctuate seasonally.

W29-3

The predictive factors of poor prognosis in Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD): a retrospective observational study

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Conflict of interest: None

[Objective] The purpose of this study is to evaluate the poor prognostic factors of SSc-ILD. [Methods] Patients diagnosed with SSc-ILD at our department from April 1, 2012 to June 30, 2022 were enrolled. We retrospectively examined the patient's clinical charactaristics. [Results] 139 cases were diagnosed with SSc and 76 cases (55%) was complicated with SSc-ILD. Among them, 60 cases of SSc-ILD were followed for more than 12 months. The progressive group (25 patients, 42%) had more frequent respiratory symptoms and higher levels of KL-6 than the non-progressive group. 14 cases (58%) in the progressive group already had extensive disease (ILD >20% or %FVC<70%) at diagnosis. In the progression group, 8 cases (33%) were negative for all of anti-Scl-70 antibody/anti-centromere antibody/anti-RNA polymerase III antibody/anti-U1-RNP antibody, which was more than the non-progression group ($p=0.04$), few cases were positive for anticentromere antibodies ($p <.001$). There was no difference between the two groups in terms of smoking history, disease type (diffuse type and limited type), skin symptoms, and joint symptoms. [Conclusions] SSc-ILD therapy should be considered in patients with extensive disease and in patients who are negative for the above four scleroderma-related antibodies.

W29-4

Clinical Utility of Progressive Pulmonary Fibrosis in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

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Conflict of interest: None

[Objective] Chronic ILD with progressive fibrosing (PF) phenotype is associated with decline in lung function and risk of mortality. Since definition of PF-ILD used in the previous clinical trial was used in clinical practice without validation, new definition of progressive pulmonary fibrosis (PPF) has been recently proposed by joint pulmonary communities. We investigated clinical utility of PPF in SSc-ILD using a single-center prospective registry. [Methods] We selected 104 patients with SSc-ILD from our SSc registry based on at least 1 year of follow-up. Baseline characteristics that predicted PPF were examined by univariate and multivariate analyses. Cumulative survival rates were compared between the groups stratified by development of PPF. [Results] During median of 50 months of follow-up, 30 (29%) and 25 (24%) patients developed PF-ILD and PPF, respectively. All patients who satisfied the PPF criteria also met the PF-ILD criteria. UIP pattern on HRCT and anti-topoisomerase I at baseline were identified as predictors for development of PPF. Cumulative survival rates tended to be lower in patients who developed PPF than in those who did not. (P=0.097). [Conclusions] PPF might be useful in predicting worse outcomes in patients with SSc-ILD.

W29-5

Clinical presentation of anti-centromere antibody-positive scleroderma in Japanese

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Conflict of interest: None

[Objective] Marker autoantibodies such as anti-Topo1 (Topo1), anti-RNA polymerase 3, and anti-centromere (ACA) antibodies are found in scleroderma (SSc). We conducted an observational study to understand the characteristics of ACA-positive patients in Japan. [Methods] Patients registered as SSc from 2008 to 2021 were enrolled. (1) Patients with skin thickening were divided into three groups: ACA-positive (Group A) Topo1-positive (Group B) and negative for all three antibodies mentioned above (Group C). (2) Patients in group A were compared with ACA-positive without skin thickening (group D). [Results] Groups A, B, and C had 160, 21, and 57 patients, respectively, and intergroup comparisons showed age (66.3, 56.4, and 63.7 for groups A, B, and C, respectively), frequency of interstitial pneumonia (IP) (14.01, 52.38, and 37.50%) and sicca symptoms (32.9, 23.8, and 17.5%). The 51 patients in group D showed a difference in frequency of IP (5.9 vs. 14.0%) and Raynaud's symptoms (RS) compared to group A. [Conclusions] ACA-positive patients were more frequent in SSc and were more elderly than previous reports. They have less frequent IP but more frequent sicca symptoms than Topo1-positive. Both IP and RS were less frequent without than with skin thickening in ACA-positive patients.

W29-6

Analysis of the association between autoantibody-profile or presence of other rheumatic diseases and treatment in patients with systemic sclerosis

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Conflict of interest: None

[Objective] To analyze the relationship between autoantibodies or the presence of other rheumatic diseases and treatment in patients with systemic sclerosis (SSc). [Methods] A total of 100 SSc patients who were still

being followed up at our hospital as of October 2022 were analyzed. [Results] Of the 100 patients, 53.0%, 15.0%, 8.0%, and 5.0% had anti-centromere, anti-Scl70, anti-RNA polymerase III, and anti-RNP antibodies, respectively. Furthermore, 8.0% had two antibodies, and 26.0% had none. Other rheumatic diseases were present in 34.0% of the patients, of which 50.0% had Sjögren's syndrome, 26.5% had rheumatoid arthritis, and 23.5% had polymyositis. SSc with the above antibodies and without other rheumatic diseases accounted for 51.0% of cases. Immunosuppressive drugs were used in 54.0% of all cases, of which 74.1% used glucocorticoids, 76.9% ($p< 0.05$) of patients without antibodies, 85.3% ($p< 0.01$) of patients with other rheumatic diseases, and 31.3% ($p< 0.01$) of patients with antibodies and no other rheumatic diseases. [Conclusion] The use of immunosuppressive drugs was low in SSc patients without complications of other rheumatic diseases.

W30-1

Characteristics of dysphagia and/or aspiration & penetration in patients with systemic sclerosis (SSc)

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Conflict of interest: None

[Objective] Our aim was to characterize dysphagia and/or aspiration & penetration in patients with SSc. [Methods] SSc who were referred and examined the videofluoroscopy (VF) at our hospital between August 2021 and May 2022 were involved. Dysphagia was recognized by the existence of the oral, pharyngeal, and esophageal (Es) residue using VF. Aspiration & penetration was evaluated by the Penetration Aspiration Scale (PAS). As patient-reported outcomes (PROs), the questionnaires for FSSG and EAT-10 were also examined. [Results] Fifty SSc were involved (Male: Female: 11:39, The age: 63.4±13.2 years). As for the extent of residue, 10 had less than half of the lower Es sphincter (LES) to tracheal bifurcation (TB), 10 had more than half of LES to TB, and 28 had above TB, by the VF. Based on PAS, 21 had penetration and 2 had aspiration. Aspiration & penetration were associated with the age of SSc onset ($p=0.04$), worsening of dyspnea ($p=0.04$), and Es residue above TB ($p=0.03$). Es residue above TB was also extracted by multivariate analysis ($p=0.046$). No association was observed between PROs and VF findings or PAS. [Conclusions] These results suggest that the severity of Es dysfunction is associated with aspiration & penetration in SSc. The development of new PROs is urgently needed.

W30-2

Transcriptome analysis of myocardium in patients with systemic sclerosis

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Conflict of interest: None

[Introduction] The pathogenic process of heart involvement associated with systemic sclerosis (SSc) involves microangiopathy and chronic inflammation, leading to the spread of patchy fibrosis throughout the myocardium. This study aimed to explore the molecular pathogenesis underlying SSc heart involvement by analyzing the transcriptome of myocardial biopsies. [Methods] Four cases each with SSc primary heart involvement or dilated cardiomyopathy undergoing endomyocardial biopsy were enrolled. Myocardial specimens were applied to RNA sequencing and SSc-specific differential gene expression (DGE) was assessed using integrated analysis involving public data (GSE116250), which included myocardial transcriptome from non-failing heart (NF, n=14), ischemic cardiomyopathy (n=13), and DCM (n=37). [Results] Compared to NF, SSc myocardium showed significantly enriched pathways related to myocardial energy metabolism such as "*Oxidative Phosphorylation*", "*Mitochondrial Dysfunction*", as well as "*Granzyme A signaling*" and "*FAT10 Signaling*". Disease-specific DGE predicted the activation of "*tRNA Splicing*" and the inhibition of "*EGF signaling*" in the SSc heart. [Conclusion] Distinct molecular transcriptome profiling was identified in the SSc myocardium.

W30-3

Research for biomarkers in the pathology of pulmonary hypertension with connective tissue disease

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Conflict of interest: None

[Objective] To clarify biomarkers reflect pathology in connective tissue disease-complicated pulmonary hypertension (CTD-PH). [Methods] Patients with suspected PH from 2015 to 2021 underwent catheterization and obtained hemodynamic including mean pulmonary artery pressure (mPAP). Serum was collected from the pulmonary artery and vein at the time of test with catheterization, and biomarkers (IL-6, IL-17, IL-12p70, MCP-1, IL-21, and TIMP-1) were measured by ELISA. The association between hemodynamic parameters and biomarkers was analyzed. Data were analyzed JMP® Pro 16.1.0. [Results] 56 cases (CTD; 33 cases, non-CTD; 23 cases) were included. Furthermore, among the CTD cases, there were 22 cases of CTD-PH (SSc-PH; 11 cases, non-SSc-PH; 11 cases). IL-6 levels were positively correlated with mPAP and WHOFC in cases in which PH was diagnosed. This correlation was observed in the CTD group but not in the non-CTD group. TIMP-1 levels were elevated only in CTD-PH, and were significantly higher in SSc-PH. Serum TIMP-1 levels were not significantly associated with mPAP. [Conclusions] It suggested serum IL-6 is associated with the pathology of all PH patients. Furthermore, it suggested not only IL-6 but also multiple biomarkers such as TIMP-1 and IL-12 were associated with the pathology of CTD-PH.

W30-4

Disease-related Organ Failure Events in Diffuse Cutaneous Systemic Sclerosis (dcSSc): Potential Surrogate of Survivals

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Conflict of interest: None

[Objective] Morbidity endpoints that predicting survivals have not been established in SSc patients. We evaluated if organ failure events of the original and revised ACR-CRISS could be a surrogate for survivals in dcSSc patients using a single-center prospective cohort. [Methods] We selected 81 patients with dcSSc based on at least 1 year of follow-up. The step 1 events of the original and revised CRISS were used as the organ failure events. Cumulative survival rates were compared between the patients stratified by occurrence of the organ failure event. Baseline features associated with the organ failure event were examined by Cox proportional hazard model. [Results] During median of 51 months of follow-up, 12 (15%) and 27 (33%) patients developed at least one organ failure event of the original and revised CRISS, respectively. Cumulative survival rates were lower in the patients who developed the organ failure event of the original or revised CRISS than in those who did not (P <0.05 and 0.12, respectively). Longer disease duration and digital ulcer were identified as baseline features associated with the organ failure event. [Conclusions] The organ failure events of the CRISS could be used as a surrogate morbidity endpoint predictive of prognosis.

W30-5

Life Prognosis and Risk Factors in Patients with Systemic Sclerosis

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Conflict of interest: None

[Objective] To elucidate the life prognosis of systemic sclerosis (SSc) patients, and to clarify the risk factors for poor life prognosis. [Methods] We analyzed the prognosis and prognostic factors of 96 SSc patients (36 males, 60 females, mean age 60 years) admitted to our department from 2008 to 2020. [Results] Patient background was diffuse cutaneous SSc; 39 patients, limited cutaneous SSc; 57 patients, 49 patients positive for anti-Scl70 antibody, 16 patients positive for anti-centromere antibody. Interstitial lung lesions (ILD) were observed in 77 patients, hand ulcers in 8, scleroderma renal crisis in 5, tricuspid valve pressure gradient (TRPG) high ≧35 mmHg in 22 during the course of the disease. 33 patients had died by the end of 2021. The causes of death were malignancies in 10 cases, heart failure in 7 cases, ILD in 4 cases, and others in 11 cases. The 5-year survival rates were compared by log-rank test as follows: male vs. female (0.735 vs. 0.989, p=0.036), positive vs. negative for anti-Scl70 antibody (0.718 vs. 0.795, p<0.001), and high vs. low TRPG (0.752 vs. 0.895, p=0.017). [Conclusions] SSc patients have a poor life prognosis. In addition to males, high TRPG levels, and Scl70 antibody positivity, the malignant tumors should be noted as significant risk factors.

W30-6

Clinical features of patients with systemic sclerosis positive for anti-SS-A antibody: A cohort study of 156 patients

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Conflict of interest: None

[Objective] Anti-SS-A antibody (SSA), which is the diagnostic markers of Sjögren's syndrome (SS), is often detected in systemic sclerosis (SSc) patients. However, some patients are only positive for SSA and not complicated with SS. We retrospectively investigated the clinical characteristics of SSc patients with SSA. [Methods] Retrospective chart reviews were performed of 156 patients with SSc at Yokohama City University Hospital from 2018 to 2021. [Results] The median age was 69.0 years. The cohort consisted of 18 males and 138 females. Thirty-nine patients had dcSSc and 117 patients had lcSSc. Forty-four patientswere positive for SSA. Among them, 24 patients fulfilled the criteria for SS. SSA-positive SSc group was significantly more common in females (P = 0.024). The proportion of patients with interstitial lung disease (P = 0.020), digital ulcer (P = 0.011), and gastroesophageal reflux disease (P = 0.012) in SSA-positive group were higher than those in SSA-negative group. The proportion of dcSSc and mRSS score in SSA-positive SSc patients without SS group were significantly high compared to those in SSA-positive SSc with SS group. [Conclusions] The population of SSA-positive SSc without SS may have a higher complication rate of organ involvement and more severe disease.

W31-1

Trunk muscle mass is associated with age and fall in patients with rheumatoid arthritis: 5-year data from CHIKARA study

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) frequently have sarcopenia. We investigated relationship between disease characteristics and trunk muscle mass, not appendicular muscle mass which is measured in sarcopenia assessment. [Methods] We investigated the body compositions, laboratory data, disease activity, physical function, and history of fall and fracture among 70 patients with RA participated in the CHIKARA study at baseline and 5 years. Relationship between trunk muscle mass and each parameter was analyzed univariately. [Results] Both appendicular and trunk muscle mass were negatively associated with SDAI (r=-0.25, p=0.04; r=0.32, p<0.01) and HAQ (r=-0.33, p<0.01; r=-0.24, p=0.04). On the other hand, only trunk muscle mass was associated with fall (r=-0.27, p=0.03). Furthermore, 5-year change in trunk muscle mass was associated with age (r=-0.34, p<0.01). [Conclusion] Age and fall were associated with trunk muscle mass, not appendicular muscle mass. It would be necessary to measure trunk muscle mass like appendicular muscle mass.

W31-2

Validity of HAQ remission as a therapy target for prevention of frailty in rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study was to examine the relationship between HAQ-DI, and frailty, including physical function measurements. [Methods] A prospective cohort study of frailty in RA patients was conducted at Nagoya University (Fairy study). Age, sex, disease duration, disease activity, and medication were collected, and physical function measurements such as walking speed, grip strength, and five times standing and sitting time, as well as physical function (HAQ-DI) and frailty (Fried's criteria) were investigated. The cut-off of physical measurements for HAQ-DI≦0.5 (remission) was calculated by ROC analysis. [Results] 243 patients were analyzed. They were 85.6% female, mean age 64.5 years, disease duration 13.1 years, disease activity (DAS28) 2.53, HAQ remission 77.1%, Physical frailty (Fried's criteria) was 20.0%. Frailty increased with age. physical function measures cut-off for HAQ-DI≦0.5 were: walking speed 1.3 m/s, grip strength 17.2 kg in women and 27 kg in men, and 5 standing 10.8 s. In patients with HAQ remission, physical frailty (Fried's criteria) were 12.6%. [Conclusions] Physical measures cut-off for HAQ remission were also commensurate with frailty criteria. HAQ remission for prevention of frailty is considered to be a reasonable treatment goal.

W31-3

Preoperative physical function (Timed up and go test) for de-frailty in joint surgery of rheumatoid arthritis

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Conflict of interest: Yes

[Objective] The purpose of this study was to verify whether or not RA patients could overcome frailty by joint surgery, to improve QOL, and to determine the preoperative timed up and go test (TUG) for achieving de-frailty. [Methods] The cut-off value of TUG for physical frailty (Fried's criterion) was calculated using ROC analysisfrom the Fairy study, a prospective cohort of RA patients. The cut-off was used in a multicenter cohort study of RA patients who were underwent joint surgery to determine frailty status before and 1 year after surgery, and the change in quality of life (ΔEQ-5D) was compared by UNIANOVA according to the success or failure of patients in escaping from frailty. [Results] 243 patients in the Fairy study, Physical frailty (Fried's criteria) was 20.0%. The TUG cut-off for frailty was 9.7 seconds. In the cohort of 139 patients underwent lower extremity joint surgery, 53.2% were judged to be frail based on preoperative TUG (≧9.7 seconds), and 31.1% improved to a TUG< 9.7 seconds after surgery. ΔEQ-5D was significantly greater in the de-flailty group (0.14 vs. 0.02). The preoperative TUG cut-off for de-frailty was 12.1 seconds. [Conclusions] Appropriately timed RA joint sugery can help patients to escape from frailty and greatly improve their quality of life.

W31-4

Predictors of frailty in patients with rheumatoid arthritis with pre-frailty~T-FLAG study using data from 2020 to 2022~

Yoshifumi Ohashi[1,5], Nobunori Takahashi[2], Yasumori Sobue[3], Mochihito Suzuki[1,4], Ryo Sato[1,2], Masataka Maeda[1], Daisuke Kihira[1], Kenji Kishimoto[1], Kenya Terabe[1], Shuji Asai[1], Toshihisa Kojima[6], Shiro Imagama[1]

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Conflict of interest: None

[Objective] To examine progressive factors of frailty in prefrail rheumatoid arthritis (RA) patients. [Methods] 287 pre-frail RA patients diagnosed by the Japanese Cardiovascular Healthcare study criteria in 2020 were included. Patients who became frailty in 2022 were assigned to the progressive and those who did not were assigned to the non-progressive groups. The adjusted odds ratio was examined by logistic regression analysis after comparing both 2020 data in univariate analysis. Also, patients were classified into the ≦low disease activity (LDA) and ≧moderate disease activity (MDA) groups to examine comorbidities. [Results] The progressive group (n=46) was older (72.1 vs. 64.7 years), had a longer disease duration (15.5 vs. 10.2 years), and had a higher DAS28-ESR) (2.67 vs. 3.08), and lower molecular-targeted drug use (44.3 vs. 24.4%) than the non-progressive group (n=241). The adjusted odds ratio was age 1.05, disease duration 1.05, molecular-targeted drug use 0.35, and DAS28-ESR 1.54. There were more patients with renal failure in the ≦LDA group than in the ≧MDA group (eGFR: 68.7 vs. 59.9 ml/min/1.73^2). [Conclusion] Treatment enhancement was necessary to prevent frailty in prefrail RA patients. Molecular-targeted drugs should also be considered for renal failure patients.

W31-5

Predictors of improvement from pre-frailty to robust in patients with rheumatoid arthritis with pre-frailty~T-FLAG study using data from 2020 to 2022~

Yoshifumi Ohashi[1,4], Nobunori Takahashi[2], Yasumori Sobue[3], Mochihito Suzuki[1,5], Ryo Sato[1], Masataka Maeda[1], Daisuke Kihira[1], Kenji Kishimoto[1], Kenya Terabe[1], Shuji Asai[1], Toshihisa Kojima[6], Shiro Imagama[1]

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Conflict of interest: None

[Objective] To investigate the predictors of improvement to the normal group in pre-frail rheumatoid Arthritis (RA) patients. [Methods] 287 pre-frail RA patients in 2020 were included. Frailty was diagnosed by Japanese Cardiovascular Health Study (J-CHS) criteria. They were divided into the improved group that improved to the normal group and the non-improved group using J-CHS 2022. The odds ratio was obtained by multiple logistic regression analysis after comparing the patient background. Each group's backgrounds in 2020 and 2022 were compared by paired t-test and Mc Nemar's test. [Results] The improved group (n =55) had a shorter disease duration (8.7 vs. 11.7 years) and a lower HAQ-DI (0.2 vs. 0.36) than the non-improved group (n =232). The odds ratio (95% confidence interval) was 0.96 (0.91-1.00) for disease duration. In the improved group, PGA (15.8 vs. 10.7) and NRS (15.1 vs. 11.3) improved, and DAS-ESR (2.68 vs. 2.39) also improved. The non-improved group had decreased renal function (eGFR: 65.9 vs. 63.5 ml/min/1.73^2) and MTX use (59.6 vs. 55.0). HAQ-DI had increase (0.36 vs. 0.42). [Conclusions] The predictive factor was disease duration. Patients with many comorbidities may be expected to improve to the normal group by treatment enhancement with molecular-targeted drugs.

W32-1

The association of between clinical background and patient reported outcome in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] To clarify the association of between clinical background and patient reported outcome (PRO) in rheumatoid arthritis patients with low grade disease activity or remission status. [Methods] We investigated HAQ, SF036, FACIT, RAPID-3 as PRO, age, disease duration, DAS-28 ESR, CDAI, VAS, anti-rheumatic drug as clincal background in rheumatoid arthritis 88 patient in low disease activity or remission for at least 6-month without serious organ failure or mental disorder. [Results] Their mean age was 66.1 year-old, 28 male, 60 female, stage was 1/61, 2/16, 3/7, 4/3, class was 1/69, 2/19, 3,4/0. Their mean disease duration was 7.5 years, mean DAS-28 ESR was 1.84. The association between their age and DAS-28 ESR in their clinical background was observed. Furthermore, role emotional in SF-36 had negative association with disease duration. In addtion, role physical, vitality, and role emotional was better in TNF inhibitor group, and role physical was also better in IL-6 group. Meanwhile, Role physical in SF-36 and MDHAQ was worsen in JAKi group than other groups. [Conclusions] PRO may be different among clinical background, and depend on the kind of antirheumatic drugs, their results should be the clue as to their therapy.

W32-2

Analysis of factors affecting each scale of SF-36 in patients with rheumatoid arthritis - TOMORROW study-

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Conflict of interest: None

[Objective] Treatment outcomes for rheumatoid arthritis (RA) have improved, however affecting factors for QOL are not well known. In this study, we investigated affecting factors for QOL in RA patients using SF-36. [Methods] We analyzed date from the TOMORROW study (UMIN 000003876), which is a 10-years prospective cohort for age and sex matched RA (n=208) and volunteers. We evaluated QOL using SF-36. We compared each factors of SF-36 for RA and Vo, and analyzed factors affecting summary score and each subscale of SF-36 in RA patients. [Results] There were 186 in Vo and 167 in RA. In RA patients, average disease duration was 22.8 year, DAS28-ESR was 3.10. In comparison with Vo, Physical Component Summary (PCS) (Vo 46.9±12.2, RA 34.1±18.0: $p<0.01$) and Mental Componen Summary (MCS) (Vo 52.2±9.5, RA 49.4±9.5: $p<0.01$) were significantly lower in the RA. In multivariate analysis, older age, the number of tender joints, VAS, mHAQ, and the use of anti-TNF inhibitor were significant decreasing factors for PCS, and only VAS was a significant decreasing factor of MCS. In subscales, high ESR values was also a significant decreasing factor in vitality. [Conclusions] In this study, RA was a significant QOL declining factor. High ESR values were associated with patient fatigue in RA patients.

W32-3

Analysis of Centralized pain in rheumatoid arthritis

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Conflict of interest: Yes

[Objective] Centralized pain: CP is a type of chronic pain and fibromyalgia is considered a typical disease. When RA was treated, tender and swelling in the joints improved on physical findings and a decrease in the inflammatory response was observed on examination, but the pain as a subjective symptom did not decrease and there were patients who persisted chronically. [Methods] 200 patients with RA SF-36 as PRO used to measure. Characteristics were analyzed compared to PROs in fibromyalgia patients, We also examined the relationship between CP and the reactivity of therapeutic drugs. [Results] In RA the SF-36 component summary were compared with the standard 50±10 according to the national standard. Physical aspects improved from 31.9±12.7 to 37.2±16.0 after 56 weeks of treat. Role and Social Component improved from 35.5±15.7 to43.7±16.2. Mental Component Summary (MCS) were from 50.4±8.6 to 50.5±8.5 after treatment. MCS was lower than 40 in 8.6%. Physical findings improved and inflammatory response was negative but there was no improvement in subjective symptoms. Decreased MCS cases are similar that of fibromyalgia patterns, and suspected the presence of Centralized Pain. [Conclusions] RA with CP may be clinically difficult to deal with and differential diagnosis is not possible.

W32-4

Real-world effectiveness and safety of tofacitinib and abatacept in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We compared the 52-week effectiveness and safety of tofacitinib (TOF) and abatacept (ABT) in patients with rheumatoid arthritis (RA) in a real-world setting. [Methods] RA patients starting TOF (n=187) and ABT (n=183) were enrolled. The inverse probability of treatment weighting (IPTW) was used to compare the effectiveness of treatments. The influence of HLA-DRB1 shared epitope (SE) alleles on effectiveness was examined. [Results] The TOF group had a significantly higher proportion of Disease Activity Score in 28-joints using erythrocyte sedimentation rate (DAS28-ESR) remission at week 52 than the ABT group. DAS28-ESR on and after week 12 was significantly decreased as the copy number increased in the ABT group, but not in the TOF group. In SE-positive patients, the proportion of remission and drug retention rate did not significantly differ between the two groups. In SE-negative patients, the TOF group showed a significantly higher proportion of remission and drug retention rate than the ABT group. Herpes zoster and some laboratory abnormalities were more frequent in the TOF group than in the ABT group. [Conclusions] The higher proportion of remission at week 52 in the TOF group was presumably due to differences in treatment response in the SE-negative patients.

W32-5

Comparison of treatment response between seropositive and seronegative patients with elderly onset rheumatoid arthritis - a study using the IORRA cohort

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Conflict of interest: None

[Objective] To evaluate the difference in treatment response between seropositive (SPRA) and seronegative (SNRA) patients with elderly onset rheumatoid arthritis (EORA). [Method] The subjects were RA patients who first enrolled in the IORRA from 2009 to 2019, and were over 65-year-old with less than 2-year disease duration. Patients were divided into two groups according to seropositivity: SPRA and SNRA groups. The primary endpoint was proportion of the patients who achieved DAS28-ESR < 2.6 at 3-year. DAS28-ESR, J-HAQ, and medications for 3-year were compared. A logistic regression analysis was conducted to evaluate the association between seropositivity and not-achieving remission. [Result] Among a total of 522 patients, 381 (female 77.7%, DAS28-ESR 3.7 ± 1.2) and 141 (female 66.0%, DAS28-ESR 3.3 ± 1.3) patients were in the SPRA and SNRA groups. The proportion of the patients with DAS28-ESR < 2.6 at 3-year was 44.0% in the SPRA group and 66.9% in the SNRA group ($p<0.01$). DAS28-ESR after 3-year was significantly lower in the SNRA group (2.8 ± 1.0 vs 2.2 ± 0.8, $p<0.01$). Seropositivity was significantly associated with non-achieving remission (odds ratio [95%CI] 2.65 [1.67-4.20], $p<0.01$). [Conclusion] Seropositivity was associated with not-achieving remission at year 3 in EORA.

W32-6

The changes in treatment, outcomes, and unfavorable clinical events in elderly-onset rheumatoid arthritis patients from the IORRA cohort

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Conflict of interest: None

[Objective] To investigate the changes in treatment, outcomes, and unfavorable clinical events in patients with elderly-onset rheumatoid arthritis (EORA). [Methods] The patients with early RA aged 65 years or older in the IORRA cohort were enrolled, and those were classified into Group A (enrollment in 2000-2008) and B (2008-2016). The patients were observed for up to 5 years. The change in disease activity was the primary endpoint, and the hazard ratios of unfavorable clinical events were analyzed. [Results] The number of patients in Group A and B were 423 and 390 patients, respectively. DAS28 was 4.1 in Group A and 3.6 in B ($p<0.01$), and J-HAQ was 0.87 in Group A and 0.76 in B ($p=0.04$). In both groups, DAS28 improved after one year and remained at the same level after two years. J-HAQ also improved after one year in both groups, but Group A showed a worsening trend after year 2. The proportion of MTX users during the observation period was 60% in Group A and 82% in B ($p<0.01$) and steroid users were 65% and 48% ($p<0.01$), respectively. Hazard ratios for clinical events were not different between the two groups.

[Conclusion] Disease control of patients with EORA improved with the progress of RA treatment, but the incidence of clinical events did not change over time.

W33-1

Recovery of muscle strength and function after total knee arthroplasty in rheumatoid patients

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Conflict of interest: Yes

[Objective] Patients suffering rheumatoid arthritis (RA) might lead to inferior recovery after total knee arthroplasty in comparison with osteoarthritis (OA) patients. The objective of this study was to evaluate the muscle strength of knee extension and flexion and function and to compare the muscle strength and function between RA and OA patients. [Methods] In total, 441 knees (73 RA knees and 368 OA knees) were included. Patients underwent total knee arthroplasty between 2012 and 2019 in our hospital. Muscle strength of knee extension and flexion was measured preoperatively and at one year after surgery. One leg standing time, 10 m walking time, and time up-and-go test (TUG) were also measured to evaluate function at the same time. [Results] In RA knees, significantly weak muscle strength of knee extension and flexion and inferior TUG were detected preoperatively. At one year after surgery, muscle strength of knee flexion was greater in RA knees. Other measurements were not significantly different. Concerning the recovery after surgery, improvement of muscle strength of knee extension and flexion and 10 m walking time and TUG was significantly greater in RA knees. [Conclusions] RA patients show greater recovery in muscle strength and knee function after total knee arthroplasty.

W33-2

Evaluation of femoral rotation deformity in rheumatoid arthritis patients with TKA

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Conflict of interest: None

[Background] There are few reports on RA knee femoral rotation. [Purpose] Preoperative CT was used to evaluate femoral rotation deformity in patients who underwent TKA for RA performed at our hospital. [Methods] Subjects underwent primary TKA for RA from March 2015 to December 2021, and femoral rotation could be evaluated by preoperative CT. 56 knees. As image evaluation, HKA were measured by full-length standing frontal Xp of both lower limbs. FRA formed by SEA and posterior condylar line (PCL) was measured as SEA. HKA of +3 degrees or more was classified into the varus knee group, and HKA of -3 degrees or more into the valgus knee group, and we investigated whether there was a difference in FRA. [Results] The average age of the patients was 68.6 years, the average HKA was 4.3°, and the average FRA was 4.0°. 34 knees in the varus knee group and 11 knees in the valgus knee group were found, and the FRA was significantly higher in the valgus knee group. [Discussion] In rheumatoid arthritis patients with valgus knee, it was suggested that bone destruction of the lateral posterior condyle of the femur may lead to high FRA. In rheumatoid arthritis, bone destruction of the lateral condyle and osteophyte formation on the medial side cause various angles of rotation.

W33-3

Changes in knee alignment of rheumatoid arthritis patients who underwent TKA in our hospital

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Conflict of interest: None

[Objective] While TKA in patients with RA (RA-TKA) has been decreased over time, RA-TKA caused by varus knee osteoarthritis (OA) has been increased. In this study, we aimed to investigate the changes in knee alignment of RA patients at our hospital. [Methods] one handred fifty five knees of 113 RA patients who underwent TKA at our hospital from 2004 to 2022 were included. 49 knees from 2004 to 2009 were included in early group (EG), 51 knees from 2010 to 2015 in middle group (MG), and 55 knees from 2016 to 2022 in late group (LG). Preoperative patient background, osteophyte score (OS), Joint space width difference (JSWD), KL grade, and FTA were compared. [Results] Age (EG: 64.3 vs MG: 69.2 vs LG: 70.2) and BIO use (EG: 4.1% vs MG: 49% vs LG: 34.6%) ware significantly lower in EG. OS (EG: 6.9 vs MG: 8.5 vs LG: 7.1) and JSWD (EG: -0.3 vs MG: -2.3 vs LG: -1.7) ware significantly higher in MG and EG, respectively. KL grade (EG: 3.7 vs MG: 3.8 vs LG: 3.5) and FTA (EG: 175.2 vs MG: 179.2 vs LG: 179.1) ware significantly lower in LG and EG, respectively. [Conclusions] Although anti-rheumatic drugs including BIO can suppress joint destruction, OA-like changes (OALC) associated with aging lead to TKA. RA-TKA cases due to OALC, such as osteophyte and decreasing JSWF, has been increasing over time at our hospital.

W33-4

Outcomes of lateral approach TKA for valgus deformity in patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] RA often shows valgus deformity. Medial approach TKA has been often utilized for even valgus deformity, but it is liable to induce the medial knee instability, subsequently early loosening of the implant. In this study, lateral approach TKA for valgus deformity in patients with RA was utilized to avoid damaging the medial component. [Methods] Eleven knees in 10 patients (mean age 61.1 years, mean follow-up 33.1 months) underwent primary TKA through the lateral approach for valgus deformity in patients with RA. ITB dissection and peroneal nerve release were performed if necessary. Radiological and clinical evaluations were performed pre and postoperatively. [Results] The average operating time was 106 minutes. Extension angle was significantly improved from the -15.0 ± 10.2 to -5.5 ± 4.2 degrees (P=0.03). FTA was significanlly corrected from 165.9 ± 4.8 to the post-operative 175.5 ± 1.8 degrees. The Knee Society Score (KSS) were also significantly improved. [Conclusions] As compared with previous reports about the medial approach TKA for the valgus knee, operating time seemed shorter, balancing between medial and lateral soft tissue was easier owing to no destruction of medial supporting components and patient satisfaction was good in the lateral approach.

W33-5

Investigate the osteotomy volume of posterior femoral condyle in TKA by pre-cut method for patients with OA and RA

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Conflict of interest: None

[Objective] The gap between RA knees may be larger than that of OA knees due to ligament laxity caused by preoperative synovitis. We investigated he volume of intraoperative posterior femoral condyle resection in RA knees with those in OA. [Methods] Ninety-eight patients (80 OA and 18 RA) underwent TKA using Kanayama's pre-cut method. After making the extension gap, the posterior femoral condyle was pre-cut by Kanayama's method. The gap was measured by using a tensor which preserved medial gap. After placement of femoral trial, the gap at 10, 30, 45, 60, 90, and 120 degrees of knee flexion was measured. [Results] The extension/flexion gap was 13.6/15.3 mm in the RA group and 13.4/15.2 mm in the OA group. The volume of additional posterior condyle osteotomy after pre-cut was 3.3 mm in the RA group and 3.2 mm in the OA group. There was no statistical difference between the two groups on any of items. There was also no statistical difference in gaps at 10, 30, 45, 60, 90, and 120 degrees of knee flexion after placement of femoral implant. [Conclusions] We investigated the volume of posterior femoral condylar osteotomy in TKA with the pre-cut method for RA and OA. There was no differ-

ence in the amount of posterior condyle osteotomy between the two groups.

W33-6

The effectiveness of cementless total knee arthroplasty in rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study was to evaluate the effectiveness of cementless TKA in RA. [Methods] Patients who underwent TKA from September 2021 through October 2022 in our institution and who had RA were included in the analyses. A total of 12 knees was devided into cementless group (6 knees, L group), and cemented group (6 knees, C group). Preoperative and postoperative (3 months after operation) Knee Society Score (KSS), KOOS, and the JOA score were obtained as patient-based functional evaluations. [Results] There was no significant difference in operative time, intraoperative bleeding, or perioperative complications between two groups. The postoperative HKA angle was 177° in L group, and 180.2° in C group (p=0.093). The delta angle was 83.8° in L group, and 86.5° in C group (p=0.021). The initial gap on X-rays in L group did not change 3 months after operation. All scores significantly improved after operation in both groups. The difference of KSS was 80.3 points in group L and 90 points in group C (p=0.71), that of KOOS was 37.3 points in group L and 27.3 points in group C (p=0.59), and that of JOA score was 23.3 points in group L and 25 points in group C (p=0.94). [Conclusions] Cementless TKA is usefull for rheumatoid arthritis patients in short-term results.

W34-1

Comparative study of clinical result in mobile-bearing total ankle arthroplasty between rheumatoid arthritis and osteoarthritis

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Conflict of interest: None

[Object] Clinical results of mobile-bearing total ankle arthroplasty for rheumatoid arthritis (RA) have been reported. However, no studies have compared osteoarthritis (OA) and RA. We investigated the difference of clinical and radiographic outcomes between OA and RA. [Methods] 22 ankles (RA) and 11 ankles (OA) were followed. The AOFAS score were evaluated as clinical outcomes. Radiographic outcomes were evaluated by the angular position of the implant, radiolucent lines, and migration. [Results] In all 33 ankles, average age, disease duration, and follow-up period were 64.9 years, 8.4 years, and 83.4 months, respectively. There were no significant differences between groups. The final follow-up AOFAS total and pain score of RA were significantly lower than these of OA (total; RA: 78.2 vs OA: 89.4; p =.044, pain; RA: 30.5 vs OA: 37.3; p =.041). There were no significant differences in other clinical and radiographic outcomes. Delayed wound healing occurred in 9.1% in RA and none in OA. Radiolucent lines were observed in 45% of both groups, and implant removal was in 9.1% and 18.2% of OA and RA, respectively. [Conclusions] The final follow-up AOFAS total and pain score were significantly lower in RA. In RA, synovitis and bone erosions in the adjacent joints might have caused pain.

W34-2

Clinical and radiographic evaluation of transfibular approach total ankle arthroplasty followed up for more than 3 years

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Conflict of interest: None

[Objective] It has been more than four years since the Trabecular Metal Ankle (TM ankle) was newly launched in Japan. In our hospital, TM ankle was used for 80 ankles. Prospective observational studies have been conducted since the start of use, and we report the 3-year results. [Methods] Between August 2018 to August 2019, a total of 24 patients with 26 feet (6 ankle osteoarthritis and 20 rheumatoid arthritis) underwent TAA using TM ankle. The JSSF ankle-hindfoot scale was used as an objective clinical evaluation, and the SAFE-Q was used as a subjective clinical evaluation before and 3 years after surgery. Implant placement angle and radiolucent line (RLL) around the prosthesis were examined for radiographic evaluation. Paired-t test was used for statistical analysis (level of significance, $p<0.05$). [Results] The mean age at surgery was 63.8 years, and the mean operative time was 171.2 minutes. The mean JSSF ankle-hindfoot scale also improved significantly ($P<0.05$). All SAFE-Q subscales were significantly improved at 3 years postoperatively (all $P<0.05$). Implant placement angles were good. No RLL was observed. [Conclusions] The 3-year mid-term results were good in objective clinical evaluation, subjective clinical evaluation, and radiographic evaluation.

W34-3

Outcome of joint-preserving surgery for rheumatoid forefoot deformity complicated by severe hallux valgus

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Conflict of interest: None

[Objective] Good results of joint-preserving surgery for rheumatoid arthritis (RA) forefoot deformities have been reported. We report the results of modified Scarf and offset-osteotomy in RA forefoot deformity with severe metatarsophalangeal angle (HV angle) of 40° or more. [Methods] Fifteen patients who underwent surgery between 2018 and 2021 and could be followed up for at least 1 year were included in this study. Radiographic evaluation included the HV angle, M1M2 angle, M1M5 angle, and Hardy classification before surgery and final follow-up. Clinical outcomes were evaluated by the JSSF RA foot and ankle scale and SAFE-Q before surgery and final follow-up. The Wilcoxon test ($P<0.05$) was used for statistical analysis. [Results] The preoperative JSSF scale was 64.7, which significantly improved to 88.6 points at final follow-up. The preoperative HV angle improved significantly from 53.9 degrees to 11.0 degrees, the preoperative M1M2, M1M5 angle improved significantly from 16.7, 35.7 degrees to 7.1, 17.7 degrees. Hardy classification 5 to 7 was 15 preoperatively and 2 at the time of the study. The recurrence of hallux valgus was 13.3%. [Conclusions] The modified Scarf and offset-osteotomy are useful in RA forefoot deformity associated with severe hallux valgus.

W34-4

Joint-preservating operation for rheumatoid patients with forefoot deformities

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Conflict of interest: None

[Objective] Since 2012, we adopted joint-preserving operations for RA forefoot surgery with metatarsophalangeal joint (MTP) reduction by shortening metatarsal bone (MT). We analyzed our results. [Methods] The amount of shortening length of the MT was decided by the length of the proximal phalanx overriding to the MT. The first MT was valgusly osteotomized at the proximal base to run parallel to the 2nd MT. Claw toe deformity with difficult reduction of proximal interphalangeal joint (PIP) was indicated PIP desis. After 3 weeks, fixing pins were removed to start passive ROM exercise. Transverse and longitudinal arch support was inserted to patient's shoes to support plantar arch to complete bone union. To assess foot function, JSSF-RA, SAFE-Q, X-ray film assessment was used. [Results] Eighteen feet of 13 women and three feet of three men were as-

sessed. Average age at the operation was 65 years with 22 years mean disease-period. Mean JSSF-RA score was improved to 75 points from 58 points. Hallux valgus angle was improved to 27 degrees from 46 degrees. Postoperative SAFE-Q was poor in pain score and shoe related score. [Conclusions] Foot function was improved by joint-preserving operation for RA foot, but patient related assessment was not satisfactory.

W34-5

Long term result of toe plasty with silicone implant to rheumatoid arthritis patients

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Conflict of interest: None

[Objective] Forefoot deformities is one of problem for rheumatoid arthritis (RA) patients. Silicone implant arthroplasty of the first MTP joint combined with oblique shortening osteotomy of the MTP joints of the lesser toes was performed in our hospital. We reviewed the long-term results (over 10 years) of this procedure. [Methods] Between 2009 and 2022, this procedure was performed on 14 feet in 10 patients with RA. Follow-up evaluation was available for 10 feet in 7 patients (5 women, 2 man). We reviewed them with medical records and X ray. [Results] Their average age was 69 years, their average follow-up period was 10.1 years. Recurrence of hallux valgus occurred in 5 foots in 3 patients and reoperation were not performed. Recurrence of callus occurred in 6 foots in 5 patients and 2 reoperation were performed. Steinbrocker classifications were class 2 for 4 patients, class 3 for 2 patients and class 1 for 1 patients at operation time. They were class 4 for 4 patients, class 2 for 2 patients and class 1 for 1 patients at final follow-up. [Conclusions] The rate of recurrence of hallux valgus was 50% and which of lesser toes was 60%. The rate of reoperation was 20%. Keeping the joint is mainstream these days so we should rethink surgical indication and operation technique.

W34-6

Long-term postoperative results of Modified scarf Osteotomy for hallux valgus deformity - comparison between RA and non-RA

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Conflict of interest: None

[Objective] For hallux valgus patients, we have been choosing the combined surgery: modified scarf osteotomy for the great toe and metatarsal shortening offset osteotomy for the lesser toes in patients with and without rheumatoid arthritis (RA). The aim of this study was to compare postoperative outcomes in RA and non-RA patients. [Methods] A retrospective observational study of 62 RA and 31 non-RA patients (mean follow-up period: 4.4 years) who underwent the surgery was completed. Radiographic evaluation and patient-standing scoring were evaluated before and after surgery. [Results] The clinical outcomes were all improved significantly with surgical treatment in both RA and non-RA groups. However, JSSF lesser scale was lower in RA group than in non-RA group both preoperatively and postoperatively. Radiographic measurements showed significant improvement in HVA, M1M2A, and M2M5A. Multivariate analysis showed that preoperative M2M5A opening was a risk factor for lesser-toe MTP joint re-dislocation in RA group. [Conclusions] The combined surgery improved radiographic measurements and patient-standing scoring regardless RA or non-RA. We should take care in cases of poor preoperative disease control or spread of M2-M5A, as these may be factors that worsen the postoperative outcome.

W35-1

Development of a Psychological Adaptation Scale for Rheumatoid Arthritis Patients

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Conflict of interest: None

We developed a psychological adaptation scale for rheumatoid arthritis patients, and verified its reliability and validity. Our survey involved 207 RA patients from RA specified five hospitals. 207 patients answered validly after seeing the leaflet handled to them by RA doctor in charge. Assuming five factors in exploratory factor analysis, Confirmatory factor analysis by Structural equation Modeling was then performed. Five factors are Being able to control the symptoms of RA, Having no negative feeling about RA, Having connections with RA patients, Being able to live without worrying RA, and Having I want to be useful to RA patients about own experience. 5-factor 25-item model was certified conformity (CFI=0.923, RAMSEA=0.059). Reliability was confirmed by Cronbach's α coefficient (α=0.906). The reliability and validity of our developed scale was proven.

W35-2

Survey of the Educational Needs of Rheumatoid Arthritis Patients

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Conflict of interest: None

[Objective] In recent years, patient education is becoming important in the treatment of RA, especially for sheared decision making. The purpose of this study was to identify the educational needs of RA patients in Japan and the factors that influence the educational needs. [Methods] A total of 344 patients with RA were included in the study. Patients' educational needs were analyzed using questionnaires covering seven areas: pain, movement, feelings, arthritis, treatments, other treatments, and support. [Results] More than 90% of the patients answered that educational needs related to "arthritis" were the highest, with "Ways my arthritis can be treated" "Ways my arthritis is affecting me" and "What might happen in the future" being particularly important. Females had higher educational needs for "movement". Lower age was associated with higher educational needs for "pain" and "other treatments", while higher VAS was associated with higher educational needs for "pain", "movement", and "feelings". [Conclusions] Efforts to educate and provide individualized care to RA patients in Japan are difficult to implement adequately, due to a shortage of knowledgeable nurses, as well as a shortage of time and places. It is important to accurately grasp the educational needs of RA patients.

W35-3

Online patient education classes for patients with rheumatoid arthritis under and post COVID-19 pandemic

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Conflict of interest: None

[Objectives] We have reported the experience of the online patient education classes for patients with rheumatoid arthritis under COVID-19 pandemic in this study. [Methods] Since June 2020, we switched the monthly patient education classes from face-to-face interaction to on line by using Zoom online meeting system. The topics of the classes included medical therapy, orthopedic surgeries, rehabilitation, infection prevention, nutrition care, oral care, music therapy, round-table talk with medical professionals, and so on. Twenty-seven classes were held and total 291 responses from attendees were collected and analyzed. [Results] Patients attended the classes from the various prefectures; not only from Hyogo, but also Hokkaido, Tokyo, Saitama, Chiba, Nagano, Aichi, Osaka, and Hiroshima. Their ages were from twenties to seventies. The classes were evaluated well by the attendees. Several personal consultations resulted in the referrals to the medical facilities in the other prefectures. [Conclusions] On line patient education classes for the patients with rheumatoid arthritis are practical and effective for the patients care under COVID-19 pandemic, probably after the pandemic, too.

W35-4

Physical Ability and Patient Health Perspectives Related to Falls in Rheumatoid Arthritis Patients

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Conflict of interest: None

[Purpose] Falls in rheumatoid arthritis (RA) affect quality of life (QOL). We conducted a prospective cohort study on frailty in RA patients at Nagoya University (Fairy study) to investigate physical ability and daily life of patients with a history of falls within 1 year. [Methods] Patients with RA were divided into two groups: those who had fallen and those who had not fallen, and the above items were compared. [Results] Patient background: 243 patients, mean age 64.5±10.4 years, BMI 22.8±14.3 kg/m2, D A S-28C R P1.8±0.8, mH A Q0.37±0.51, K C L7.9±.3.4, B D I -II 10.5±8.0, M T X users 78 patients (32%), women 85%, and men 85%. (%), 85% female, 40% B I O and J A K use, 43 (17.6%) had fallen within 1 year, the fall group had higher D A S28C R P (2.1 VS 1.8, $p<0.05$), H A Q (0.5 VS 0.3, $p<0.05$) and in physical ability, 5 sit tests (13.0 V S10 seconds, $p<0.05$), 2-step test (1.12 VS 1.21 m, $p<0.05$), and grip strength (18.1 V 20.9 kg $p<0.05$). There were differences in health views in “I think my own health condition is not good” and “I think my walking speed is getting slower than before”. [Conclusion] The physical characteristics of the rheumatoid arthritis patients who fell and their perceptions of their own health were clarified.

W35-5

JIA Transitional to Preconception Care by Nurses as a Countermeasure for D2T RA

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Conflict of interest: None

[Objective] From the perspective of D2TRA countermeasures, the significance and challenges of preconception (PC) care initiated during the JIA transition by nurses will be discussed. [Methods] The subjects were 624 RA female patients who visited our clinic in September 2022, and their medical history was investigated retrospectively. The WoCBA generation with age of onset between 18 and 45 years was 201/624 (32.2%) patients. 20 WoCBA generation patients were introduced to PC care with the addition of nurses, and 5 patients experienced delivery of 8 healthy children. we present the current status of care and measures regarding the risk of progression to D2TRA. [Results] We experienced a case of RF-positive polyarticular JIA (JIA), in which she was unable to obtain consent for continued biologics after an unexpected pregnancy, following the issue of withdrawal of MR live vaccination leading to relapse of RA disease activity and bone destruction progression due to interruption. Challenges remained in the care of this generation in terms of suppression of D2TRA progression. [Conclusions] The role of nurses in the field is significant in the transition to adulthood with JIA, as there are many sensitive issues for young women.

W35-6

What we have learned after 10 years since the establishment of the Rheumatology Care Study Meeting

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Conflict of interest: None

[Purpose] The Gifu Rheumatology Care Study Meeting was established in 2012. Ten years have passed, and we look back on its activities. [Achievements] Study meetings were held in several districts in the prefecture, and 21 meetings were held over a 10-year period. The meetings consisted of lectures and panel discussions related to rheumatology care. Topics ranged from drug therapy, infection control, psychological support, physical therapy, and medical services such as physical disability and long-term care insurance. The number of participants ranged from 10 to 49, with an average of 26.4. Participants commented that it is good to be able to compare the current situation through information exchange with healthcare professionals from other facilities. [Conclusion] The following issues have been highlighted. Although the goal was to hold the conference throughout the prefecture, the conference has been held mainly in Gifu City due to the availability of venues and transportation convenience. Since the beginning of 2020, the frequency of the event has been drastically reduced due to the difficulty of holding the event in person due to the outbreak of the new coronavirus infection. The number of care nurses in the prefecture has been decreasing.

W36-1

Physical Activity of Rheumatoid Arthritis Patients with Foot Impairment - Comparison with Healthy Individuals Using Propensity Score Matching

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Conflict of interest: None

[Introduction] Sarcopenia in rheumatoid arthritis (RA) is a serious problem even in Japan, where it is reported to be about three times higher than same age group. In this study, we compare physical activity in patients with foot deformity with that of healthy subjects in order to explore methods of therapeutic intervention. [Subjects and Methods] Twenty-three RA patients (all female) with foot deformity and healthy controls were enrolled in the Kyotamba Town Health and Longevity Study. Propensity scores were calculated by using age and body mass index as covariates, and 20 RA patients and 20 healthy subjects were extracted after matching. [Results] The mean SDAI and mean HAQ of RA patients were 8.0 (±8.2) and 0.9 (±0.7), respectively. In terms of physical activity, the mean calorie consumption was 214.2/282.8 kcal/day (RA/healthy subjects) ($p = 0.038$) and mean daily steps were 3939/6852 ($p = 0.002$), which were statistically significant. However, there were no significant differences in sedentary time 729/708 minutes/day, low intensity activity 299.8/349.0 minutes/day, and medium intensity activity 11.8/16.7 minutes/day. [Conclusion] Differences in number of steps and metabolic rate were found, suggesting that disease-related physical disability may occur on a single activity scale.

W36-2

Estimating the effect on skeletal muscle mass of replacing sedentary behavior in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Sedentary behavior (SB) in RA patients decrease skeletal muscle mass. In this study, we investigated the effects on skeletal muscle mass of replacing SB with light-intensity (LPA) or moderate-to-vigorous-intensity physical activity (MVPA) in RA patients. [Methods] Thirty female RA outpatients were included in the study. Physical activity using accelerometer and skeletal muscle mass using a body composition were measured. The changes predicted by replacing 10 minutes per day of SB with LPA or MVPA were analyzed by multiple regression analysis using the Isotemporal Substitution model model (objective variable: skeletal muscle index, explanatory variables: LPA time, MVPA time, and accelerometer wearing time). [Results] The mean age, disease duration, HAQ were 65.4 years, 21.9 years, and 0.9, respectively. The mean skeletal muscle index, SB time, LPA time, MVPA time, and accelerometer wearing time were 5.4 kg/m2, 724 minutes, 299 minutes, 14 minutes, and 1036 minutes, respectively. The estimated change in skeletal muscle mass was 0.02 kg/m^2 when replacing LPA (p=0.04) and 0.26 kg/m^2 when replacing MVPA (p=0.01). [Conclusions] Replacing SB with LPA or MVPA may improve skeletal muscle mass loss in RA patients. The longitudinal studies requires investigation in future studies.

W36-3

Walking habits in elderly rheumatoid arthritis patients can reduce the incidence of new lumbar spine compression fractures after 1 year

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Conflict of interest: None

[Objective] Walking is recommended for elderly rheumatoid arthritis (RA) patients. We reported that walking had a positive effect on spinal longitudinal alignment and disease activity at 1 year. On the other hand, there are no reports on the incidence of new vertebral compression fractures (VF). The purpose of this study was to prospectively evaluate the effect of walking on the incidence of new VF after 1 year in elderly RA patients. [Methods] 87 elderly patients with RA who were able to complete the initial survey, 81 were able to complete the follow-up survey one year later. The walking group was asked to walk twice a week (30 mins or above for each time) for a year. The initial evaluation items were age, sex, weight, BMI, period of illness, drug administration, blood collection, disease activity, thigh bone density, and functional impairment index. VF was investigated at the initial evaluation and 1 year later. [Results] The number of walking group contained 40 subjects (49.4%). The incidence of new VF cases at one year was 7.5% in the walking group and 24.3% in the non-walking group, indicating a significantly lower incidence in the walking group. [Conclusions] Walking habit in elderly RA patients can reduce the incidence of new VF at 1 year.

W36-4

Long-term outcomes of hip prosthesis with acetabular reconstruction using Graft Augmentation Prosthesis II acetabular shell

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Conflict of interest: None

[Objective] The long-term results of hip arthroplasty (THA) with acetabular reconstruction using the Graft Augmentation Prosthesis (GAP) II shell were investigated. [Methods] Between 2002 and 2011, 22 hips in 19 patients were retrospectively evaluated for pathophysiology, surgical outcomes, complications, and radiographic findings. Long-term outcomes were calculated using Kaplan-Meier curves. Risk factors for revision were also analyzed using Cox regression analysis. [Results] Age at surgery was 60.5 years. The pathology included 9 OA, 5 RA, 5 osteonecrosis, and 3 rapid fracture hip arthroplasty. The degree of labral defect was AAOS classification type III in all cases. Excluding revisions, the observation period was 145.8 months (55-204 months). Revisions occurred in 6 patients with 6 hips (27.3%: 4 loose, 2 infected) at an average of 74.7 months (6-125 months) postoperatively. The calculated implant survival rate was 70.6% at 15 years. Risk factors for revision included granular bone graft (vs. block bone graft: hazard ratio 8.524, $p < 0.005$). [Conclusions] The long-term outcome of THA with acetabular reconstruction using bone grafting with GAPII shells was about 70%. It was suggested that the shape of the grafted bone influenced the results.

W36-5

Trial of ROM exercise from early phase after total ankle arthroplasty

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Conflict of interest: None

[Objective] Range of motion (ROM) and gait training after artificial ankle arthroplasty (TAA) should be started after the wound heals. In recent years, we have performed TAA with a modified anterior-lateral approach, which has shortened and stabilized wound healing (Foot Ankle Orthop. 2021). Therefore, we decided to start range of motion and gait training early after surgery, and confirmed its safety. [Methods] Four patients underwent TAA using a modified anterior-lateral approach. Passive ROM exercise was started on the 3rd day after the surgery, and full-weight walking was started on the 14th day. [Results] In 4 cases, no exudate was observed at the wound site after ROM training was started, and suture removal was completed in an average of 13.5 days after surgery. No wound opening after suture removal was observed. One month after surgery, the range of motion was 17.5±2.5 degrees for dorsiflexion and 38.8±5.5 degrees for plantar flexion. The JSSF ankle/hindfoot scale improved from 33.3±19.3 points before surgery to 89.8±2.8 points after surgery. [Conclusions] Currently, ROM training starting 3 days after TAA with a modified anterior-lateral approach is safe and does not interfere with wound healing. A dramatic advance in post-TAA rehabilitation treatment was expected.

W36-6

Three cases of reversed shoulder arthroplasty using allograft or wedge-shaped baseplate for glenoid bone defects due to rheumatoid arthritis

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Conflict of interest: None

[Objective] When undergoing reversed shoulder arthroplasty (RSA), particularly for small Japanese women with rheumatoid arthritis (RA), severe glenoid defects make it difficult to place a base plate. [Methods] Three patients who underwent RSA using allograft or wedge-shaped base plate for severe glenoid defects were included in the study. All patients were female and the mean age was 79.7 years old. A 3D model of the scapular was created in using a 3D printer from preoperative CT data, and simulated surgery was performed using surgical instruments. RSA was performed after determining whether to use allograft or wedge-shaped baseplate. [Results] The mean follow-up was 28.7 months, and none of the

patients had any postoperative complications, including implant dislocation. The mean range of motion improved from 70° preoperatively to 120° postoperatively in flexion, and the JOA score improved from 48.3 points preoperatively to 75.7 points postoperatively. [Conclusions] RA patients have severe glenoid defects and the humeral head is also deformed, making autograft difficult. Preoperative 3D models were created and simulated surgeries were performed to provide reference for intraoperative procedure and appropriate bone grafting and implant selection.

W37-1

Safety and Efficacy of Upadacitinib (UPA) in Japanese Patients with Rheumatoid Arthritis (RA) and Inadequate Response to Conventional Synthetic DMARDs: Results Through 5 Years from the SELECT-SUNRISE Study

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Conflict of interest: Yes

[Objective] To evaluate the efficacy and safety of UPA in Japanese RA patients (pts) up to 5 yrs in a long term extension (LTE) of SELECT-SUNRISE. [Methods] Pts who completed the wk12 double-blind period proceeded to a blinded LTE to continue UPA 7.5 mg, 15 mg or 30 mg QD while pts randomized to placebo were switched to 7.5 mg, 15 mg or 30 mg QD. UPA 30 mg QD were switched to 15 mg QD prior to marketing approval. [Results] Of the 197 pts, 187 (95%) completed wk12 and entered LTE. During the LTE, 66 (33.5%) pts discontinued study drug: due to adverse events (AEs, 21.3%), withdrawal of consent (6.1%), loss to follow-up (0.5%), lack of efficacy (0.5%), COVID-19 infection or logistic restrictions (0.5% respectively) or other reasons (4.1%). Clinical outcomes improved and maintained thru wk260 as demonstrated by 57%, 45% and 56% achieving CDAI remission with UPA7.5, 15 and 30 mg (AO). The incidences rate of serious AEs (n/100 PYS) in UPA 7.5 mg, 15 mg and 30 mg were 7.8, 14.0 and 14.2 and serious infections for 3.5, 4.9, 8.8; HZ for 5.9, 9.8, 11.8; MACE for 0.8, 0.4, 0.5; VTE for 0, 0, 0.5; malignancy for 0.4, 1.2, 0.5. [Conclusions] Efficacy of UPA was maintained thru 5 yrs. The safety profile was consistent with earlier time points and with an integrated phase3 safety analysis of UPA in RA.

W37-2

Real world data of Efficacy and Safety of Upadacitinib in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Purpose: Upadacitinib (UPA) is the fourth JAK inhibitor approved in Japan for rheumatoid arthritis (RA) in September 2017. We need data on the safety and efficacy of UPA in real clinical practice. We report here on the efficacy and safety of UPA of 44 post-marketing cases. **Method:** We evaluated safety and efficacy up to 6 months after the start of UPA. We evaluated efficacy by DAS28-ESR, DAS28-CRP, SDAI, and CDAI at 1, 2, 3, and 6 months after the start of UPA, and the incidence of adverse events evaluated as safety from 44 patients (mean age 66.5 y.o., 29 patients female, 12.5 years duration). **Result:** Continuation rate at six months was 70%. MTX was co-administrated in 17 patients and 34 had been experienced with bio/ts DMARDs. The efficacy was already found at 1 month. Eight of 44 patients experienced with adverse events (two early gastric cancer, two herpes zoster, one liver function abnormality, one lung field shadow, one cellulitis, and one Pseudomonas aeruginosa bacteremia/pneumonia). There was no difference in efficacy between patients co-administrated with and without MTX. **Conclusion:** UPA significantly reduced disease activity as early as 1 month after initiation, suggesting that UPA may be effective for patients who wish to obtain early efficacy.

W37-3

The status and effectiveness of upadacitinib for patients with rheumatoid arthritis in Tsurumai Biological Communication Registry

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Conflict of interest: None

Objective: This study aimed to investigate the status and effectiveness of the treatment of updacitinib (UPA) for patients with rheumatoid arthritis. Methods: 64 RA patients who were treated with UPA were included. We investigated the status of UPA treatment for patients in TBCR. The change of SDAI, rate of discontinuation of UPA, and incident rate of herpes zoster infection were investigated. The overall patients' mean age was 68.8±11.9 years, 83% were female, the mean disease duration was 12.3±11.8 years, the mean Rheumatic Disease Comorbidity Index (RDCI) was 1.4±1.5, concomitant MTX/glucocorticoid were 58%/48%. The rate of previous treatment of bDMARDs was 83%. The change of SDAI was from 22.0±13.5 at baseline to 10.0±10.8 after 4 weeks and 4.4±5.2 after 24 weeks. The rate of remission was 61.5% at 24 weeks. There were no significant variables in baseline characteristics that are associated with the achievement of remission. Four patients discontinued treatment of UPA. The incident rate of herpes zoster was 3.36 (100 patients-year). Conclusion: The mean age of patients who were treated by UPA was higher, the concomitant of MTX was lower, and previous treatment of bDMARDs or JAK inhibitor was higher. UPA btreatment reduced SDAI titer and induced 61.5% of patients for remission.

W37-4

The effectiveness of concomitant methotrexate in upadacitinib treatment for rheumatoid arthritis patients

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Conflict of interest: None

Object: This study aimed to investigate the effectiveness of concomitant methotrexate (MTX) in upadacitinib (UPA) treatment for rheumatoid arthritis (RA). Methods: A total of 64 RA patients were divided into non-concomitant MTX group (N group) and concomitant MTX group (M group). We investigated the change of SDAI and the rate of discontinuation. Results: 31 were in N group and 33 were in M group. Patients in N group were a significantly higher proportion of previous bDMARDs/JAK inhibitor treatment (N: 97%, M: 70%) and comorbidities include lung disease (N: 39%, M: 15%) and diabetes mellitus (N: 29%, M: 6%). Although there were not significant differences, the mean age was higher in N group than in M group (N: 71.5±10.8, M: 66.2±12.4). Mean SDAI significantly decreased in both groups (N: 22.7±13.6 to 4.4±4.1, M: 21.4±13.5 to 4.4 ±6.5). The patients who were discounted were one patient in N group and three patients in M group while there were no significant differences between the two groups by Cox Hazard models analysis. The patients with herpes zoster were two only in N group. Conclusion: There were no significant differences in the effectiveness of UPA between the concomitant MTX or not. These results suggested that UPA will be a useful treatment for RA patients who are intolerant to MTX.

W37-5

Efficacy and safety evaluation of JAK1 selective inhibitor upadacitinib long-term administration

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Conflict of interest: Yes

[Objective] We evaluated the efficacy and safety of the JAK1 selective inhibitor upadacitinib. [Methods] 104 patients started treatment with upadacitinib. Disease activity evaluation was evaluated by CDAI. [Results] In 104 patients the average treatment weeks was 48.5 weeks. Treatment continuation rate was 92.9% at 12 weeks and 75.9% at 26 weeks, and there was no significant difference between the phase II initiation group and the phase III initiation group (Log-rank p=0.3813). CDAI improvement rate was 73.0% at 12 weeks and 77.1% at 26 weeks. There was no significant difference in CDAI improvement rates between Phase II and Phase III initiation groups at 12 and 26 weeks (Wilcoxon p=0.5265, p=0.4433, respectively). There was no significant difference in the CDAI improvement rate among preadministered TNF inhibitors, non-TNF inhibitors, JAK inhibitors, and the number of b/tsDMARD in the Phase III initiation group (both nonparametric multiple comparisons, p>0.05). None of the 4 patientswho discontinued due to side effects had MACE or malignancy. There were no major adverse events influenced by more than one CV risk. Herpes zoster (11 cases) and herpes simplex (7 cases) were relatively common. [Conclusions] Upadacitinib shows early and sustained efficacy regardless of treatment phase.

W37-6

A clinical study of the efficacy and safety of upadacitinib for 2 years in 22 patients with D2TRA in our clinic

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Conflict of interest: None

[Objective] To verify the efficacy and safety of upadacitinib for 2 years in patients with D2TRA. [Method] 22 patients with D2TRA from April to October 2020 (average below) Age: 69.8 Years: male to female ratio: 2:20 Years of disease: 6.83 years Disease stage: Stage 2.64 Class 1.83 RF208.2 ACPA295.1 MMP362.4 CRP3.96 MTX11/22 cases (average 6.8 mg/w) PSL6/22 cases (average 2.41 mg/day) Bio JAK use 4.6 drugs (1-9 drugs + Lcap) DAS28-CRP5.71 e-GFR 65.6 mL J- HAQ1.48 Administer UPA 15 mg to these patients DAS J-HAQ MMP3 US-GS score PD score improvement will be evaluated from 12 weeks to 96 weeks. [Results] DAS52w 1.84 (P<0.001) Significantly improved at 96 w1.94 (P<0.001). The average MMP3 level 96 w was 38.8 ng/mL (P<0.005), showing a significant decrease. US showed significant improvement at 96w GS1.41 (P<0.04) PD0.36 (P<0.003). At 96 w after administration, DAS28 was 3.2 or less in 16 cases and 2.6 or less in 14 cases. VZV was 2 cases, Of the 6 cases in which administration was discontinued, 2 cases had an insufficient effect, 2 cases had blood disorders, and 1 case each had vasculitis and NTM disease. [Discussion] Significant improvement in D2TRA pathology was observed at 96 w, and DAS3.2 or less was 73%, and DAS 2.6 or less was 64%, achieving a high remission rate.

W38-1

Genetically confirmed VEXAS syndrome with relapsing polychondritis in a patient with poor vacuoles in cells of bone marrow aspiration: a case report

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Conflict of interest: None

An 80-year-old man visited his previous doctor at the dermatology department due to swelling, heat, and pain in the left ear. He was treated with antimicrobial agents; however, he still had erythematous infiltration, severe pain, general malaise, and weight loss. He was then referred to our department. In addition to polyarthritis, recurrent polychondritis was suspected based on the findings of redness and swelling of both the auricular surfaces and episcleritis. VEXAS syndrome was suspected due to cytopenia, and a skin biopsy specimen indicated neutrophilic infiltration. Mean corpuscular volume (MCV) was normal. Bone marrow aspiration was performed; however, the findings were insignificant, although a few granulocytes and erythroblasts showed vacuolated images. Treatment with glucocorticoids improved the skin rash and arthralgia and decreased the CRP level. Genetic testing of the UBA1 gene revealed a somatic UBA1 variant (c. 121A>C: p. Met41Leu), and a diagnosis of VEXAS syndrome was confirmed. The patient responded well to azathioprine (50 mg) combined with prednisolone (10 mg). Herein, we report the case of genetically confirmed VEXAS syndrome with relapsing polychondritis in a patient with poor vacuoles in the cells of bone marrow aspiration and normal MCV.

W38-2

Two cases of VEXAS syndrome

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Conflict of interest: None

VEXAS syndrome is an acquired autoinflammatory disease. There is a somatic mutation in the *UBA1* gene on the X chromosome. [Case] Case 1: A 61-year-old male. He has fever and skin eruption. And he wad diagonosed with Sweet's disease. After steroid pulse, treatment with prednisolone (PSL) and colchicine was started. After treatment with azacitidine, PSL was gradually decreased. After the operation, fever and skin eruption developed. He was diagnosed with recurrence of Sweet's disease, and the dose of PSL was increased. Cyclosporine and tocilizumab were administered, but the condition recurred. A somatic mutation (c. 122T>C: p. Met41Thr) of the *UBA1* gene was found. Case 2: A 72-year-old male.

He had fever and cough. Chest CT showed peribronchovascular interstitium, thickening of the interlobular septum, and patchy opacities. He was diagnosed as organizing pneumonia, and PSL was started after steroid pulse. Endoxan, azathioprine, and tacrolimus were administered. He was diagnosed as MDS. Azacitidine was started. A somatic mutation (c. 121A>G: p. Met41Val) of the UBA1 gene was found. [Discussion] VEXAS syndrome should be differentiated in elderly men with recurrent fever and MDS, as well as skin lesions or organizing pneumonia.

W38-3

A case report of hip joint destruction caused by pustulotic arthro-osteitis treated with total hip arthroplasty

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Conflict of interest: None

[Case] We describe the case of a 61-year-old woman who felt pain with her right hip 30 years ago and then got pustular rashes on both palms and soles. She was admitted to a dermatology clinic and was diagnosed with palmoplantar pustulosis. C-reactive protein (CRP) was 1.13 mg/L. Rheumatoid factor and anticyclic citrulline peptide were within normal ranges. Hip x-ray showed severe joint degeneration, so we diagnosed her with pustulotic arthro-osteitis (PAO). Guselkumab removed pustular rashes and pain of another joint arthritis, but hip pain was not gone. Then we approached this case with total hip arthroplasty (THA), as a result, her hip pain passed away. [Clinical Significance] We considered this report was incredibly valuable because hip arthritis of PAO was rare and we found only a few report that described THA as a treatment for severe hip joint destruction by PAO. Severe hip joint destruction by PAO should be considered to approach THA for an ADL improvement of PAO patiants if any medication cannot remove hip pain.

W38-4

A case of HDR syndrome complicated with pustular psoriasis and psoriatic arthritis successfully treated with biologics

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Conflict of interest: None

HDR (hypoparathyroidism, deafness and renal dysplasia) syndrome is a syndrome characterized by hypoparathyroidism, sensorineural hearing loss and renal dysplasia. This syndrome is caused by mutation of GATA-3. We describe a case of HDR syndrome complicated with pustular psoriasis and psoriatic arthritis successfully treated with biologics. [Case] A female patient in her twenties had childhood onset hearing loss and psoriasis which was treated with topical ointment and phototherapy. At the initial evaluation, she was noticed to have hypoparathyroidism and renal dysplasia. Aggravation of her psoriasis was also noted. Genetic test revealed a heterozygous missense mutation of c. 1186G>A (p. Ala396Thr) in exon 6 of the GATA3, which were a novel mutation of HDR syndrome. Remission of skin lesions were obtained with an IL-17 inhibitor and alteration of an IL-17 inhibitor to a TNF-inhibitor brought remission in her joint symptoms. [Clinical Significance] GATA-3 is important not only in the organ formation but also in the Th2 induction of T cells. Reduced expression of GATA-3 in the psoriatic skin is also reported. This case is important to further understanding of GATA-3 in the pathological mechanism of psoriasis.

W38-5

Bimekizumab (BKZ) in bDMARD-Naïve Patients (pts) with Psoriatic Arthritis (PsA) and Skin Involvement: Analysis of Radiographic Progression at Week (Wk) 16 of BE OPTIMAL, a Phase 3, Multicenter, Randomized, Placebo (PBO)-Controlled, Active Reference Study

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Conflict of interest: Yes

Objective: To assess radiographic progression with BKZ in PsA pts from BE OPTIMAL Methods: BE OPTIMAL was 16 weeks (wks) double-blind, PBO-controlled; 36 wks treatment-blind. Pts randomized 3:2:1 BKZ 160 mg every 4 wks (Q4W): PBO: adalimumab (ADA) 40 mg Q2W. Wk16 radiographic progression (vdHmTSS) reported by baseline (BL) psoriasis (radiographic set: ≧1 study drug dose received; valid hands, feet radiographs at screening). Results: Radiographic set: 824/852 (96.7%) pts (PBO/BKZ/ADA: 269/420/135), 409/824 (49.6%) BL BSA≧3% (50.2%/50.0%/47.4%). Mean (SE) vdHmTSS CfB, overall: 0.31 (0.09)/0.01 (0.04)/-0.03 (0.07); BSA<3%: 0.18 (0.08)/0.01 (0.05)/-0.01 (0.09); BSA ≧3%: 0.45 (0.15)/0.01 (0.06)/-0.06 (0.11). Pts with no radiographic progression (vdHmTSS CfB≦0.5), overall: 78.8%/85.7%//8.5%; BSA<3%: 82.8%/88.1%/81.7%; BSA≧3%: 74.8%/83.3%/75.0%. Similar outcomes observed in BSA≧3-10% and >10%. Mean (SE) vdH erosion, joint narrowing sub-score CfB, overall: 0.28 (0.08)/0.01 (0.03)/-0.02 (0.05), 0.06 (0.03)/0.01 (0.02)/-0.04 (0.06); BSA<3%: 0.14 (0.07)/-0.01 (0.03)/-0.02 (0.07), 0.04 (0.03)/0.03 (0.03)/0.02 (0.05); BSA≧3%: 0.43 (0.14)/0.03 (0.04)/-0.02 (0.08), 0.08 (0.06)/-0.02 (0.03)/-0.09 (0.12). Conclusions: BKZ demonstrated inhibition of radiographic progression as early as Wk16 in bDMARD-naïve, PsA pts with psoriasis skin symptoms.

W38-6

Bimekizumab (BKZ) Treatment in bDMARD-Naïve Patients (pts) with Active Psoriatic Arthritis (PsA): 52-Week (Wk) Efficacy and Safety Results from BE OPTIMAL, a Phase 3, Randomized, Placebo (PBO)-Controlled, Active Reference Study

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Conflict of interest: Yes

Objective: To report Wk52 BKZ efficacy, safety in PsA patients from

BE OPTIMAL Methods: BE OPTIMAL (NCT03895203) was 16 wks double-blind, PBO-controlled; 36 wks treatment-blind. Biologic DMARD-naïve pts were randomized 3:2:1 BKZ 160 mg every 4 wks (Q4W): PBO: adalimumab (ADA) 40 mg Q2W. PBO pts received BKZ 160 mg Q4W (PBO/BKZ) from Wk16. Results: 821/852 (96.4%) pts completed Wk16; 761 (89.3%) Wk52. At Wk52, PBO/BKZ, BKZ, ADA pts with ACR50: 53.0%, 54.5%, 50.0%; PASI100 (for pts with baseline [BL] psoriasis, BSA≧3%): 65.0%, 60.8%, 48.5%; minimal disease activity: 53.7%, 55.0%, 52.9%; DAPSA≦14; low disease activity/remission: 55.2%, 57.1%, 52.9%. Clinical joint, skin efficacy responses sustained in BKZ pts (Wk16-52). At Wk52, no radiographic progression (vdHmTSS CfB≦0.5): 87.3% PBO/BKZ, 89.3% BKZ, 94.1% ADA (radiographic set; observed case). To Wk52, BKZ/ADA pts with ≧1 TEAE: 79.1%/80.7%; most common TEAE: nasopharyngitis (12.0%/8.6%). Discontinuation due to TEAE: 21 (3.0%)/7 (5.0%). *Candida* infections (high level term): 7.7%/0.7%; all mild/moderate, none systemic. 1 oral candidiasis led to discontinuation. Conclusions: Clinically meaningful improvements in efficacy outcomes with BKZ at Wk16 in bDMARD-naïve, active PsA pts sustained to Wk52. BKZ well tolerated; no new safety signals observed.

W39-1

Clinical and renal pathological features predicting complete clinical response in crescentic lupus nephritis

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Conflict of interest: None

[Objective] To determine the clinical and pathological features predicting complete clinical response (CCR) after induction therapy in crescentic lupus nephritis (LN). [Methods] Patients with biopsy proven class III or IV LN from 2008 to 2017 were divided into two groups according to the presence of cellular crescentic lesions. Cumulative CCR rates were compared between the two groups, and independent factors associated with CCR were investigated. [Results] Among 73 patients included, 30 had crescentic lupus nephritis (CLN) and 43 did not. There was no significant difference in cumulative CCR rate between patients with and without CLN (83% vs 84%, p=0.96). Multivariable analysis revealed that interstitial fibrosis was associated with CCR in both CLN and non-CLN patients (OR: 0.01, p<0.01; OR: 0.08, p=0.04, respectively). We next divided CLN patients into two groups according to the interstitial fibrosis less than 25% or not, and found significantly higher cumulative CCR rate in patients with interstitial fibrosis less than 25% (p<0.01). [Conclusions] Interstitial fibrotic lesions predict CCR after induction therapy in crescentic LN.

W39-2

A prompt initiation of re-induction therapy may be important for flared patients with lupus nephritis class III or IV

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Conflict of interest: None

[Objective] To investigate the prognostic factors in patients with lupus nephritis (LN) class III or IV who flared after maintenance therapy. [Methods] We examined patients with biopsy proven LN class III or IV and were observed more than 5-years from 2008 to 2017. Cumulative renal remission rate was compared between newly diagnosed and flared patients. We investigated the prognostic factors for re-induction failure in flared patients. [Results] We enrolled 80 patients (42 in newly diagnosed and 38 in flared) and a significantly lower cumulative renal remission rate was observed in flared patients than newly diagnosed patients (p=0.03). In patients who flared, re-induction failure was observed in 10 patients (26.3%) and they had a longer duration of LN (p=0.02), eGFR (p=0.07), and a longer duration of persistent proteinuria after flare (p<0.001). Multivariate analysis revealed more than 3-months of the duration of persistent proteinuria after flare was associated with re-induction failure (OR: 1.56, p<0.001) and the duration was positively correlated with chronicity index in renal pathology (r=0.53, p<0.001). [Conclusions] A prompt initiation of re-induction therapy may be important for flared patients with LN class III or IV.

W39-3

Early clinical response to induction therapy predicts remission achievement in lupus nephritis class III/IV

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Conflict of interest: None

[Objective] To identify the prognostic factors associated with remission achievement at one year after induction therapy in lupus nephritis (LN) class III/IV. [Methods] We reviewed consecutive patients with biopsy proven LN class III/IV from 2008 to 2017. We divided patients into two groups according to remission achievement at one year after induction therapy and compared clinical characteristics. Remission was defined complete clinical response (CCR, UPCR<0.7 g/gCr) according to 2019 EULAR/ERA-EDTA recommendations. [Results] 44 patients who had detailed data after treatment were included in the analysis. At one year, 34 patients (77.2%) achieved CCR. At baseline, patients with CCR tended to show a lower serum creatinine level (p=0.08) and a lower UPCR (p=0.05). After induction therapy, patients with CCR showed a greater reduction of UPCR at 6 months. The cut-off value of UPCR reduction rate at 6 months for CCR at 1 year was 50.7% (AUC 0.79, p=0.04) and its achievement was independently associated with CCR at 1 year (odds ratio 28.3, p<0.01). Patients with UPCR -50.7% at 6 months also showed a significant reduction in UPCR at 3 months (p<0.01). [Conclusions] 50% reduction of UPCR at 6 months after induction therapy can predict remission achievement at one year in patients with LN.

W39-4

Low intensity of C1q deposition with renal immunofluorescence predicts poor renal prognosis in class III/IV/V lupus nephritis

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Conflict of interest: None

[Objective] To elucidate renal histological findings associated with deterioration of renal function in lupus nephritis (LN). [Methods] Patients with biopsy-proven LN class III/IV/V from 2008 to 2017 were included and classified into two groups: patients with deterioration of renal function which was defined as more than 30% decline in eGFR from baseline and those without. Renal histological findings and clinical characteristics at the time of LN diagnosis were compared. [Results] Sixty-nine patients (class III/IV 34; class III/IV+V 21; class V 14) were include in the analysis. Renal function was deteriorated in 12 patient (17.4%). Intensity of C1q deposition in renal immunofluorescence (IF) was significantly lower in patients with deterioration of renal function than those without (1+ vs 2+, p=0.029). We compared clinical characteristics between patients with and without low intensity of C1q deposition (<2+ staining). Patients with low intensity of C1q deposition had a lower positivity of serum anti-dsDNA antibody (75 vs 96%, p=0.04), a lower serum C3 levels (54 vs 40 mg/dl, p=0.03), and a higher cumulative deterioration rate of renal function (p=0.002). [Conclusions] A low intensity of C1q deposition in renal immunofluorescence predicts poor renal prognosis in LN class III/IV/V.

W39-5

Development of a quality indicator set related to pregnancy and delivery for systemic lupus erythematosus in Japan

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Conflict of interest: None

[Objects] The aim of this study was to develop a quality indicator (QI) set related to pregnancy and delivery systematically for Japanese SLE patients. [Methods] We used a validated process that combined available scientific evidence and expert consensus to develop a QI set related to pregnancy and delivery for SLE. First, we performed a literature review to retrieve all clinical practice guidelines (CPGs) and QI development studies. Second, we extracted the candidate QI items related to pregnancy, delivery, and breast-feeding. Third, we used a modification of the RAND/ UCLA Appropriateness Method. [Results] We found 7525 articles through the initial search. Finally, 32 literatures were identified. We selected the remaining 41 indicators as the final QI set through the RAND/UCLA Appropriateness Method. The areas covered included pregnancy planning, testing, and treatment.

W39-6

Pregnancy outcomes in patients with systemic lupus erythematosus with or without taking immunosuppressant agents

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Conflict of interest: None

[Objectives] Pregnancy in women with systemic lupus erythematosus (SLE) show worse pregnancy outcome and more complication than the general population. This study examined maternal and fetal outcomes among SLE women with or without taking immunosuppressant agents (IS). [Methods] We retrospectively analyzed 29 pregnancies in 21 women previously diagnosed with SLE who gave birth at our hospital from April 2004 to July 2022. [Results] The median age at SLE diagnosis was 22 years, conception was 30 years, dose of prednisolone was 5 mg/day, SLEDAI-2K was 2, and antiphospholipid syndrome complicated with 13.8%. Lupus flare, preterm delivery, and low birth weight were observed 3.4%, 10.3%, and 27.6%, respectively. Hypertensive disorders of pregnancy, preeclampsia, and threatened premature delivery were observed 17.3%, 3.4%, 3.4%, respectively. IS was administered 34.5% of pregnancies. No significant differences were observed between with or without taking IS in rate of pregnancy complication, fetal complication, lupus flare, preterm delivery, and APGAR score. Low birth weight was tended to more frequency in IS taking group, but not significancy (50% vs. 15.8%, p=0.007). [Conclusions] This study indicated that administration of IS did not affect maternal and fetal outcomes.

W40-1

Efficacy and safety of belimumab treatment for systemic lupus erythematosus in our department

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Conflict of interest: Yes

[Objective] To investigate the efficacy and safety of belimumab (BLM) for systemic lupus erythematosus (SLE). [Methods] From February 2018 to March 2021, 34 SLE patients (1 male and 33 females) who started BLM at our department were retrospectively examined. [Results] The mean age was 35.0±10.7 years, and the reason for starting treatment was to reduce PSL in 16, exacerbation of skin rash in 9, exacerbation of arthritis in 5, and others in 3. Hydroxychloroquine was used in 24, mycophenolate mofetil (MMF) and tacrolimus (TAC) in 16, azathioprine (AZA) and TAC in 3, TAC in 5, MMF in 3, and AZA in 1. Disease progression occurred in 5, including worsening renal function, nephrotic syndrome flare-up, Libman-Sacks endocarditis, and skin rash exacerbation in 2. 3 patients discontinued BLM, and 1 patient relocated before 52 weeks; 90.1% (30/33) patients continued at 52 weeks. PSL dose and CH50 were improved from baseline to 52 weeks: a mean PSL dose (13.7±6.2 mg/day vs. 8.9±6.6 mg/day, $p<0.01$) and a mean CH50 (29.3±10.7 U/mL vs 36.2±12.5 U/mL, $p<0.01$). Adverse events were herpes zoster in 2, gastroenteritis in 2, cellulitis in 1, worsening perianal abscess in 1, cystitis in 1, and common cold in 7. [Conclusions] BLM effectively reduced PSL dose and SLE activity without severe adverse effects.

W40-2

Positioning of Belimumab in treatments of SLE in our clinical practice

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Conflict of interest: None

[Objective] We aimed to summarize and analyze the positioning of Belimumab in treatments of SLE patients. [Methods] We investigated the patients backgrounds at administration and clinical courses throughout the observation period of 95 SLE patients treated with belimumab from February 2018 to September 2022 in our institution. [Results] At baseline, median age was 42 (18-75) years, median disease duration 10 years, cSLEDAI≧4 were 22.8%, low complement were 48.9%, positive anti-ds-DNA antibody were 28% and approximately 90% were in maintenance therapy. Serum C3 and anti-ds-DNA antibody were significantly improved in administered at the maintenance phase. The trend of increasing serum C3 was not significantly different after 12 weeks. Some cases, anti-ds-DNA antibody were began to be decreased after 52 weeks. The LLDAS achievement rate increased from 21.5% to 39.2% after 52 weeks. The mean PSL dose were decreased 12.2 mg/day to 5.9 mg/day after 156 weeks. In 7 of 8 patients with active lupus nephritis, urinary protein was reduced or in remission after 52 weeks, regardless of the negative serum immunologic activity at administration. The retention rate was 85.7% (52 weeks), 75.4% (156 weeks). [Conclusions] Belimumab could improve serum immunologic activity and reduce dose of PSL.

W40-3

Effect of belimumab on clinical profiles and daily living score in patients with systemic lupus erythematosus (SLE) -activities of daily living score-

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Conflict of interest: None

[Objective] We have examined the effect of belimumab in patients with SLE. [Methods] We selected 36 cases (F/M 30/6) from 2018 to 2022 in patients with SLE treated with belimumab (BE) to clarify the effect of BE on immunological data, disease activities (SLEDAI), activities of daily living score (AS) (Lupus 26: 849, 2017), and dose of PSL after treatment for 6 months (M), 12 M and 24 M. [Results] Mean BMI and duration of disease were 20.5±3.7 kg/m2 and 15.7±13.8 years. Two cases could not continue due to arthralgia and loss of hair within 24 M. After treatment with BE for 6 M and 12 M, anti-dsDNA antibodies (AU/ml) were significantly decreased for 12 M and 24 M, respectively ($p<0.05$) and C3, C4 and CH50 (U/ml) were significantly increased for 6 M and 12 M ($p<0.05$). Levels of SLEDAI score were significantly decreased for 6 M and 12 M. Doses of PSL (mg) were significantly decreased ($p<0.05$-0.02, before 10.8±10.6, 6 M 6.1±3.7, 12 M 5.7±3.0). AS scores were also significantly improved ($p<0.01$-0.05), before 28.4±14.2, 12 M 14.8±15.8, 24 M 16.8±10.9). [Conclusions] Effects of BE on immunological data, disease activities, and daily living scores, induction of clinical remission and dose reduction of prednisolone were tolerable without major adverse effects in patients with SLE.

W40-4

Withdrawal of Belimumab after over 24-week treatment in patient with SLE

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Conflict of interest: None

[Objective] There is concern in clinical practice whether withdrawal of belimumab (BEL) after achieving low disease activity in SLE will result in a flare of disease activity. [Methods] We retrospectively observed changes in disease activity after 24 and 48 weeks of BEL discontinuation in SLE patients who used BEL for more than 24 weeks and discontinued BEL after achieving SLEDAI 4 or less at our hospital. The endpoints were prednisolone (PSL) dose and SLEDAI. [Results] Seven SLE patients who met the above criteria were on BEL for 707±441 days. None had a flare of BILAG A or B at 24 or 48 weeks after BEL discontinuation. SLEDAI at BEL discontinuation and 48 weeks after discontinuation was not significantly different (2.7±1.3 to 2.4±1.1), and the significant reduction in disease activity was maintained when comparing BEL induction and 48 weeks after discontinuation ($p<0.05$, ANOVA). There was also no significant increase in PSL dosage from 3.7±2.1 mg to 2.7±1.1 mg at BEL discontinuation and 48 weeks after discontinuation. [Conclusions] SLE patients who achieved SLEDAI 4 or less after 24 or more weeks of BEL treatment did not have flares of disease activity or increased PSL use even 48 weeks after discontinuation of BEL.

W40-5

Time course analysis of clinical symptoms and immunocompetent cells in patients with SLE treated with belimumab

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Conflict of interest: None

[Objective] In this study, we analyzed the efficacy of BLM in clinical practice and its effect on immunocompetent cells. [Methods] We analyzed the patient background, clinical symptoms, laboratory findings, and changes in immunocompetent cells before and after the introduction of BLM in 28 patients with SLE treated with BLM at our department. [Results] Twenty-six patients were female and two were male. Induction treatment was median PSL 10 mg, concomitant medications were HCQ 61%, CyA 43%, TAC 29%, MMF 29%, MZR 14%, IVCY 7%. Disease activity at the time of BLM introduction was a median anti-dsDNA antibody titer of 24 IU/mL, median SLEDAI-2K titer of 6, and BILAG B or higher was common in cutaneous mucosal and renal symptoms. Interestingly, there were differences in the temporal changes after the introduction of BLM in each clinical symptom category. In addition to changes in B-cell subsets, analysis of immunocompetent cells showed changes in non-B-cell groups that correlated with disease activity. [Conclusions] The efficacy of BLM in clinical practice was demonstrated, suggesting that the onset of action varied with each clinical condition. Analysis of immunocompetent cells suggested that BLM may also affect B cells and other immunocompetent cells.

W40-6

Three patients with lupus nephritis difficult to continue or refractory to standard therapy responded to belimumab

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Conflict of interest: None

[Clinical Significance] We experienced a case in which disease activity was reduced by the addition of belimumab in a patient who was refractory or difficult to continue remission induction therapy with standard therapy. Case 1: 39-year-old female, She was diagnosed with lupus nephritis type IV 17 years of age, and had frequent interruptions in recent years. She had nephrotic syndrome, and was started on steroid pulse therapy and hemodialysis. MMF was added, but was discontinued due to decreased cytopenia. After adding intravenous belimumab, her urinary protein creatinine ratio (U-P/Cr) was normalized. Case 2: 48-year-old female, diagnosed with lupus nephritis type III+V 3 years ago. She was treated with MMF, TAC and PSL, but after the PSL dose was reduced, she repeatedly relapsed with increased proteinuria, so belimumab infusion was added. After the addition, proteinuria improved. Case 3: 49-year-old woman with alveolar hemorrhage and acute renal failure. She was started on dialysis, steroid pulse, IVCY, and immunoadsorption therapy, but she developed pancytopenia and was unable to continue IVCY, so belimumab self-injection was introduced. Her renal function did not recover and she required maintenance dialysis, but her SLE activity was stabilized.

W41-1

A case of MPO-ANCA positive EGPA with a single pulmonary nodular lesion responding to mepolizumab

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Conflict of interest: None

A 74-year-old woman developed purpura on her lower legs, drop foot, and paresthesia in her extremities a year ago. She had a history of eosinophilic sinusitis and sinobronchial syndrome several years ago. She was diagnosed with EGPA based on positive MPO-ANCA, increased peripheral blood eosinophil count, and skin biopsy results. She started on high-dose oral PSL and a course of intravenous immunoglobulin therapy. Since she reduced PSL to 7 mg/day, she showed increased eosinophil count in peripheral blood and recurrent inflammatory findings three months before, although MPO-ANCA was negative. A 15 mm size nodule shadow appeared in the right lung on CT, and she was admitted to our hospital. Beta-D-glucan, cryptococcal antigen, T-SPOT. TB test and MAC antibodies were negative. According to a bronchoscopy, cytology was class I, and bacterial and mycobacterium cultures were negative. Although we couldn't obtain a tissue biopsy of the lesion, the pulmonary nodule was considered likely to be an EGPA-related granuloma. She was started on mepolizumab while maintaining steroid dosage for diagnostic treatment. Then, the size of the pulmonary nodule shrank, and CRP improved. Reports on the efficacy of mepolizumab in different organ lesions are still scarce. More case

reports are needed.

W41-2

Two cases of eosinophilic granulomatosis with polyangiitis (EGPA) who achieved steroid (GC)-free remission with meolizumab (Mepo) despite persistent high IgE levels

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Conflict of interest: None

Clinical trials have proven that Mepo is effective in maintaining remission and reducing GC dose in EGPA therapy. We'd like to reduce the GC-related adverse events, and avoid relapses. We have to be cautious with abnormal lavoratory data. We report 2 of the 14 GC-free remission cases during Mepo administration at our hospital remained high IgE levels. Case 1: 23 year old male with rhinitis. In 2017, he developed eosinophilia, purpura, neuropathy, and diagnosed with ANCA-negative EGPA. We treated with GC and azathioprine. After 3 years, relapsed occured and Mepo 300 mgsc q4W was administrated. After 9 months, though IgE levels were 1300 IU/ml, GC-free remission was achieved Case 2: 77 year old male visited our hospital with muscle pain and eosinophilia after asthma attack in 2010, We diagnosed as ANCA-positive EGPA and treated with moderate dose PSL. After reducing the PSL to 2.5 mg, ANCA was reelevated, and Mepo was administarated. After 3 years, though IgE was 12000, GC-free remission was achieved. Clinical significance: GC reduction should be cautious during EGPA treatment because there are no reliable indicators to predict relapse. Though high IgE levels during Mepo administration may not affect the achievement of GC reduction/free unless accompanied by other abnormalities.

W41-3

Therapeutic approach to Refractory Patients with Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: None

[Objective] In active and severe patients with EGPA, cyclophosphamide (CYC) has been used in addition to glucocorticoids (GC), and recently rituximab (RTX) has also been considered, although the details are unclear. We report the therapeutic approach for patients with severe refractory EGPA. [Methods] We retrospectively studied 46 patients of EGPA attending our hospital between 2000 and 2022. We analyzed each organ involvement, ANCA positivity, the treatment response, and relapse with immunosuppressants, mepolizumab (MEP), and intravenous immunoglobulin therapy (IVIG). [Results] Among all patients treated with GC, we administered CYC, IVIG, MEP, azathioprine (AZA), mycophenolate mofetil (MMF), methotrexate (MTX), and RTX to 9, 16, 20, 17, 4, 5, and 2 patients respectively. One patient with refractory enterocolitis was treated with GC, AZA, and MEP. Although peripheral blood eosinophils disappeared, numerous eosinophilic inflammations remained in the intestinal tract, and RTX was effective. Another patient with refractory sinusitis and peripheral nerve lesions was treated with IVCY and MEP inadequately, but RTX and sulfamethoxazole/trimethoprim were effective. [Conclusions] Refractory gastrointestinal tract, peripheral nerve lesions, and sinusitis were successfully treated with RTX.

W41-4

Relapse Rate and Effect of Steroid Reduction with Mepolizumab in Maintaining Remission of EGPA

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Conflict of interest: None

[Background] EGPA has different treatment strategies depending on the severity of the disease at diagnosis. We investigated the relapse rate and the effect of steroid reduction with mepolizumab in 10 patients with EGPA treated with mepolizumab. [Methods] We compared the relapse rate and steroid reduction effect within 1 year in 20 patients with EGPA newly diagnosed at our department from April 2018 to March 2022. [Results] The median age at onset was 52 years, and the male-to-female ratio was 2:3. 10 of the 20 patients were positive for MPO-ANCA, and the median eosinophil count at onset was 7890/μg, which was markedly high. Neuropathy was the most common organ disorder in 85% of the patients. 11 patients had a FSS of 1 or higher, and 9 patients had a FSS of 0. 5 patients with FSS 1 or higher and 5 patients with FSS 0 received mepolizumab as remission maintenance therapy. 4 patients in the mepolizumab group discontinued steroids within 4 months of remission therapy, 6 continued on low-dose steroids but had no relapse, and the steroid dose and relapse rate were lower than in the group not receiving mepolizumab. [Conclusions] Mepolizumab may be effective in preventing relapse and reducing steroid use regardless of disease severity when introduced early in maintenance therapy.

W41-5

Characteristics of GC-free 14 patients among 25 patients treated with mepolizumab for eosinophilic granulomatous polyangiitis

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Conflict of interest: None

[Objective] We examined the characteristics of EGPA patients who achieved GC-free remission by administering Mepo. [Methods] Age, sex, presence or absence of ANCA, duration of disease, induction therapy, period until introduction of Mepo and administration period, eosinophils (Eos) and CRP/IgE levels were retrospectively examined. [Results] Median age of onset 53 years, 11 females, disease duration 5 years, 8 ANCA+at onset, Eos 6476/μl, CRP 5 mg/dl, and IgE 776 IU/ml. 14 cases achieved GC-free, age 52 years old, female 8 cases, disease duration 3 years, ANCA positive 6 cases, from onset to Mepo introduction 1 years, Mepo administration period 2 years. Eos7500/479, CRP2.3/0.04, IgE775/173 at the time of diagnosis/installation. 6 cases (43%) with GC pulse at induction, 42.5 mg/day initial dose of PSL, 7 cases (50%) receiving CY. Eos29/CRP0.03/IgE65 when GC-free was achieved, and the PSL doses in non-achieved cases was 2 mg/day. [Conclusions] Mepo administration achieved GC-free in more than half of the patients, and the ANCA-positive patients also followed a favorable course. There was a tendency to achieve early GC-free by early introduction in cases with a short disease period.

W41-6

Influence of early use of mepolizumab on glucocorticoid-free remission of eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] Achieving glucocorticoid (GC)-free remission on eosinophilic granulomatous polyangiitis (EGPA) patients is difficult. In Japan, mepolizumab (MPZ) was approved for EGPA for insufficient GC effect in July 2016, but its efficacy in an early stage is unknown. [Methods] In EGPA patients who started treatment at our department from July 1, 2016 to October 31, 2020, glucocorticoid (GC)-free remission rates after 2-year treatment were compared between early mepolizumab group (started within 30 days) and the other group. Inverse propensity score weighting analysis (IPTW) was used to control for confounding factors such as cyclophosphamide use (within 30 days), BVAS and revised five factor score. [Results] A total of 22 patients were included. MPZ was used concomi-

tantly with GC in 14 cases, in 6 of whom it was started within 30 days of treatment commencement. The GC-free remission rates 2 years after the start of treatment in the early MPZ group vs the other group were 50% (3/6) vs 6.3% (1/16) (Fisher's exact test: p=0.046), unadjusted odds ratio 16.0, ITPW adjusted odds ratio 19.2 [1.21-304], p=0.036. [Conclusions] The GC-free remission rate after 2 years was higher in the group that received early mepolizumab.

W42-1

Remission induction therapies and their outcome with ANCA-Associated Vasculitis (AAV) in our department

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Conflict of interest: None

[Objective] To clarify remission induction therapies and their outcome in patients with AAV in our department. [Methods] We reviewed all patients with AAV induction therapy in our department from 2013 to 2021 and retrospectively selected clinical data from their medical records. We defined the remission as those who had Birmingham Vasculitis Activity Score version 3 (BVAS) less than 1, prednisolone (PSL) use less than 10 mg/day, and no flare at 52 weeks. [Results] There were 28 microscopic polyangiitis (MPA) patients, 9 granulomatosis with polyangiitis (GPA), and 5 eosinophilic granulomatosis with polyangiitis. The median age of each AAV patients was 72, 63 and 72 years old, and males were 29, 58 and 33%, respectively. The median score of BVAS before induction therapy was 14, 16 and 14, respectively. There were more patients in remission in corticosteroid (CS) monotherapy group compared with intravenous cyclophosphamide plus CS therapy group. Patients with MPA and GPA not in remission had diabetes mellitus (67 and 75%) and infection (56 and 50%), respectively. [Conclusions] The remission rate was lower in patients with diabetes and infections. It is desirable to use immunosuppressive drugs as much as possible to attain remission, and CS therapy for as short a period as possible.

W42-2

Treatment and Prognosis in Patients with ANCA-associated Vasculitis (AAV) in Each Period

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Conflict of interest: None

[Object] To investigate treatment and prognosis in patients with AAV by period of diagnosis. [Methods] We retrospectively collected clinical information from patients with AAV who had attended our department since January 2012. The clinical feature of patients diagnosed between 2007 and 2011 (Group A), between 2012 and 2016 (Group B), and between 2017 and 2022 (Group C) were compared. [Results] 134 cases were enrolled; mean age was 67 y/o, female was 62%, MPA 59, GPA 47, EGPA 28, group A 20, group B 52, and group C 59. No significant difference was found in each group, except ILD (group A 35%, group B 40%, group C 60%, P=0.05), steroid monotherapy (60%, 42%, 24%, P<0.01), and RTX (0%, 6%, 18%, P=0.03). Mortality tended to be higher in group A (35%, 17%, 11%, P=0.05), but overall survival was comparable (P=0.73, log-rank). The most common causes of death were malignancy (N=3) in group A, AAV (N=3) and infectious disease (N=3) in group B, and AAV (N=5) in group C. Compared to nonfatal cases, fatal cases had more MPA (78% vs 37%, P<0.01), p/MPO-ANCA (96% vs 65%, P<0.01), ILD (78% vs 42%, P<0.01), and mean age (75 vs 65 y/o, P<0.01) and CRP (8.4 vs 6.1 mg/dL, P=0.04) were higher. [Conclusions] The prognosis of AAV has not improved over time. More appropriate treatment is desirable.

W42-3

A case series of microscopic polyangiitis (MPA) without rituximab (RTX) as remission induction therapy

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Conflict of interest: None

[Objective] In recent years, RTX has become the standard treatment for MPA. However, the question arose as to whether RTX should be selected to all patients. In this study, we examined cases of MPA treated with remission induction therapy without RTX. [Methods] We retrospectively reviewed the clinical characteristics, treatment course, and relapse/complications of patients classified as MPA using the 2022 ACR/EULAR classification criteria and treated with induction remission therapy without RTX. [Results] 8 patients were studied. The mean age was 84.5 years, the mean MPO-ANCA antibody titer was 107.0 IU/ml. All patients had systemic symptoms. 4 patients had pulmonary involvement (2 with interstitial pneumonia and 1 with nodular shadows), 1 with glomerulonephritis, and 1 with purpura. All patients were started on high-dose steroids, and all went into remission. Immunosuppressive drugs were MZB in 3 cases, MTX in 3 cases, and AZA in 2 cases. The mean time to reduction to PSL10 mg was 16 weeks, and 32 weeks to 5 mg. No relapse or serious infection was observed in all patients. [Conclusions] In very elderly MPA patients with mainly systemic symptoms, induction remission therapy with other immunosuppressive agents instead of RTX is considered to be feasible.

W42-4

The efficacy and safety of rituximab in patient with ANCA associated vasculitis as the first remission induction therapy

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Conflict of interest: None

[Objective] Purpose is to reveal the efficacy and safety of rituximab (RTX) in patients with ANCA-associated vasculitis (AAV) as the first remission induction therapy. [Methods] We investigated the medical records of 32 AAV patients (22 MPA, 10 GPA) who had visited our hospital until March 2022. The observation period was 6 months from the start of RTX. [Results] At the time of RTX induction therapy, the median age was 74 years old, the median PSL dose was 40 mg/day, and BVAS score was 19. At six months, 23 cases (71.9%) in remission (BVAS=0), PSL dose was 10 mg/day. The adverse events were as follows, 18 infections in 13 cases (CMV 8, viral infection 3, Herpes Zoster infection 2, PCP 1, and so on), 2 thrombosis, and 1 malignancy. The risk factor of the severe infection at baseline was mPSL pulse therapy (P<0.03). ANCA type, titer, and disease classification were not related to disease flare-up. [Conclusions] With the Median dose of glucocorticoid (less than 0.5 mg/kg/day), RTX was effective for AAV, but the infection rate was higher than the result of Remit-JAV cohort.

W42-5

Efficacy and safety of RTX therapy for AAV in Japan: Clinical research using the J-CANVAS registry

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Conflict of interest: None

[Objective] To analyze the efficacy of rituximab (RTX) in maintaining

remission in ANCA-associated vasculitis (AAV) from data in the J-CANVAS registry. [Methods] Of the 262 first-onset AAV patients registered in this statistics, Using Fisher's exact test, we compared the rate of achieving remission between a group that received RTX during both the induction and maintenance periods and a group that received only the induction period. Using the same analysis method, Comparison with the group administered only the maintenance period of remission, and we also compared two groups with the same patient background age and RTX administration time. [Results] In the group that received RTX during the induction and maintenance periods, the group that received only the induction period, and the group that received only the maintenance period, the remission rates at 48 weeks after the start of treatment were 89%, 73%, and 54%, respectively. There was no significant difference in the comorbidity The analysis results suggested that regular administration was more important and useful than the number of administrations during the induction period. [Conclusion] We confirmed that regular administration of RTX was effective as a maintenance therapy for AAV up to 48 weeks after the start of treatment.

W42-6

The evaluation of Glucocorticoid -free achievement in Systemic vasculitis syndrome

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Conflict of interest: None

The evaluation of Glucocorticoid-free achievement in Systemic vasculitis syndrome [Objective] To examine treatment course of systemic vasculitis syndrome (SVS), especially focused on characteristics of the patients achieved glucocorticoid-free (GCF). [Methods] Fifty-two patients of SVS from April 2016 to December 2021 were retrospectively analyzed. [Results] The patient characteristics were as follows: giant cell arteritis (GCA) (n=3), Takayasu arteritis (TAK) (n=3), microscopic polyangiitis (MPA) (n=19), granulomatosis with polyangiitis (GPA) (n=4) and eosinophilic granulomatosis with polyangiitis (EGPA) (n=8). Twenty-two patients (42.3%) were achieved GCF: GCA (n=10; 55.6%), TAK (n=2; 66.7%), MPA (n=6; 31.6%) and EGPA (n=5; 62.5%). In GCA, Tocilizumab (TCZ) had the contribution to achieve GCF in 7 out of 8 patients (87.5%). On the other hand, no statistical significance both BVAS and FFS was found between achievement group and non-achievement group in MPA. Only 4 patients successfully achieved the GCF with remission only with PSL administration (66.7%). In EGPA, 4 out of 5 patients administered Mepolizumab (MEP) were led to GCF (80%). [Conclusions] Our study suggests that severe MPA is difficult to achieve GCF, and co-treatment with TCZ or MEP has the tendency for achieving GCF in GCA or EGPA, respectively.

W43-1

A disintegrin and metalloprotease -15 and Vascular endothelial cadherin is expressed on psoriatic arthritis

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Conflict of interest: None

[Objective] A disintegrin and metalloprotease (ADAM) -15 is a protein expressed in the cell membrane surface, and we have reported that it is concerned with angiogenesis in RA. Vascular endothelial (VE) -cadherin is a protein concerned with the adhesion formation of vascular endothelial cells. We found that ADAM-15 and VE-cadherin were elevated in serum and joint fluid in RA. But no association between ADAM-15 and VE-cadherin in psoriatic arthritis (PsA) has been reported. [Methods] To examine whether ADAM-15 and VE-cadherin was expressed by PsA serum, enzyme linked immune sorbent assay (ELISA) were performed. We investigated whether there is a relationship between serum ADAM-15 and VE-cadherin levels in PsA and clinical symptoms. To investigate correlation between ADAM-15 and VE-cadherin, Spearman's rank correlation coefficient test was performed. [Results] ADAM-15 and VE-cadherin in PsA were significantly elevated compared with NL. Serum levels of ADAM-15 and VE-cadherin in PsA patients with enthesopathy lesions were significantly lower than those without enthesopathy lesions. ADAM-15 and VE-cadherin were correlated. [Conclusions] ADAM-15 and VE-cadherin are expressed on PsA serum. These data show ADAM-15 and VE-cadherin is correlated in PsA.

W43-2

The clinical characteristics of refractory psoriatic arthritis

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Conflict of interest: None

[Objective] Difficult-to-treat rheumatoid arthritis (D2T RA) has been defined, whereas such a definition is lacking for psoriatic arthritis. The purpose of this study was to identify cases of difficult-to-treat psoriatic arthritis (D2T PsA) based on the tentative similar definition and to clarify their clinical characteristics. [Methods] PsA cases who had been attending our department, and met the following criteria were considered D2T PsA: (1) history of inadequate response to two or more b/tsDMARDs, (2) active disease, and (3) current condition was perceived as clinically problematic by the physician or patient. Patient characteristics were investigated retrospectively for these cases. [Results] Thirty-five PsA cases were selected, of which eight (22.9%) met the criteria for D2T. D2T cases had a significantly higher prevalence of fibromyalgia and respiratory disease than non-D2T cases. On the other hand, no significant differences were detected in activity indices such as CRP, MMP-3, and PASI. In addition, D2T cases had a significantly longer time from the onset of joint symptoms to diagnosis. [Conclusions] Fibromyalgia is more frequently complicated in D2T PsA, suggesting that it is important to address pain symptoms.

W43-3

Cardiovascular risk assessment in patients with psoriatic arthritis (PsA)

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Conflict of interest: None

[Objective] We evaluated coronary artery disease (CAD) risk, the disease activity and CAD risk management in patients with PsA. [Methods] We calculated the 10-year estimated CAD risk by the Suita score in 28 patients with PsA. We examined traditional CAD risk factors, frequency of indication for preventive treatment in patients at intermediate to high risk of CAD. The correlation between the Suita score and PsA disease activity indices was investigated. [Results] The frequency of hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM) were 57.1%, 67.9%, 25.0%. Fifty percent of the patients had an intermediate CAD risk and 17.9% had high risk. Among patients at intermediate and high CAD risk, the prevalence of untreated HT, DL, and DM was 18.2%, 46.2%, and 44.4%, and 55.6%, 71.4%, and 60.0% were inadequately treated, respectively. No significant correlation was found between the Suita score and the PsA disease activity indices. [Conclusions] Nearly 70% of PsA patients were at intermediate and high CAD risk, and many of them were untreated or inadequately treated for CAD risk factors. CAD risk should be assessed in patients with PsA regardless of disease status, and therapeutic management of CAD risk factors should be implemented in high-risk patients.

W43-4

Gender differences among patients with psoriatic arthritis

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Conflict of interest: None

[Objective] Psoriatic arthritis (PsA) occurs slightly more often in men. Reports from Westerners are accumulating that peripheral PsA is more common in women, while axial PsA and severe PsA are more common in men. We investigate gender differences in Japanese PsA. [Methods] We analyzed 249 patients diagnosed with PsA in our department's spondyloarthritis registry (TOSPAR) for patient background, disease activity, bone destruction, and response to molecularly targeted therapies. [Results] The male to female ratio is 1.6:1. Peripheral PsA was similar in both sexes, but axial PsA was significantly more frequent in males. Male PsA had significantly higher rates of comorbid hypertension, dyslipidemia, hyperuricemia, diabetes, and obesity. Female PsA had significantly higher patients global assessments and pain. Therefore, both AS-DAS and DAPSA were higher in women. On the other hand, bone destruction progression was significantly greater in males. There were no differences in response to molecularly targeted therapies between men and women. [Conclusions] Japanese PsA also showed gender differences similar to those of Westerners, suggesting that disease control in PsA requires gender-specific treatment in addition to molecularly targeted therapies.

W43-5

Examination of DISH (diffuse idiopathic skeletal hyperostosis) complication rate on CT evaluation, sacroiliac joint condition and patient background in psoriasis patients

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Conflict of interest: None

[Objective] To examine the complication rate of DISH in psoriasis patients and the risk factors for DISH based on patient backgrounds and sacroiliac joint (SIJ) fusion. [Methods] In the past two years, the psoriasis patients who underwent thoracoabdominal CT were examined by the backgrands of patients, erosion/fusion of SIJ and DISH on CT images. A t-test and a chi-square test were used, and the significance level was set at 0.05. [Results] Of the 58 psoriasis patients (44 men, mean age 60.5 years, mean disease duration 10.3 years), 17 (29%) had DISH. Patient age, age at onset, SIJ fusion rate, hypertension, and cardiovascular disease comorbidity rate were significantly higher in the DISH group. Multivariate logistic analysis revealed that the risk factors for DISH in psoriasis patients were patient age (odds ratio 1.07, p=0.015) and SIJ fusion (odds ratio 7.73, p<0.01). As a result of the ROC analysis, the odds ratio for DISH in patients aged over 60 was 10.6 (AUC = 0.75). SIJ erosion+; 17 (29%), PsA; 11 (19%) did not differ significantly by DISH (p =0.056,0.368, respectively). [Conclusions] Elderly psoriasis patients have a high risk of DISH complication and may be included in axial joint lesions due to SIJ fusion of DISH.

W43-6

A case of adult-onset hypophosphatasia (HPP) complicated with psoriatic arthritis

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Conflict of interest: None

A 33-year-old man with five years of back pain and psoriatic plaques at his hands was referred to us. The level of C-reactive protein or erythrocyte sedimentation rate was not elevated, and no autoantibodies were detected. HLA-B27 was negative, and a magnetic resonance imaging scan did not detect sacroiliac joint inflammation. His serum alkaline phosphatase (ALP) level by the Japan Society for Clinical Chemistry (JSCC) method was 100-110 U/L (the standard level was 106-322 U/L). Musculoskeletal ultrasonography detected enthesitis in his fingers. He was diagnosed with psoriatic arthritis (PsA), and anti-TNF-α agents improved his systemic pain. However, the levels of muscle and joint pain elevated again, and his gripping power was gradually lowered. Four years later, the method of evaluating serum ALP levels in Japan was changed from the JSCC method to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) method, and his serum ALP level was about 25 U/L (the standard level was 38-113 U/L). The level of urine phosphoethanolamine was 122.7 μmol/L (the standard level is <65.5 μmol/L). Examination of the ALPL gene detected reportedly pathogenic variants: 979T>C and 529G>A. He was finally diagnosed with adult-onset hypophosphatasia (HPP) complicated with PsA.

W44-1

Differences in HLA-A and B genotypes in patients with spondyloarthritis (SpA) and palmoplantar pustulosis osteoarthritis (PAO) with axial lesions in our hospital

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Conflict of interest: None

[Objective] We investigated the differences in the HLA-A and B genes of patients with axial lesions classified as SpA and PAO at our hospital. [Methods] In 170 patients with axial lesions classified as SpA and PAO and consented to the patient, HLA-A and B typing were performed using the PCR-rSSO method. Allele frequencies from 40902 Japanese bone marrow donors were used for comparison. [Results] B27 and B54 (OR 9.1, 2.2) were at a high risk of developing SpA with axial lesions. B27, B75, B7, B13 and B51 (OR 124.3, 4.2, 3.6, 2.7, 2.2) were at a high risk of developing ankylosing spondylitis. B75, B46, B60 and B7 (OR 12.6, 4.3, 2.2, 2.0) were at a high risk of developing nr-axSpA. B55 and B61 (OR 3.2, 2.6) were at a high risk of developing PAO. A24 (OR 3.06) were at a high risk of developing SpA with axial lesions. A11 and A31 (OR 2.34, 2.20) were at a high risk of developing PAO. [Conclusions] There was a clear difference in allele frequencies between SpA and PAO.

W44-2

The incidence and HLA phenotype of reactive arthritis in Japanese patients with bladder cancer following intravesical BCG therapy: prospective study

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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, a reactive arthritis (ReA) and the frequencies are known as about 0.5 to 5.7% in Western countries. [Objective] To prospectively evaluate the incidence and HLA typing of ReA in Japanese patients with bladder cancer following iBCG therapy. [Methods] The clinical findings of Japanese patients who received iBCG (n = 90) for bladder cancer from January 2018 to October 2022 were prospectively assessed, with specific attention to patients with ReA. We also looked at HLA typing

of patients with ReA. [Results] Patient age was 74 ± 9 and male/female ratio was 76/14. Of the 90 cases, ReA, uveitis and conjunctivitis were revealed in 2 (2.2%), 0 (0%) and 4 (4.4%), respectively. Notably, HLA-B27 was not detected in ReA patient. [Conclusions] Although this was 5-year prospective study, the incidence of ReA in Japan was 2.2% 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.

W44-3

Determination of whole sequences of KIR genes using long-read sequencing and its application for genetic study of KIR in ankylosing spondylitis

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Conflict of interest: None

[Objective] HLA-B27 is strongly associated with susceptibility to ankylosing spondylitis (AS). HLA-B27 is one of the ligands for killer cell immunoglobulin-like receptor (KIR) expressed on NK and T cells, suggesting a possibility that HLA-KIR interaction may contribute to the pathogenesis of AS. *KIR* genes are highly polymorphic and homologous to each other, which makes the genetic analysis using short-read sequencers highly challenging. In this study, to examine the association of *KIR* genes and AS, we made an attempt to sequence entire *KIR* genes including non-coding regions, and to determine *KIR* alleles, by long-read sequencing. [Methods] Whole length of each *KIR* gene was amplified by PCR and the amplicons were sequenced by PacBio Sequel sequencer. Using the obtained data, *KIR* consensus sequences and *KIR* alleles were determined. [Results] By comparing the *KIR* consensus sequences of the samples and the IPD-KIR Database, it was possible to determine the five digit *KIR* alleles, defined by coding region variants. In addition, multiple variants in non-coding region, which have not been registered in the database, were newly detected. [Conclusions] Our data showed that it is possible to conduct *KIR* allele typing and to detect new *KIR* alleles by long-read sequencing.

W44-4

Evaluating Numeric Rating Scale Versions of the 3 and 4 Visual Analog Scale (3/4-VAS) Composite Measures in Patients with Active Psoriatic Arthritis from the SELECT-PsA Program

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Conflict of interest: Yes

[Objective] Evaluate the ability of 3/4-numeric rating scales (NRS) scores to assess treatment response in SELECT-PsA 1 and 2, as well as the correlation of 3/4-NRS with other common disease activity measures. [Methods] 3-NRS scores were determined using the mean of SAPS questions 1-10, physician's and patient's global assessment of disease activity; 4-NRS scores were determined using SAPS, physician's global assessment, patient's assessment of pain, and BASDAI question 3. Correlations between 3/4-NRS with other disease activity measures were determined for UPA 15 from both trials and ADA for SELECT-PsA 1. [Results] A total of 1281 and 423 patients were included from SELECT-PsA 1 and 2, respectively. For both cDAPSA and 3/4-NRS scores, UPA 15 showed clear numerical improvements compared with PBO at wk 24 in both trials. Moderate correlations were observed between 3/4-NRS and DAPSA/cDAPSA ($r = \sim 0.4$, $P < 0.0001$), as well as HAQ-DI and SF-36. Nominally significant but weaker correlations were detected for joints, skin, and other disease activity assessments. Similar overall results were observed for ADA. [Conclusions] 3/4-NRS scores correlated well with other clinical and patient reported outcome measures, supporting 3/4-NRS as a viable and easy to use tool in daily clinical practice.

W44-5

The study of spinal ankylosing factors in patients with axial spondyloarthritis treated with biologics

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Conflict of interest: None

[Objective] We analyzed the spinal ankylosis progression and the associated factors in ax-SpA patients treated with bDMARDs. [Methods] Present study included patients with spondyloarthritis who met the ax-SpA classification criteria of the ASAS from March 2014 to November 2022. Total of 60 cases was included, but 37 cases were excluded according to exclusion criteria, remaining 23 cases were retrospectively analyzed. The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) (0-72) was used to evaluate spinal lesions, and the difference between the base mSASSS score and the 2 years after mSASSS score was defined as the degree of ankylosis progression. We analyzed the age, disease duration, sex, type of disease, use of NSAIDs and csDMARDs, biologics, ESR, CRP, VAS, HAQ, and baseline mSASSS values as the correlated factors. [Results] The average ankylosis progression were 2.16 (-1-9). The ankylosis progressed significantly in high mSASSS at baseline ($r=0.62$, $p=0.021$) and the no use of csDMARDs ($p=0.033$). There was no significant difference between the TNFα inhibitor group and the IL-17 inhibitor group ($p=0.15$). [Conclusions] High baseline mSASSS levels and no use of csDMARDs were risk factors for spinal ankylosis in ax-SpA patients treated with bDMARDs.

W44-6

Radiological Features and Clinical Variability of SAPHO Syndrome

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Conflict of interest: None

[Objective] The purpose of this study is to analyze and discuss the radiological characteristics and clinical diversity of Japanese patients with SAPHO syndrome. [Methods] Radiographic and clinical information was retrospectively reviewed in 115 Japanese patients (female/male: 81/34, mean age at onset: 48.7 years) diagnosed with SAPHO syndrome from 2007 to 2020. [Results] Among the 115 patients, 70 (60.9%) had complications of palmoplantar pustulosis, acne, or psoriasis. Imaging studies included bone scintigraphy in 71 patients, PET in 23, MRI in 58, and CT in 70. The most frequent lesions were arthritis of the sternoclavicular and sternocostal joints and bone thickening in 96 cases (83.4%). Spinal lesions including sacroiliac arthritis were observed in 85 cases (73.9%). Aseptic osteitis was observed in 95 patients (82.6%). Peripheral aseptic osteitis was observed in 22 patients, and tibia was involved in 12 patients. The mean CRP level at the initial visit was 1.18 mg/dL, which was within the normal range in 71 patients. Bone biopsies were performed in 20 cases of osteitis of the spine and limb bones, all with a diagnosis of aseptic osteitis. [Conclusions] SAPHO syndrome was frequently associated with sternoclavicular joint lesions and dermatological manifestations.

W45-1

4 cases of new-onset immune-mediated inflammatory diseases (IMIDs) post COVID-19mRNA vaccination

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Conflict of interest: None

COVID-19 mRNA vaccine may induce IMIDs due to its adjuvant and molecular mimicry. We report 4 cases diagnosed with new-onset IMIDs, of which manifestations appeared within a week after 2nd or 3rd vaccinations and required immunosuppressive therapies including glucocorticoid (GC). [Cases] Case 1: 27-year-old male presenting fever, oral ulcer, and butterfly rash from five days after the 3rd vaccination, was diagnosed with SLE by low complements, anti-nucleolar and anti-ds-DNA Ab positivity and received GC therapy. Case 2: 53-year-old female having arthralgia and myalgia two days after the 2nd dose of vaccination, followed by persistent dyspnea and general fatigue, was treated with GC and tacrolimus (TAC) under the diagnosis of anti-ARS+PM with ILD. Case 3: 78-year-old male developed general malaise four days after the 3rd dose of vaccination, followed by fever, polyarthralgia, skin rash and ferritin elevation, which was diagnosed as adult Still's disease (ASD) and improved by GC. Case 4: 68-year-old female with RA and SSc had arthralgia within 12 h from the 3rd dose of vaccination and was diagnosed with ASD by persistent rash and increased CRP and ferritin. Tocilizumab in addition of GC and TAC achieved remission. [Conclusion] IMIDs onset following COVID-19 vaccination should be considered.

W45-2

A case of anti-MDA5 antibody-positive interstitial pneumonia initially diagnosed to be scleroderma that could be treated as an outpatient

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Conflict of interest: None

[Case] 50 years old, female. [Current history] She visited another doctor because of arthralgia and generalized swelling of fingers. She had Raynaud's phenomenon and periungual hemorrhage. She was diagnosed as localized systemic scleroderma based on positive anti-centromere antibody. Glucocorticoid (GC) 10 mg/day was started. [Clinical Coarse] Lung exam showed vesicular sounds. Blood exam results showed LD 416 U/l, CRP 0.64 mg/dl, KL-6 493 U/ml. Chest X-ray showed decreased permeability in the lung base. MTX 6 mg/week was started. Chest CT showed interstitial pneumonia in bilateral lower lungs, which was thought to be NSIP with high cellular component. A few weeks later, dyspnea appeared and GC 40 mg/day was started. The anti-MDA5 antibody was found to be over 3,000 index, and KL-6 610 U/ml and ferritin 622 ng/ml was showed. After our discussing, treatment was continued as outpatient. The patient's respiratory symptoms did not worsen, but KL-6 increased gradually. So tacrolimus and mycophenolate mofetil were added, and the clinical symptoms stabilized. [Clinical Significance] The images of this case suggest the possibility of a disease other than scleroderma. This case is useful for future treatment, as which may be treated on an outpatient depending on the circumstances.

W45-3

Study on 7 cases of CTD-PAH treated with immunosuppresive agents

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Conflict of interest: Yes

[Objective] To elucidate the clinical outcome of immunosuppressive therapy for CTD-PAH. [Methods] Cases of CTD-PAH treated mainly by immunosuppression, were analysed using our patient database (2013-2022). [Results] 7 patients were extracted and the characteristics as follows; all patients were women, mean age at the treatment was 50.4 ± 19.9 (SD) years old. The background disease was SLE (n=3), Sjögren's syndrome (n=2) and systemic sclerosis (n=2). All patients were treated with corticosteroids, of whom 2 combined with cyclophosphamide, and 5 with mycophenolate mofetil. 6 patients were administered selective pulmonary vasodilators, and all received diuretics. Right heart catheterization was performed in 6 patients before and after the treatment, which showed the decrease of pulmonary artery pressure (41.3 mmHg±12.7 mmHg to 26 mmHg±7.9 mmHg). The follow-up period was 23 ± 17 months, and 6 patients (85%) were alive in 2022. One fatal case was an 84-years patient with Sjögren's syndrome; she died of respiratory failure by bacterial pneumonia. [Conclusion] The prognosis of CTD-PAH patients at our department was better than previously reported. The immunosuppressive therapy was also successful in SSc-PH patients, suggesting the pathophysiology may be partly immunological or inflammatory.

W45-4

The clinical features of chronic thromboembolic pulmonary hypertension associated with connective tissue disease

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Conflict of interest: None

[Purpose] CTEPH associated with CTD has no established treatment algorithm because of its rarity. We aimed to investigate the clinical features of CTEPH with CTD. [Methods] Six patients of CTEPH with CTD who underwent RHC in our department from 2010 to 2021 were enrolled as CTD group. Twelve patients with CTEPH without CTD who underwent RHC in the department of cardiology were selected as the control group by matching age, sex and mean pulmonary artery pressure. The clinical characteristics such as PVR change after 1 year were compared. [Results] The CTD group included 1 case of SLE, 3 cases of SSc, and 3 cases of APS. Pulmonary artery wedge pressure (11.8±5.0 mmHg) and interstitial lung disease complication rate (50%) in the CTD group were significantly higher than that in the control group ($p<0.05$). The rate of treatment by BPA in CTD group was significantly lower than that in control group. PVR after 1 year in the control group improved markedly ($P<0.01$), but not in the CTD group ($p=0.2$). However, PVR in the 3 patients in the CTD group who underwent BPA reached normalization. [Conclusion] CTEPH with CTD may have category 2 (PH associated with left heart disease), or 3 (PH associated with lung disease/hypoxia) PH. BPA may be an effective treatment in CTEPH with CTD.

W45-5

The efficacy and safety of nintedanib in patients with connective tissue disease-related interstitial lung disease (CTD-ILD) at our institution

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of nintedanib (NTB) and its effect on serum biomarkers in patients with progressive fibrosing connective tissue disease-related interstitial lung disease (CTD-ILD) treated with immunosuppressive therapy. [Methods] We studied patients diagnosed with CTD-ILD who met the criteria for progressive fibrosing interstitial lung disease and were treated with NTB. Efficacy was evaluated by changes in FVC (%, mL), the monthly rate of decline in FVC (%/M), and serum biomarkers. Safety was evaluated by the occurrence of adverse events. [Results] The mean age of 22 patients was 64.8 years, the mean duration of ILD was 9.0 years, and the mean FVC (%, mL) were 57.1 (%) and 1617.3 (mL). Mean FVC (%, mL) increased at 6 and 12 months and the monthly rate of decline in FVC (%/M) improved. Serum KL-6 was significantly decreased after 6 and 12 months. Adverse events (AE) were nausea in 2 patients, diarrhea in 12 patients, headache in 1 patient, and elevations in liver enzymes in 2 patients, and the dose of NTB was reduced in 11 patients. No patient discontinued NTB due to AEs. [Conclusions] The efficacy and safety of NTB in progressive fibrosing CTD-ILD were

confirmed in clinical practice. We discuss the effect of concomitant immunosuppressive therapy.

W45-6

Involvement of cytoskeleton-related signaling in the pathogenesis of renal fibrosis through focal adhesion formation

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Conflict of interest: None

[Objective] Renal injury contributes to the prognosis of various autoimmune disorders. Renal fibrosis is a common pathway of progressive renal injury, therefore, clarifying the mechanisms of renal fibrosis is vital. Cell activity is regulated by the microenvironment through focal adhesion. In addition, lysyl oxidase (LOX) family is a family of collagen-crosslinking enzyme, leading to the stabilization of fibrosis. In this study, we hypothesized that actin cytoskeleton-related cell signaling (MRTF-SRF signaling) is involved in the formation of focal adhesion and LOX family expression. [Methods] Renal fibroblasts (RFB) were used to determine the activity of MRTF-SRF signaling by TGF-β1 in promoter assay. Expressions of focal adhesion components and LOX family were also estimated by the stimulation with TGF-β1. [Results] TGF-β1 enhanced MRTF-SRF signaling in RFB. TGF-β1 induced LOX family expression dependent on MRTF-SRF signaling. In addition, TGF-β1 upregulated the expression of focal adhesion components (integrins and ILK) through MRTF-SRF signaling. In contrast, the inhibition of focal adhesion components suppressed TGF-β1-induced LOX family expression. [Conclusions] MRTF-SRF signaling may regulate LOX family expression directly and indirectly through focal adhesion formation.

W46-2

Comparison of the inhibitory effect of tocilizumab and etanercept on the progression of joint erosion in rheumatoid arthritis treatment

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Conflict of interest: None

Objectives: We compared the efficacy of tocilizumab and etanercept in inhibiting the radiographic progression of joint destruction in rheumatoid arthritis. Methods: Overall, 187 patients treated with etanercept or tocilizumab were selected. To adjust for baseline patient characteristics between the tocilizumab and etanercept treatment groups, a propensity score matching was performed. Radiographic progression of joint destruction was compared between patients treated with tocilizumab or etanercept. Clinical disease activity index (CDAI) and modified health assessment questionnaire (mHAQ) scores at the administration of biologic treatment and after 12 months of tocilizumab and etanercept therapy were measured and compared to radiographical parameters between the groups. Results: The Proportion of patients with no Sharp erosion score progression was significantly higher with tocilizumab treatment than with etanercept treatment (p=0.032). Multivariate analysis demonstrated that Sharp erosion score was significantly associated with baseline CDAI (odds ratio, 1.05; 95% confidence interval, 1.003-1.099, p=0.037). Conclusions: Tocilizumab treatment suppressed joint erosion progression compared to etanercept, and the progression correlated with baseline CDAI.

W46-3

The effects of treatment response in difficult-to-treat rheumatoid arthritis patients treated with IL-6 receptor inhibitor, abatacept and JAK inhibitor

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Conflict of interest: None

[Objective] The aim of this study was to evaluate the clinical response in D2TRA patients treated with IL-6Ri, ABT and JAKi. [Methods] This study included 138 RA patients met D2TRA criteria (IL-6Ri 31, ABT 31, JAKi 76). Effectiveness of each bDMARDs/JAKi were evaluated for 24 weeks. [Results] Drug retention rate at 24 weeks were 67.7% in IL-6Ri, 74.2% in ABT, 61.8% in JAKi group. DAS28-ESR was decreased in IL-6 and JAKi group between 24 weeks (IL-6Ri; $p<0.01$, ABT; 0.06, JAKi; $p=0.02$), and CDAI was decreased in all groups between 24 weeks (IL-6Ri; $p<0.01$, ABT; $p<0.01$, JAKi; $p<0.01$). Though improvement ratio of DAS28-ESR at 24 weeks was higher in IL-6i group than in other groups (IL-6Ri vs ABT; $p<0.01$, IL-6Ri vs JAKi; $p<0.01$, ABT vs JAKi; $p=0.51$), that of CDAI was not different between groups ($p=0.43$, $p=0.82$, $p=0.51$). Multivariate linear regression analysis revealed that high ACPA ($\beta=0.24$, $p=0.04$) and high DAS-ESR at baseline ($\beta=0.54$, $p<0.01$) inhibited the improvement of DAS28-ESR. Type of bDMARDs/JAKi ($\beta=-0.15$, $p=0.16$) did not affect the DAS28-ESR improvement. [Conclusions] Drug retention rate and clinical efficacy of D2TRA patients were not different among IL-6Ri, ABT and JAKi. In DT2RA patient, high ACPA and high disease activity were the risk factor to inhibit the clinical response.

W46-4

Comparison of continuation rate and effectiveness of IL-6 inhibitors and JAK inhibitors in patients with rheumatoid arthritis complicated with interstitial pneumonia

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Conflict of interest: None

(Purpose) Rheumatoid arthritis (RA) patients with interstitial lung disease (ILD) may find it difficult to treat. We compared the continuation rate and efficacy of IL-6 inhibitor (IL-6i) and JAK inhibitor (JAKi) in RA patients with ILD. (Methods) Thirty-six RA patients with ILD (IL-6i: 24 cases, JAKi: 12 cases) who received IL-6i or JAKi. Comparisons were between the two drugs in terms of patient background, continuation rate for 1 year after initiation, and changes in DAS28-ESR and CDAI in continuation cases. (Results) There was no significant difference in the patient background. There was no significant difference in the 1-year drug continuation rate (IL-6i: 46%, JAKi: 58%, $p = 0.73$), and the most common reason for discontinuation was insufficient efficacy (IL-6i: 54%, JAKi: 40%). The most common was infection, followed by infection (IL-6i: 23%, JAKi: 20%). Changes in DAS28-ESR (IL-6i; -1.95, JAKi: -1.07, $p = 0.39$) and changes in CDAI (IL-6i; -10.7, JAKi: -10.9, $p = 0.97$) in patients treated for 1 year Improvement was observed in both drugs, and no significant difference was observed between the two drugs. (Conclusion) There was no clear significant difference in the continuation rate of IL-6i, JAKi, and improvement in disease activity in RA with ILD.

W46-5

Sarilumab of 2nd line using of biologic agents has a good and comparable clinical efficacy to 1st line using in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the clinical efficacy of Sarilumab (SAR), inhibitor of IL-6 receptor, in 2nd line using of biologic agents (Bio) in patients with rheumatoid arthritis (RA). [Methods] We evaluated the disease activities in 29 RA patients for 52 weeks after starting administrations of SAR. [Results] The mean DAS28-CRP at baseline (BL) was 4.42, and 2.96 at 4 weeks (W) ($p<0.001$), 2.37 at 12 W ($p<0.001$), 2.40 at 24 W ($p<0.001$), 2.49 at 36 W ($p<0.001$), and 2.18 at 52 W ($p<0.001$). DAS28-CRP significantly decreased after 4 W from BL. When looking at the clinical courses after starting SAR as 1st and 2nd line Bio, the mean DAS28-CRP of 1st SAR (N=10) and 2nd SAR (N=11) groups were 5.02 and 4.02 at BL ($p=0.054$), 3.29 and 2.35 at 4 W ($p=0.164$), 2.66 and 1.58 at 12 W ($p=0.055$), 2.45 and 1.73 at 24 W ($p=0.088$), 2.61 and 1.69 at 36 W ($p=0.084$), 2.17 and 1.56 at 52 W ($p=0.218$), respectively. DAS28-CRP significantly decreased after 4 W from BL in both groups ($p<0.05$). There were no significant differences in DAS28-CRP of both groups, and SAR, even under 2nd line using, showed good clinical efficacy. [Conclusions] SAR of even 2nd line using had a good and comparable efficacy to 1st line using, although 2nd line using of Bio is usually considered that the clinical efficacy is less than 1st line using.

W46-6

The safety and efficacy of peficitinib 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 peficitinib in daily clinical practice, and factors related to them. [Methods] Patients with rheumatoid arthritis who were enrolled in the FIT-RA by March 2022 and who received peficitinib were included in the study. The drug retention rate, DAS28-CRP, and adverse events during 12 months observation periods were investigated, and Cox regression analysis was performed to identify factors associated with the drug retention rate. [Results] Fifty-three patients were included. Age 68.0 years [56.5-75.5] (median, IQR), 46 (86%) were female. The continuation rate at 12 months was 66%; DAS28-CRP remission was 18% at baseline and 47% at 12 months. Adverse events included one case of herpes zoster (incidence rate 2/100 patient-years) and one case of infection leading to drug withdrawal. Previous JAK inhibitor use was significantly associated with lower continuation rate during 12 months (HR 2.76, p=0.047), but previous biologic agent use was not (HR 0.61, p=0.228). [Conclusion] Peficitinib showed efficacy and safety in real clinical practice although previous use of other JAK inhibitors may lower drug retention rate.

W47-1

Investigation of IP-10-producing cells in anti-MDA-5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objective] Last year we reported that serum IP-10 levels were elevated in patients with anti-MDA-5 antibody-positive dermatomyositis (DM) and they rapidly decreased in parallel with a decrease in interferon (IFN)-α levels. In this study, we investigated IP-10-producing cells. [Methods] We performed immunohistological analysis of IP-10-expressing cells in the skin tissue of one patient. We next sorted peripheral blood mononuclear cells (PBMCs) of healthy volunteers into monocytes and non-monocytes, and evaluated IP-10 production on type I IFN stimulation *in vitro*. [Results] In the skin tissue, IP-10-positive cells were mostly CD68-positive, indicating that they were of monocyte/macrophage-lineage cells. Monocytes derived from PBMCs produced IP-10 on type I IFN stimulation *in vitro*, in a dose-dependent manner. Non-monocytes produced only a small amount of IP-10. [Conclusions] Monocytes/macrophages infiltrating the skin lesions of anti-MDA-5 antibody-positive DM were indicated to produce IP-10, and monocytes were shown to produce IP-10 on type I IFN stimulation *in vitro*. Monocytes may infiltrate the skin lesions in an autocrine manner. The type I IFN/IP-10 axis may be important not only as a marker of disease activity but also as a therapeutic target in this life-threatening disease.

W47-2

Urinary Beta-2 Microglobulin is an Accurate Prognostic Marker in Dermatomyositis Patients with Interstitial Lung Disease Positive for Anti-MDA-5 Antibody

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Conflict of interest: None

[Objective] Interstitial Lung Disease (ILD) accompanied with anti-melanoma differentiation-associated gene 5 (MDA5) antibody-positive dermatomyositis (DM) is usually rapidly progressive and life-threatening. In this study, we assessed the utility of urinary Beta-2 microglobulin (β2MG) as a disease activity marker and prognostic marker in anti-MDA5 antibody-positive DM. [Methods] Anti-MDA5 antibody-positive DM patients admitted to our department were classified into survival and death groups, and urinary β2MG and other data were retrospectively extracted and analyzed. [Results] Urinary b2MG levels before treatment were significantly lower in the survived patients than those in the dead patients (239 and 647 mg/gCr, respectively, $p = 0.025$), while serum ferritin, KL-6 and creatinine levels were not significantly different between the two groups. In addition, when comparing the data at the time of admission and after treatment, urinary β2MG after treatments decreased significantly in the survival group while it increased significantly in the death group. [Conclusions] A high urinary β2MG level may be a prognostic marker for anti-MDA5 antibody-positive DM patients with ILD. Furthermore, elevated urinary β2MG during treatment suggests treatment resistance and poor prognosis.

W47-3

Inferring the pathogenesis of anti-MDA5 antibody-positive dermatomyositis and effective therapeutic targets - differences from anti-ARS antibody-positive dermatomyositis and Characteristics of surviving cases in peripheral blood gene expression

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Conflict of interest: Yes

[Objective] To Infer the pathogenesis of anti-MDA5 antibody-positive dermatomyositis and effective therapeutic targets [Methods] Total of 31

DM cases were investigated, including anti-aminoacyl-tRNA synthetase positive (ARS) DM (n=12), MDA5 DM (n=7) and others (n=12). Peripheral blood was drawn at baseline and 2 to 3 months after treatments. Total RNAs were subjected to gene expression analysis. [Results] The hierarchical clustering with expression profiles of peripheral blood at baseline showed major 3 clusters. ARS and MDA5 DM were clearly discriminated if differentially expressed genes (DEGs) between these subtypes of DM were analyzed. By GO enrichment analysis, the terms, such as related to "defense response to virus" including "type 1 IFN signaling pathway" were found in the DEGs. We also investigated the DEGs of peripheral blood at 2-3 months after treatment between survival and fatal cases in MDA5 DM. We found that suppressing RIG-I like receptor and type 1/2 IFN signaling were the keys for survival. [Conclusions] MDA5-DM is possible to be caused by MDA5-mediated hyper-activation of RIG-I-like receptor signaling. The use of depletion of B-cells to effectively lower anti-MDA5 antibody titers and the use of JAK inhibitors to suppress type 1/2 IFN signaling seemed to be reasonable.

W47-4

Clinical features and cytokine profiles of anti-MDA5-antibody-positive patients with anti-ADAR antibody

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Conflict of interest: None

[Objective] Adenosine deaminase acting on RNA (ADAR) is a double-stranded RNA editing enzyme that edits A-to-I RNA that converts adenosine to inosine. We previously reported that anti-ADAR antibody (Ab) was frequently found in anti-MDA5 Ab-positive patients. In the present study, we examined clinical features and cytokine profiles of anti-MDA5 Ab positive patients with anti-ADAR antibody. [Methods] The participants were 26 patients with anti-MDA5 Ab-positive dermatomyositis who were admitted to our department. To detect anti-ADAR Ab, we made ELISA using ADAR as an antigen and measured anti-ADAR IgG Ab. [Results] The anti-ADAR Ab was detected in 9 of the 26 patients (34.6%). Anti-ADAR Ab-positive patients were four males and five females with an average age of 54.6 years. When comparing anti-ADAR Ab positive and negative patients, no differences were found between the two groups in clinical features, including fever, arthralgia, ILD, or pneumomediastinum, and in laboratory findings, including serum ferritin levels. However, IP-10 and TNF-α levels were elevated in anti-ADAR Ab-positive patients. [Conclusions] In anti-MDA5 Ab positive patients, there was no difference in clinical features and laboratory findings between anti-ADAR Ab positive and negative patients.

W47-5

A case of anti-MDA5 antibody-positive dermatomyositis after COVID-19

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Conflict of interest: None

[Case] 33-year-old male. On May 1, he was diagnosed as having COVID-19 and had a persistent cough even since. From mid-June, muscle pain, muscle weakness and skin eruption on the fingers appeared. Because an increase of CK and KL-6 values was pointed out, he visited our hospital on September 9. Because heliotrope rash and Gottron's sign were observed and SpO_2 at rest was 94% (under 4 L/min of oxygen), anti-MDA5 antibody-positive dermatomyositis was strongly suspected. He was admitted on the same day and treatment with mPSL pulse, tacrolimus, intravenous cyclophosphamide and plasmapheresis were started. Anti-MDA5 antibody titer before treatment was 3180 index. After treatment, hypoxemia and chest CT findings were improved along with the decreased anti-MDA5 antibody titer, ferritin and KL-6 values. [Discussion] To our knowledge, this is the first case that developed anti-MDA5-positive dermatomyositis after SARS-CoV-2 infection. Although it is well known that MDA5 recognizes double-stranded RNA viruses as an intracellular virus sensor, the association of COVID-19 and anti-MDA5 antibody production is not clear. Some sequelae after COVID-19 have been reported, but we should take care of the development of severe manifestations related to systemic autoimmune disorders.

W47-6

Examination of the formula to decide the starting dose of tacrolimus based on CYP3A5 genotype

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Conflict of interest: None

[Objective] The use of tacrolimus (TAC) is increasing in the treatment of interstitial lung disease in dermatomyositis (DM-ILD). Genotype of CYP3A5 was reported to play an important role in pharmacokinetics of TAC and several reports showed that the blood concentration of TAC in patients with a CYP3A5 *1 allele was lower than those with CYP3A5 *3/*3. In our previous study, we made the formula to decide the starting dose of TAC for attainment target trough concentration based on CYP3A5 genotype. In this study, we examined of the formula. [Methods] We decided the starting dose of TAC by using the formula, for treatment of the patients with DM-ILD (*3/*3 6, *1 allele 6) visiting our hospital between November 2019 and October 2022. [Results] The significant correlation between the predicted and observed trough concentration of *3/*3 group were shown in initial and second measurement date. *1 allele group were no correlation. [Conclusion] Although the formula which we made for attainment target trough concentration of *3/*3 group was useful for deciding the starting dose of TAC, *1 allele group were not useful.

W48-1

Cluster analysis to identify different phenotypes in patients with anti-synthetase antibodies

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Conflict of interest: None

[Objective] To characterize homogeneous subgroups using cluster analysis in a cohort of anti-synthetase antibody-positive patients with significant heterogeneity. [Methods] Ninety-nine consecutive patients with anti-synthetase antibodies detected by RNA immunoprecipitation who visited our hospital from August 2014 to October 2021 were included regardless of clinical diagnosis. A multiple correspondence analysis followed by hierarchical clustering was performed to aggregate the patients into subgroups. [Results] Three subgroups were identified. Cluster 1 corresponded to 26 patients who had anti-Jo-1, EJ, or OJ, most commonly diagnosed with interstitial pneumonia with autoimmune features (58%). Patients in this cluster were frequently complicated with rapidly progressive interstitial lung disease (42%) and malignancy (27%). Cluster 2 included 52 patients who were positive for anti-Jo-1, PL-7, PL-12, or EJ, and had dermatomyositis-specific rash (77%), muscle weakness (40%), fever (31%), mechanic's hand (79%), and arthritis (39%). Cluster 3 corresponded to 21 patients characterized by increased frequencies of anti-KS (76%) and clinical features of systemic sclerosis. [Conclusion] Patients with anti-synthetase antibodies were classified into three different phenotypes.

W48-2

Prognostic factors for mortality and risk factors for recurrence of anti-aminoacyl-tRNA synthetase syndrome

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Conflict of interest: None

[Objective] To investigate life prognostic factors and risk factors for recurrence in patients with anti-aminoacyl-tRNA synthetase syndrome (ASS). [Methods] We identified 63 ASS patients followed at Kyoto University Hospital from 2005 to 2021. Kaplan-Meier's survival curve and univariate and multivariate Cox regression analysis were used to explore prognosis factors and risk factors for recurrence retrospectively. Anti-ARS Abs were screened by RNA immunoprecipitation (RNA-IP). [Results] Multivariate analysis revealed that life prognostic factors for mortality were rapidly progressive interstitial lung disease (RP-ILD) (HR: 20.5 95%CI: 1.60-262.3), malignancy (HR: 16.6 95%CI: 1.44-190.2) and Male (HR: 13.7 95%CI: 1.80-104.3). Fever (HR: 3.97 95%CI: 1.67-9.41) and anti-PL12 antibody (HR: 2.73 95%CI: 1.16-6.43) were identified as risk factors for recurrence. [Conclusions] RP-ILD and malignancy were detected as prognostic factors for mortality in ASS patients. The patients with fever and anti-PL12 antibody had recurrence more frequently.

W48-3

Effect of nintedanib on the progression of ILD associated with anti-synthetase syndrome

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Conflict of interest: None

[Objective] To determine the effect of nintedanib (NIN) on the progression of ILD associated with anti-synthetase syndrome (ASS-ILD). [Methods] Participants were ASS-ILD patients who were administered NIN. Changes in symptoms, CT imaging, and serum KL-6 and SP-D levels were compared between 6 months before and after the administration of NIN. [Results] This study included 12 cases (3 males and 9 females, a mean age of 65.8 years, a mean disease duration of 84 months). Symptoms worsened in 6 cases in the 6 months before NIN but improved in 4 cases and worsened in 2 cases in the 6 months after NIN (p=0.43). CT imaging showed deterioration in 10 cases 6 months before NIN, but 2 cases had improvement, and 4 cases had worsened after NIN (p=0.04). KL-6 levels had increased in 4 cases before NIN. The increase and decrease were found in 6 and 4 cases after NIN. An increase in SP-D levels had increased in 2 cases before NIN. The increase and decrease were found in 4 and 1 cases after NIN. The dose of glucocorticoid was reduced in 5 of 9 cases less than the dose the relapse developed before NIN. [Conclusion] NIN may suppress the worsening of CT images, but not symptoms and relapse in ASS-ILD. A discrepancy was found between the change in KL-6 and SP-D levels and that in imaging and symptoms.

W48-4

Examination of clinical features of anti-ARS antibody-positive cases

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Conflict of interest: None

[Objective] We examined anti-ARS antibody-positive cases from our institution and reported that IP is more common than myositis and eruption as a symptom. We further increased the number of cases and examined them. [Methods] From 2016 to September 2022, 136 patients who were positive for anti-ARS antibody index 25 or higher at our hospital were examined for age, sex, diagnosis, symptoms, anti-ARS antibody subtype, and treatment. [Results] The average age of anti-ARS antibody-positive patients was 63.4±13.4, with 54 males and 82 females. The symptoms were IP in 124 cases, myopathy in 50 cases, rash in 36 cases, arthralgia in 57 cases, and Raynaud's symptom in 15 cases. IP alone was the most common in 62 cases. In the IP group, 4 patients who were hospitalized with acute interstitial pneumonia and died within 1 month due to resistance to steroid treatment were observed. EUROLINE Myositis Profile 3 was measured in 103 patients. There were 31 cases of Jo-1, 16 cases of PL-12, 16 cases of EJ, 9 cases of PL-7. Sixteen patients in the Jo-1 group relapsed, but no recurrence was observed in the PL-7 group. [Conclusion] Anti-ARS antibody-positive patients are mainly IP, and the recurrence rate differs depending on the subtype.

W48-5

Two cases of anti-ARS antibody-positive polymyositis complicated by gangrene of the fingers

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Conflict of interest: None

Case 1. A 75-year-old woman, who has been treated for polymyositis (PM) and interstitial lung disease (ILD) with positive anti-ARS antibody (anti-PL-7 antibody) developed cyanosis of both fingers. Soon after that, the tip of the left third finger became gangrenous, and she was referred to our hospital. Hand angiography showed stenosis of peripheral hand vessels, and capillaroscopy revealed microbleeding. Anti-phospholipid antibodies, ANCA, and systemic sclerosis-related autoantibodies were negative. She was treated with intravenous cyclophosphamide (IVCY). Case 2. A 63-year-old man developed gangrene of the fingers. He also presented with ILD, elevated creatine kinase levels, and positive anti-ARS antibody (anti-EJ antibody) and was diagnosed with PM. He was treated with methylprednisolone pulse therapy, high dose oral corticosteroids, and IVCY. His gangrenous fingers were treated with incisional drainage, antibiotics, and prostaglandins. Recently severe digital ischemia in patients with anti-ARS antibodies has been reported, and Raynaud's phenomenon and myositis are suggested to be predictive factors. As there have been reports of cases in which digital lesions improved with immunosuppressive therapy, immunosuppression may be effective in some cases.

W48-6

A case of interstitial lung disease with anti-Pl-7 antibody-positive dermatomyositis in which rituximab and plasma exchange therapy were effective

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Conflict of interest: None

[Case Description] A 73 years old woman presented one week of, fatigue, muscle pain, skin eruption, and cough since the day before admission. On physcial and laboratory examination, Gottron's signs, respiratory failure, and interstitial opacities in the lung field were found, anti-MDA5 antibody was negative, but anti-Pl-7 antibody was positive, and then she was diagnosed as a rapidly progressive interstitial pneumonia associated with dermatomyositis. After the corticosteroid pulse therapy, multidrug immunosuppressive therapy with PSL 1.0 mg/kg/day, TAC, and IVCY was introduced. However, oxygenation worsened, so the corticosteroid half-pulse therapy was introduced on the 10th day of admission. In addition, plasma exchange (PE) was introduced, IVCY was discontinued and was switched to RTX on the 12th day of admission. On the 49th day, oxygen became unnecessary, and the patient was discharged on the 65th day. [Clinical Significance] We experienced anti-Pl-7 antibody-positive dermatomyositis that was remissioned by RTX and PE. There are few reports of RTX for anti-Pl-7 antibody-positive interstitial lung disease. In this case, which suggests the involvement of B cells in the pathology, we considered the possibility that it was related to therapeutic responsiveness.

W49-1

Examination of the cut-off value of skin sclerosis in scleroderma using ultrasonic shear wave elastography

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Conflict of interest: None

[Objective] Ultrasound Shear Wave Elastography (SWE) was used to quantify skin sclerosis in scleroderma and examine the cut off value of skin sclerosis. [Methods] Subjects were 78 cases positive for either anti-Scl-70 antibody, anti-centromere antibody, or anti-RNA polymerase III antibody (SSc group: average age 50 years ± 14.5, 74 females, 4 males) and 20 ANA negative healthy controls (mean age 47.1 ± 15.9 years, 15 females, 5 males) were used as control group. [Method] The E Elastocity (kPa) values of total 18 sites, 10 sites on the proximal phalanx and 8 sites on the middle phalanx of the left and right fingers, were measured by SWE. [Results] Cut-off values were calculated by ROC analysis for the SSc group with sclerodactyly (27 cases) and the control group. The maximum value was 56.47 kPa, with a sensitivity of 45.01% and a specificity of 99.44. % The SSc group was divided into the group with sclerodactyly and the group without sclerodactyly, and the cut-off value was calculated. The maximum value was 73.92 kPa, with a sensitivity of 32.64% and a specificity of 99.90. [Conclusions] In cases between the two cut-off values, other evaluation methods such as strain elastography, changes in dermal layer structure on B-mode images, and vascular narrowing should be considered.

W49-2

Characterization of systemic sclerosis (SSc) patients who developed hyperCKemia

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Conflict of interest: None

[Objective] SSc occasionally develops hyperCKemia. The characteristics of SSc patients with hyperCKemia were investigated. [Methods] The patients were classified into two groups: the high CK level group (>150 mg/dl) and the normal CK level group (≦150 mg/dl). Age, gender, disease type, comorbidities, disease-specific antibodies, mRSS levels, and KL6 levels were compared in these two groups. [Results] In these 358 cases, the mean age was 62.9 ± 12.8, and the male-to-female ratio was 1:16. Forty-four patients (12.3%) showed hyperCKemia. The mean CK level in the high CK level group was 409 ± 609 mg/dl. There were no differences between the two groups in age, gender, or disease type. HyperCKemia was significantly associated with the muscle symptomatic group and the anti-centromere antibody negative group. There were no differences in pulmonary hypertension, interstitial pneumonia, or mRSS levels between the two groups. CK levels above 300 mg/dL were frequently accompanied by calcinosis. [Conclusions] Elevated CK levels in SSc patients were not associated with prognostic factor and the severity of fibrosis A Higher CK level is an indicator of skin calcification. This observation suggests conditions related to elevated CK level cause calcinosis in SSc.

W49-3

Forearm porphyrin levels evaluated by digital imaging system are increased in patients with systemic sclerosis compared with patients in pre-clinical stage

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Conflict of interest: None

[Objective] We hypothesized that changes in skin characteristics on the forearm could be useful for early diagnosis of systemic sclerosis (SSc). We used digital imaging system (VISIA) to investigate this possibility. [Methods] Twenty-eight Japanese patients who were diagnosed with typical or very early diagnosis of SSc (VEDOSS) were enrolled in this study, and ten of age- and gender-matched patients with other disorders were included as a control. Eight skin characteristics were analyzed. [Results] The scores of WRINKLES, TEXTURE, PORES and PORPHYRINS were higher in SSc subjects with sclerotic forearm skin (SSc forearm+) and those without (SSc forearm-) than in the non-SSc control subjects. Also, the scores of SPOTS, TEXTURE, PORES, UV SPOTS, BROWN SPOTS and PORPHYRINS were elevated in SSc forearm+ and SSc forearm- patients compared with those with VEDOSS. We found statistical significance in the difference in score of PORPHYRINS between SSc forearm- and VEDOSS ($p = 0.044$), and between SSc forearm+ and VEDOSS groups ($p = 0.012$). [Conclusions] VISIA may be used to differentiate VEDOSS from SSc cases. Our study also suggests that the porphyrin research may lead to a better understanding of SSc pathogenesis.

W49-4

The clinical manifestation of scleroderma renal crisis does not always match the renal histopathology

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Conflict of interest: None

[Background] Scleroderma renal crisis (SRC) has been classified according to the presence or absence of clinical hypertension. In Japan, SRC is classified into narrowly-defined SRC, which is malignant hypertension, and SRC with thrombotic microangiopathy (TMA) and microscopic polyangiitis (MPA). This classification is based on glomerular lesions only. [Methods] We retrospectively compared the clinical findings and renal histopathology of 8 patients with SRC who underwent kidney biopsy at our hospital. [Results] All 8 patients presented with hypertension, and 2 patients had malignant hypertension. Pathologically, there was a thrombus in the glomerulus and in the interlobular artery in 4 cases, which were pathologically diagnosed as TMA. However, 3 of the 6 patients with TMA clinically had no thrombus, which was inconsistent with the pathology. [Conclusion] The classification by the presence or absence of hypertension has no clinical significance. It is also necessary to evaluate also the upstream arteries. Although the clinical manifestation does not always coincide with the pathological findings, and treatment in the acute stage should be based on the clinical findings, Kidney biopsy is useful in understanding the pathophysiology and determining the course of further treatment.

W49-5

Examination of autoantibodies in anti-centromere antibody-positive cases

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Conflict of interest: None

[Purpose] In this study, we compared the positive rate of autoantibodies in ACA-positive cases with anti-SS-A antibody-positive cases. [Methods] ubjects were 101 ACA-positive and ASA-negative cases (ACA alone group), 319 ACA-negative and ASA-positive cases (ASA alone group), and 42 ACA-positive and ASA-positive cases (co-positive group). [Results] The positive rate of anti-thyroid peroxidase antibody was 26% in the ACA alone group, 31% in the ASA alone group, and 44% in the co-posi-

tive group. The positive rate of anti-mitochondrial M2 antibody was 35% in the ACA alone group, 14% in the ASA alone group, and 48% in the co-positive group, showing a significant difference between the three groups ($p<0.0001$). RF positivity was 17% in the ACA alone group, 63% in the ASA alone group, and 46% in the co-positive group ($p<0.0001$). ACPA positivity was 17% in the ACA alone group, 30% in the ASA alone group, and 15% in the co-positive group ($p=0.1026$). [Conclusions] Hashimoto's disease and PBC are known complications of SS, but in this study, the autoantibody positive rate was higher in ACA-positive cases than in ASA-positive cases. It has been reported that ACA-positive PBC is likely to cause portal hypertension, and it was considered necessary to screen ACA-positive patients for PBC.

W49-6

On Characteristics of Myocardial involvement of SSc

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Conflict of interest: None

[Objective & Methods] Eight cases of SSc with myocardial involvement were investigated to elucidate its characteristics. [Results] Age 43-82 yo (m=70), seven were female. Mostly dSSc patients except one. Comorbidities included renal crisis (7), interstitial pneumonitis (7), digit necrosis (3), lung cancer (3). Labolatory data showed high titers of BNP; 14.3-4095 (m=1266) and KL-6; 198-6750 (m=1497). ANA were all positive, other auto-Ab were as follows; Topoisomerase Ab (4/8), Centromere Ab (2/7), RNP3 (2/5). All cases but one complicated with concentric hypertrophy (one with eccentric hypertrophy), two cases showed outflow obstruction like HOCM. Severest case was a woman in her 40s, having past history of renal crisis suffered lethal refractory heart failure with CAVB in spite of pacemaker insertion. [Conclusions] Renal crisis, and IP were thought to be risk factors of myocardial involvement of SSc. Some cases were consulting with cardiologist independently. We should not hesitate order sonographic exam for screening, especially SSc patients with risk factors.

W50-1

Therapeutic Effects of Rituximab on cutaneous manifestations of Systemic Sclerosis

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Conflict of interest: None

[Objective] Systemic sclerosis (SSc) is a refractory autoimmune disease that causes skin sclerosis, blood flow disorders in various organs. In September 2021, the indication of rituximab (RTX) was expanded to SSc. Our department has been treating patients with rapidly progressing skin hardening, which has a very high risk of affecting life prognosis. In this study, the course of disease was retrospectively examined. [Methods] Twelve SSc patients who visited our department were diagnosed according to the 2013 ACR/EULAR classification criteria. The disease type was diffuse cutaneous SSc in all cases. The mean age of SSc patients was 49.6 ±21.8 years, the duration of illness was 7.8±9.9 years, and the total skin thickness score (TSS) was 24.8±8.3. [Results] TSS in SSc patients was 19.3±9.9 at 1 month, 18.2±10.2 at 3 months, 16.8±10.4 at 6 months, and 15.6±10.3 at 1 year after the administration of rituximab. Two years had passed for 6 patients, and many of them had a good response, with a TSS of 8.8±7.4. RTX has a good therapeutic effect, but there are some cases where the effect is poor. [Conclusions] RTX is a treatment that can be expected to be effective in SSc, but there are cases where the effect is poor, so it is necessary to accumulate cases in the future.

W50-2

Efficacy and safety of nintedanib in interstitial lung disease associated with connective tissue disease

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Conflict of interest: None

[Objective] This study aimed to evaluate whether low-dose initiation and escalation of nintedanib (NTD) improves drug continuation rates and usefulness in interstitial lung disease associated with connective tissue disease (CTD-ILD). [Methods] We included 48 patients who initiated NTD in our hospital from December 2018 to September 2022. We examined the discontinuation rates due to adverse events, overall continuation rates, maintenance doses, cumulative doses, the change in forced vital capacity (FVC), and adverse events from medical records. We compared the outcomes between the high-dose initiation (HD) group and the low-dose initiation (LD) group. [Results] Patient characteristics of the two groups showed no apparent differences, and the discontinuation rate due to adverse events and the overall continuation rates were identical in both groups. Although the maintenance doses of NTD were similar in both groups, the cumulative doses were significantly higher in the HD group than in the LD group. Changes in FVC were markedly greater in the HD group than in the LD group. Adverse events resulting in dose reduction or discontinuation were in 31 patients, with 18 seen at the 300 mg doses. [Conclusions] The low-dose initiation of NTD achieved no improvement in drug continuation rates.

W50-3

A case of successful immunosuppressive therapy in a patient with PVOD-like morphology during exacerbation of CTD-PAH caused by long-term MCTD~SSc+SS

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Conflict of interest: None

[Case] A 54-year-old woman was treated with pulmonary vasodilators for CTD-PAH caused by MCTD~SSc+SS for 30 years, with a history of induction-therapy by steroid pulse and POCY. Even under the administration of Masitentan 100 mg, Riociguat 4.5 mg, and Celexipag 2.8 mg, dyspnea on exertion worsened and she was admitted to the hospital. Chest CT showed lobular central shadows, which suggested PVOD. As a possible treatment before lung transplantation, we attempted enhancement of immunosuppressive therapy with high-dose steroids and MMF. Celexipag was gradually decreased because of doubt on drug-induced overdilation of pulmonary vein. In the clinical course, lung shadows, oxygen demand, and exercise tolerance improved, and BNP (738 to 316 pg/ml) and TRPG (65 to 49 mmHg) were both reduced. [Clinical Significance] In this case, we tried immunosuppressive therapy as a possible treatment for long-term CTD-PAH before lung transplantation, and the patient responded well to the therapy, suggesting that inflammatory causes may be present even in chronic CTD-PAH.

W50-4

A case of systemic sclerosis after COVID-19 vaccination, was worse skin sclerosis, interstitial pneumonia with pleuritis despite early treatment with rituximab

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Conflict of interest: None

[Case] A 38-year-old man noticed swelling of his face, stiffness of his fingers after COVID-19 vaccination in September 2021. He visited Sagamihara National Hospital due to being worse the symptoms at the end of May 2022. Severe sclerosis was observed on both arms, the face, neck, and around chest, with Raynaud's phenomenon, fingertip ulcers, and interstitial pneumonia. Anti-Scl-70 antibody was positive. He was diagnosed with systemic sclerosis. From June, he was treated with rituximab (RTX) (375 mg/m^2 each week for 4 weeks). However, his skin sclerosis, interstitial pneumonia were worse with CRP elevation and pleuritis. Antibacterial treatment for 2 weeks was not effective, and the neutrophil CD64 molecule expression count (as a marker for infection) was low. We considered that the symptoms were not infection and the flare of systemic sclerosis. Treatment of prednisolone (PSL) 30 mg/day and cyclophosphamide pulse therapy (IVCY) were initiated. CRP became negative, and pleuritis and interstitial pneumonia were improved. He is continuing IVCY every 4 weeks and tapering PSL dose. [Discussion] Despite early RTX treatment, the disease was worse and improved with PSL and IVCY therapy. We report a valuable case because there is still insufficient information about RTX for sclerosis.

W50-5

A case of systemic scleroderma and autoimmune hepatitis which treated with rituximab

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Conflict of interest: None

[Case] 51-yo. female. She was diagnosed systemic scleroderma 4 years ago. She was started to treat with rituximab (RTX) due to rapid progressive skin sclerosis in February X. RTX was effective, and skin score become better. In June X, B cell count increased, and she felt her skin was harder. We planned to restart RTX, however laboratory test revealed severe hepatic damage. A liver biopsy was performed on June 29 X. As a result of liver biopsy, autoimmune hepatitis (AIH) was diagnosed, and treatment was started with PSL. After that, we started administering RTX in August X for exacerbation of skin sclerosis. In addition to improving skin sclerosis, liver function also improved promptly. Since then, PSL has been gradually decreasing, but there have been no signs of recurrence of AIH. [Clinical Significance] The efficacy of RTX for skin sclerosis in SSc has been shown in the DESIRES study. In this case, liver damage appeared at the same time as the number of B cells increased, suggesting the onset of AIH as a pathology similar to immune reconstitution syndrome. There are several reports that RTX was effective against refractory AIH, and in this case as well, RTX was effective not only for skin sclerosis of SSc but also for AIH.

W50-6

Heating of the upper extremities increases Angiopoietin-1 concentrations at fingertips and also induces improvements in capillary morphology

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Conflict of interest: Yes

[Objective] Angiopoietin-1 (Angpt1) is a vascular stabilizing factor, and its decrease may trigger capillary twisting and branching. Angpt1 has been reported to be decreased in systemic sclerosis (SSc), and we have reported that heating of the elbows with disposable warmers increases Angpt1 levels at the fingertip as well as alleviating Raynaud's phenomenon in patients with SSc. (Mod Rheumatol. 2022; 32: 351) Here, we observed whether the increase in Angpt1 caused by heating alters the morphology of the capillaries in the nail fold. [Methods] The participants underwent six capillaroscopy examinations (Cap) every four weeks, and both elbows were heated with warmers during the 2nd to 4th Cap. Fingertip blood samples were taken at the same time of 2nd, 3rd, 4th, 5th Cap to measure Angpt1 level. [Results] Twenty SSc patients participated in the study. The fingertip Angpt1 averaged 1918 pg/mL before warming and increased to an average of 5172 pg/mL at 4 weeks after the start of heating. The rate of front-most capillaries with normal hairpin-loop shape averaged 20.2% in the two times Caps before heating but increased to 26.6% in the two times Caps during heating. [Conclusions] Heating of the elbows increases Angpt1 level at the fingertips and also induces an improvement in capillary morphology.

W51-1

Synovial Tph cells of rheumatoid arthritis are pleiotropically involved in the pathogenesis

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Conflict of interest: None

[Objective] Peripheral helper T (Tph) cells involved in B cell help and ectopic lymphoid structure formation are present at the RA inflammatory sites. However, it has not been elucidated how Tph cells are involved in RA pathogenesis other than antibody production. We analyzed Tph cells and other CD4$^+$ T cell subsets at the RA inflammatory sites using single cell RNA sequencing (scRNA-seq). [Methods] We analyzed 9 patients with ACPA-positive RA, who underwent total knee arthroplasty or joint puncture between 2020 and 2022. All patients were female, the mean age was 64 (34-80) years, and the mean DAS28-ESR was 4.06 (1.58-5.41). We isolated CD4$^+$ T cells from synovial tissue, synovial fluid and peripheral blood, and conduced scRNA-seq, flow cytometry and in vitro analysis. [Results] scRNA-seq identified CD4$^+$ T cell clusters such as Tph cells, regulatory T cells, and cytotoxic T cells. The frequency of Tph cells significantly correlated with disease activity. Tph cells were classified into 2 clusters by chemokine receptors. In response to RA disease activity, Tph cells expressed signature genes, which target various immune cells. [Conclusions] Tph cells are involved in RA pathogenesis by targeting various immune cells in the inflammatory tissue.

W51-2

Analysis of autoimmune response in lung and salivary gland lesions of anti-ARS antibody syndrome

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Conflict of interest: None

[Objective] The aim of this study was to analyze in detail the humoral immune response in lungs and salivary glands of patients with anti-ARS antibody (Ab) syndrome. [Methods] Ab-secreting cells were single-cell sorted from BALF of 3 serum anti-Jo-1 and 3 anti-EJ Ab-positive ILD patients each, and the sequences of Abs were obtained, from which 119 and 81 monoclonal Abs were produced, respectively. In addition, 76 and 23 Abs were produced from salivary glands from 1 serum anti-Jo-1 and 1 anti-EJ antibody-positive patient each. The autoreactivity of the Abs were

examined. Anti-ARS Ab-producing cells in salivary glands were detected by immunostaining. [Results] Of the BALF-derived Abs from serum anti-Jo-1 and anti-EJ Ab-positive patients, 14.3% and 53.4% bound Jo-1 and EJ, respectively; anti-Ro52 Abs were also found in 8.4% and 6.9%. Furthermore, 22.4% and 60.9% of salivary glands-derived Abs also recognized Jo-1 and EJ, and 5.3% and 26.1% recognized Ro52. In salivary gland tissues, there were cells co-stained with anti-CD138 Abs and GFP-fused recombinant autoantigens, confirming that autoantibodies are also produced in salivary glands. [Conclusions] We revealed that anti-ARS and anti-Ro52 Abs were produced in lung lesions and salivary glands.

W51-3

Low avidity, which is observed in anti-citrullinated protein antibodies, is not a general feature of autoantibodies

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Conflict of interest: None

[Objective] Production of ACPA is implicated in the pathogenesis of RA. It has been reported that the avidity of ACPA is lower than that of antibodies against foreign antigens, but it is unclear whether low avidity is a general feature of autoantibodies. So we compared avidity of some autoantibodies with ACPA. [Methods] RA (n=180), SLE (n=10), CREST syndrome (n=12), MCTD (n=7) patients were included. some RA patients have Sjogren syndrome (n=14) or Hashimoto thyroiditis (n=10). Avidity of antibodies against 4 citrullinated peptide antigens (CCP, fibrinogen, a-enorase, vimentin), 3 foreign antigens (influenza HA, diphtheria toxin, measles), and 5 autoantigens (dsDNA, centromere, U1-RNP, SS-A, TPO) was measured by adding 1M of NaSCN to ELISA. [Results] All ACPAs showed lower avidity than antibodies against foreign antigens, whereas the avidity of other autoantibodies, except for anti-dsDNA antibody, was comparable to that of antibodies against foreign antigens. The avidity of anti-dsDNA antibody was lower than ACPA. There was a correlation in the avidity between some ACPAs. [Conclusions] Low avidity is not a general feature of autoantibodies, but implies distinct mechanism of ACPA and anti-dsDNA antibody production. The correlation in the avidity between ACPAs implies cross-reactivity.

W51-4

Expression patterns of cytokine genes in human dendritic cell-derived osteoclasts and effects of JAK inhibitors

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a systemic autoimmune disease with synovitis and joint destruction. The JAK inhibitor partially corrects inflammation and immune abnormalities by acting on the pathopoietic cells. On the other hand, we have found dendritic cell-derived osteoclasts (DC-OCs) in the synovium of RA patients and characterized their role in pathogenesis. However, the expression of cytokines in the DC-OC and the effects of JAK inhibitors remain unclear. [Methods] We compared the expression of cytokine genes in DC-OCs and monocyte-derived osteoclasts (Mo-OCs) by quantitative PCR. Monocytes and immature dendritic cells (DCs) were treated with the JAK inhibitors Tofacitinib (Tofa) and Baricitinib (Bari), and the differentiation of DC-OCs was examined. [Results] In the DC-OC differentiation system, the expression of *IFN-γ* and *HTRA1*, but not *L-1β*, *IL-6*, and *TNF-α* decreased in DC-OCs compared to Mo-OC. The number of TRAP-positive cells decreased in a dose-dependent manner (0.01, 0.1, 1 μM) when monocytes, but not immature DC were treated with Bari and Tofa. [Conclusions] *IFN-γ* decreased in DC-OCs may suppress osteoclast differentiation. JAK inhibitors may also play a role in suppressing bone destruction by having inhibitory effects on DC-OC differentiation.

W51-5

Expression patterns of intronic microRNAs and host genes in fibroblast-like synoviocytes

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Conflict of interest: None

[Objective] Genetic loci, including intronic microRNAs (miRNAs), produce miRNA and host protein transcripts. There might be an enhancement or suppression of function between miRNA and its host protein as a result of their influence on each other, but this is currently unclear. We investigated the expression pattern of intronic miRNAs in fibroblast-like synoviocytes (FLS). [Methods] RNA was extracted from FLS harvested from patients with rheumatoid arthritis. miRNA expressions were comprehensively analyzed using next-generation miRNA sequencing. FLS were stimulated with several cytokines and the expression levels of the intronic miRNAs and their host genes were analyzed using RT-qPCR. [Results] Among 1,881 miRNAs, 75 with read counts >1000 were identified. Of the 75, 18 (24%) were intergenic miRNAs and 28 (37%) were intronic miRNAs. Analysis of the top eight candidates in FLS stimulated with cytokines revealed that some miRNAs, such as miR-21-5p and miR-93-5p, were upregulated in parallel with host genes. [Conclusion] Intronic miRNAs have biological functions, and their interaction with host genes emphasize their biological significance. Further investigations of the identified candidates will help elucidate the function of FLS in joint diseases.

W51-6

Proinflammatory roles synovium-resident macrophages in the pathogenesis of rheumatoid arthritis

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Conflict of interest: None

[Objective] Synovium-resident macrophages (SRMs) are involved in the maintenance of tissue homeostasis. In rheumatoid arthritis (RA), monocyte-derived macrophages are considered important in inflammatory pathology. However, the functions of SRMs in RA pathogenic conditions are not well understood. In this study, we analyzed the response of SRMs to various inflammatory stimuli. [Methods] Macrophages were isolated from synovial tissue of non-inflammatory osteoarthritis patients collected at the time of arthroplasty and cultured with immune complexes and cytokines related to RA pathophysiology. Monocyte-derived macrophages were used as controls to compare changes in surface molecules and gene expression. In addition, various stimulated SRMs and fibroblasts were co-cultured, and changes in the gene expression of fibroblasts were analyzed. [Results] Stimulation with TNFα+PGE2 or TNFα+IFNγ or immune complex stimulation resulted in decreased surface expression of MerTK and CD163 and increased gene expression of TNFα, IL1-β, HBEGF, and SPP1 in monocyte-derived macrophages, while SRMs showed little change in these expressions. However, fibroblasts showed increased expression of inflammatory genes such as IL6. [Conclusions] SRMs play proinflammatory roles during the inflammatory process of RA.

W52-1

The regulatory mechanisms of a low molecular weight compound, BIK387, BAFF signaling inhibitor, in suppression of B cell function

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Conflict of interest: None

[Objective] We discovered a BAFF signaling inhibitor, BIK-387, which shows suppressive effect on production of autoantibody *in vivo*. In this study, we investigated the mechanisms of BIK387 on B cell function in both mice and human cells. [Methods] Splenic lymphocytes from MRL/lpr mice orally received BIK387 and BIK387-treated human PBMC were stimulated with anti-IgM, CD40, IL-21 and BAFF for 7 days. Cell proliferation, the expression of cell surface markers (mice: B220, CD19 and CD138; human: CD19, CD38, IgD and CD138), production of anti-dsDNA antibody and IgG, and the gene expression were analyzed by XTT assay, FACS, ELISA and qPCR, respectively. [Results] Proportion of B cells and plasma cells, production of IgG and anti-dsDNA antibody, and the expression levels of *Blimp1* and *IRF4* in splenic lymphocytes of the MRL/lpr mice were reduced as compared with the control. Moreover, BIK387 suppressed proliferation of human PBMC and proportion of plasma cells among the cells. IgG production and the expression levels of *IRF4* and *Blimp1* were also suppressed in the cells. [Conclusions] Our data suggest that BIK387 suppresses B cell function by inhibition of B cell differentiation in both mice and human and that the compound has the possibility as an oral drug to treat autoimmune diseases.

W52-2

Butyric acid suppressed migration of human monocyte derived Dendritic Cell by inhibiting Actin polymerization

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Conflict of interest: None

[Objective] Butyric acid (BA) is known to improve chronic inflammation such as inflammatory bowel disease and arthritis. dendritic cells (DC) activate locally inflamed, migrate to regional lymph nodes, and activate naive T cells. We investigated the effect of butyric acid on the migration ability of human dendritic cells. [Methods] CD14+ Monocytes were purified by positive selection from PBMC. Cells were cultured in the presence of GM-CSF and IL-4 for 5 days. After culturing for 5 days, cells were matured with LPS for 24 hours. BA was administered at different dose or period. Cell were analyzed surface antigen by flow cytometry, migration assay, Actin staining and western blot (WB). [Results] BA downregulated the CCR7 expression of DC and migration toward both CCL21 and FBS. BA changed the cell morphology as a round shape and poor formation of dendrites and pseudopodia. It suggested that BA acts on the cytoskeleton. Actin staining revealed that BA inhibited actin polymerization of DC in a dose-dependent manner. WB revealed that BA decreased expression of mDia1, RhoA, and CDC42. The amount of β-actin was not downregulated. Rho activator improved DC migration and actin polymerization. [Conclusions] Butyric acid suppresses migration of DC by inhibiting mDia1 medicated actin polymerization.

W52-3

Clock Controlled Gene Tef Regulates Cell Proliferative Activity and TNF-alpha production

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Conflict of interest: None

[Objective] We have reported the expression of various clock genes in leukocytes from RA patients correlates with their disease activities. However, the central role of clock genes on the joint destruction of RA remains unclear. The aim of this study is to examine the roles of clock genes on the pathogenesis of RA. [Methods] After transfected siRNA of clock related genes including *Tef*, RA-FLS were stimulated with or without IL-6/sIL-6R (100 ng/ml) or TNF-α (10 ng/ml) to examine the cell viabilities by WST-8 assay. Mouse embryonic fibroblasts (MEFs) were isolated from of *Tef*-/- or wild-type mouse embryos to measure cell viabilities by WST-8 assay and Foci-formation assay. Expressions of *TNF-α* and *IL-6* mRNA in spleen of *Tef*-/- or wild-type mouse were measured by RT-qPCR. [Results] By silencing *Tef,* cellular viabilities were significantly increased under the stimulation of IL-6/sIL-6R and TNF-α. Also, cellular viabilities and the number of formed focus were significantly increased in *Tef*-/- MEFs compared to wild type. In addition, Expressions of *TNF-α* mRNA in spleen of *Tef*-/- mouse were increased compared to wild-type mouse. [Conclusions] The results suggest that clock related gene *Tef* is involved the pathogenesis of RA by affecting cellular viabilities and TNF-α production.

W52-4

Immuno-pathogenic analysis of idiopathic multicentric Castleman disease (iMCD-NOS), an intractable rare disease, using xenopeltid immunodeficiency mice

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Conflict of interest: None

[Objective] Castleman disease (CD) is a rare lymphoproliferative disorder characterized by hyper gamma-globulinemia and chronic inflammation. Among them, idiopathic multicentric Castleman disease (iMCD-NOS) has a poor prognosis and its pathogenesis is largely unknown, [Methods] To clarify the molecular pathogenesis of iMCD-NOS, immunodeficient mice xenotransplanted with patients lymph node cells exhibited iMCD-NOS like inflammation with body weight loss and elevation of human gamma-globulin (IgG, IgA, IgE), indicating that the iMCD-model mice has been established. [Results] Expansion of $CD4^{+}PD\text{-}1^{high}CXCR5^{-}CCR2^{+}$expressing peripheral helper T cell (Tph) was observed in the spleen and liver and showed a increase of CXCL13 chemokine with IL-6 elevation in the sera of mice. The expression of CXCL13 was detected in Tph cells. Depletion of human $CD3^{+}$Tcells from grafts failed to induce iMCD like lethal inflammation in grafted model mice. Furthermore, an anti CXCL13 antibody also blocked the development of lethal inflammation and improved the survival in the grafted mice. [Conclusions] There data suggested that CXCL13 producing Tph cell with activation of B cell and IL-6 play a critical role in the pathogenesis of iMCD, indicating that iMCD-NOS is an T cell abnormal immunoregulatory disorder.

W52-5

Oxytocin expression kinetics, analgesic and antidepressant mechanisms in a reserpine-induced fibromyalgia rat model

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Conflict of interest: None

[Objective] To evaluate the reserpine repeated administration fibromyalgia (FM) model and to assess oxytocin (OXT) expression kinetics and its effects. [Methods] OXT-mRFP1 transgenic (Tg) rats and OXT DREADDs Tg rats were used. Saline or reserpine was administered for 3 days, von Frey test and forced swim test were performed. Hypothalamic OXT-mRFP1 fluorescence intensity and the number of TPH-ir cells in dorsal raphe (DR) and TH-ir cells in locus ceruleus (LC) were measured. *OXT* mRNA was measured using *in situ* hybridization. OXT DREADDs Tg rats were divided into saline or CNO groups after reserpine administration, and von Frey test and forced swim test were performed. After administration of OXT receptor antagonist (OXTR-A), the rats were treated with CNO, then, were performed the von Frey test. [Results] Mechanical nociceptive threshold was decreased and immobility time was prolonged. FM model does not change intensities of OXT-mRFP1 fluorescence. TPH-ir cells in DR and TH-ir cells in LC were decreased. Oxytocin neuron activated by

CNO in FM model of OXT DREADDs, therefore mechanical nociceptive threshold and depression were improved. The effects of CNO are ablated by co-treatment with OXTR-A. [Conclusions] Increasing endogenous OXT in FM may have analgesic and antidepressant effects.

W52-6

Spatiotemporal analysis of gene expression associated with plastic brain changes in mouse models of arthritis

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Conflict of interest: None

Objective: Rheumatoid arthritis (RA) is complicated by psychiatric symptoms such as depression. There are many reports of organic abnormalities in RA brain. But it is unclear when these abnormalities appear and where they are distributed. In this study, we analyzed the spatiotemporal gene expression changes in the arthritis model mice brain. Methods: Collagen induced arthritis (CIA) mice were generated. Whole brains were collected at five stages of arthritis and divided into six sections. RT-PCR was performed using RNA extracted from the divided brains, and the expression of proinflammatory cytokines, glial markers, and neurogenesis-related factors were semi-quantified. Results: IL1β and DDIT4 were induced at formative stage in a wide range of brain regions. IL6, ITGAM and NR3C1 were induced at pre-onset stage, especially in the olfactory bulb (OB). IL6 expression in the OB was correlated with loss of body weight and appetite. Conclusion: Induction of IL1β and DDIT4 suggest that plastic changes may occur in a wide range of brain regions during arthritis formation. Gene expression characteristic of the OB suggested that brain abnormalities existed prior to the onset of arthritis and may be associated with clinical symptoms.

W53-1

Clinical features of osteomyelitis of the jaw in patients with rheumatic diseases

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Conflict of interest: None

[Objective] The risk factors for the development of osteomyelitis of the jaw (ONJ) in rheumatic diseases (RD) are unknown because of the low incidence. In this study, we aim to clarify the clinical problems in cases of ONJ associated with RD. [Methods] We retrospectively identified cases of ONJ from the medical records of outpatients with RD and analyzed the clinical characteristics of these patients. [Results] Twenty-eight patients with RD, including 24 patients with rheumatoid arthritis (RA), had ONJ. There were 26 females. The mean age was 66.4±12.1 years at the onset of osteomyelitis of the jaw. Fifteen patients (53.5%) underwent tooth extraction prior to osteomyelitis and 10 (35.7%) had dental infection. 21 patients received bone resorption inhibitors, 15 (71.4%) for treatment and 6 for prevention. Steroids and immunosuppressive drugs (IS) were administered in 19 and 20 patients, respectively. Patients with RA had low disease activity, but 21 of 23 patients (91.3%) had Steinbrocker's stage IV. [Conclusions] RA is the most common RD associated with ONJ, and they had osteoporosis and advanced bone destruction. Dental infections were more common in RD patients with ONJ, and IS therapy was used for RD, suggesting that oral hygiene was important in the prevention of ONJ.

W53-2

Eye complications and related factors in rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify the effects of recent advances in drug therapy on ocular complications associated with rheumatoid arthritis (RA). [Methods] We investigated the presence and frequency of ocular symptoms in 341 RA patients, and analyzed factors related to ocular complications. [Results] Complicated eye disease was observed in 145 patients (42.5%) consisting of 74 cases of cataract (21.7%), 44 of dry eye (12.9%), 20 of glaucoma (0.6%), 6 of keratitis (0.02%), and 32 of other diseases. The patients were divided into group A with dry eye and group B without dry eye. There was no significant difference in average age between groups A and B (69.5 years vs. 66.3 years, respectively). Disease duration was significantly different between groups A and B (24.4 years vs. 14.9 years, respectively). A group without dry eye (group B') matched for disease duration with group A was analyzed by stage and class. There were no significant differences in Stage I, II/III, IV, and Class 1, 2/3 between the two groups. [Conclusions] Dry eye was associated with disease duration, but no other related factors were identified. Detailed evaluation of disease activity is necessary to prevent the occurrence of ocular complications.

W53-3

Relationship between glucocorticoid-induced adrenal insufficiency and Health-related Quality of Life (HRQOL) of patients with autoimmune diseases

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Conflict of interest: None

[Objective] To determine how glucocorticoid-induced adrenal insufficiency is related to HRQOL in patients with rheumatic diseases. [Methods] This cross-sectional study included patients with rheumatic disease who underwent adrenocorticotropic hormone (ACTH) tests to assess adrenal function. At the same time, HRQOL was assessed using the SF-36, and the presence of adrenal insufficiency symptoms was also investigated using a questionnaire to analyze the relationship with adrenal function. [Results] Fifty-three of 89 (59.5%) patients with rheumatic disease had insufficient adrenal response. Eight subscales of the SF-36 showed no significant differences between patients with and without insufficient adrenal response, and the 3-component summary score was similar. In terms of adrenal insufficiency symptoms, the proportion of patients with decreased motivation was significantly higher in the insufficient adrenal response group. [Conclusions] In patients with rheumatic diseases, glucocorticoid-induced adrenal insufficiency was not related to HRQOL. However, decreased motivation is associated with insufficient adrenal response, and this symptoms should be kept in mind in patients on long-term glucocorticoids.

W53-4

Efficacy and safety of nintedanib in progressive fibrosing interstitial lung disease (ILD) in patients with connective tissue diseases

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of NTN in CTDs patients with ILD in our institute. [Methods] Thirteen patients with CTDs who had received concomitant NTN for relapse of ILD in our department by September 2022. Patients were prospectively followed up according to the examination schedule, and KL-6, SP-D, %VC, and K-BILD scores were analyzed at 12 months. [Results] The mean age was 59.3±15.1 years. The mean disease duration was 66.8±52.3 months. The underlying diseases were polymyositis/dermatomyositis in 5 cases, systemic scleroderma in 3, rheumatoid arthritis in 3, mixed connective tissue disease in 1, and microscopic polyangiitis in 1 case. Steroid dosage at baseline was 11.1±13.4 mg/day of prednisolone (PSL) equivalent, KL-6 was 1404.0±1244, SP-D was 133.0±66.4 ng/ml, %VC was 71.3±15.8%, and K-BILD score was 72.1±21.9. At 12 months after NTN commencement, the dose of PSL was 5.3±2.6 mg/day, KL-6 was 1133.2±907.2, SP-D was 158.8±127.9 ng/ml, %VC was 73.9±19.8%, and the K-BILD score was 73.6±16.9. Although

there were no significant change from the baseline in each items, PSL dose and %VC were slightly improved. Adverse events were observed in 4 patients. [Conclusions] This study will suggest that concomitant NTN might enable to reduce the dose of PSL and prevent progression of ILD.

W53-5

The Efficacy and safety of nintedanib in connective tissue disease - associated interstitial lung disease (CTD-ILD)

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Conflict of interest: None

[Objective] To elucidate the efficacy and safety of nintedanib in CTD-ILD in our department. [Methods] Twenty-one CTD patients were retrospectively analyzed about the efficacy and safety under the administration of nintedanib between January 2020 and September 2022. [Results] Baseline patient-characteristics (n=21) was as follows; systemic sclerosis (28.6%), rheumatoid arthritis (28.6%), ANCA-associated vasculitis (14.3%), anti-synthetase syndrome (14.3%), Sjögren's syndrome (9.5%) and IgG4-related disease (4.7%). Mean age was 71.2 ± 1.9 years, and observation period was 10 ± 2 months. NSIP was the most common CT-imaging pattern (61.9%). Serum level of KL-6 was 1452.8 ± 219.3 U/ml at baseline and 1153.7 ± 224.0 U/ml after treatment (follow-up period: 8.3 ± 2.1 months), there was no statistical significance (*P=0.34*). Sixteen adverse events were revealed; gastrointestinal symptom (n=12), liver enzyme dysfunction (n=8). Although dose reduction was necessary in 95.2%, the treatment persistence rate was 95.2%. [Conclusions] In our study, nintedanib in CTD-ILD resulted in no significant decrease about KL-6 value, but the value had the tendency of decrease, and the treatment persistence rate was over 95%. It is suggested that nintedanib in CTD-ILD might inhibit the progression.

W53-6

Clinical efficacy and safety profile of nintedanib in patients with CTD-ILD

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Conflict of interest: None

[Objective] To clarify the effect of nintedanib (NTB) on CTD-ILD patients. [Methods] The subjects were patients who started treatment with NTB at our hospital and had a confirmed diagnosis of CTD. 1) Background, hematological findings and lung function, and clinical course were analyzed. 2) Adverse events were analyzed, and the patients were divided into two groups based on the appearance of gastrointestinal symptoms (GS) and the continuation status due to them, and the background was retrospectively compared. [Results] 1) 38 cases (male: 13/female: 25), age: 60.3 ± 12.8 years, clinical diagnosis: SSc 23, RA: 11, SS: 7, PM: 4, MPA: 2 (including overlapped). KL-6 at the baseline: 1177.9 ± 916.5 U/ml, %VC: 70.7 ± 21.4%, no significant difference was observed after half a year. 19 were evaluated by CT after the start of NTB, and 6 got worse (31.6%). None had an acute exacerbation in 33.9 person-year. 2) Adverse events: GS 29, liver injury 8, fatigue 1. SSc cases were significantly more common in 29 with GS than 9 without GS (72.4% vs 22.2%, P=0.016). Of 29 with GS, 6 who discontinued had significantly shorter days to GS than 23 who did not (12.7 ± 10.8 vs 114.6 ± 110.1, P < 0.01). [Conclusions] Whereas NTB may suppress acute exacerbation of CTD-ILD, GS were more common in SSc.

W54-1

The study of effect of initial dose of glucocorticoids and its duration on the development of osteonecrosis during remission induction therapy in patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] We define the trends in the development of osteonecrosis (aseptic necrosis; AN) and changes in glucocorticoid dosage in patients with systemic lupus erythematosus (SLE). [Methods] SLE patients who received pulse therapy or prednisolone (PSL) ≧1 mg/kg/day from October 2006 to September 2022 were retrospectively evaluated. [Results] AN developed in 17 of 88 SLE patients. 11 cases (64.7%) occurred within 2 years. Significantly more AN occurred in patients who received pulse therapy (p<0.01). Of the 83 patients who started with PSL 1 mg/kg/day, 40 (48.1%) were still taking the same dose at 4 weeks, and AN occurred in 16 patients and was significantly more frequent (p<0.01). Among those receiving pulse therapy, 31 patients with PSL 1 mg/kg/day at 4 weeks had significantly more AN than those with less than (p<0.01). Among 2 years of observation, significantly more AN occurred within 2 years in the 4-week initial dose continuation group (p=0.01). In cases with onset after 2016, both pulse therapy (p=0.02) and 4-week dose continuation (p<0.01) decreased. AN during the first 2 years has decreased in recent years: 3/49 (6.1%) vs. 8/39 (20.5%). [Conclusion] 4-week continuation of high-dose glucocorticoid for induction therapy in SLE may be a risk for the development of osteonecrosis.

W54-2

The effectiveness of Nintedanib for PF-ILD in reducing the markers of pulmonary fibrosis and sparing corticosteroids

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Conflict of interest: None

[Objective] Nintedanib (NTB), anti-fibrotic drug, has recently been approved for progressive fibrosing interstitial lung disease (PF-ILD) and widely used for various kinds of ILD including connective tissue diseases (CTD)-ILD. Because of the lack of the evidence of effectiveness of NTB for PF-ILD, we aimed to unveil the effectiveness and adverse events of NTB on PF-ILD in our hospital. [Methods] Thirty-two PF-ILD patients, including 29 CTD-ILD patients, were enrolled. We assessed drug retention rate and the effects on serum KL-6 and SP-D and corticosteroids (CS) sparing. [Results] Drug retention rate at 2 year was 76% using Kaplan-Meyer method. SP-D, KL-6 and CS dose were significantly reduced in 3, 6 and 12 months, respectively. In 23 patients, who continued NTB for more than 6 months, NTB dose was significantly higher in those whose KL-6 reduced more than 10% in 6 months than in others. ROC analysis showed the cut-off value 200 mg, sensitivity 100% and specificity 63%. Although diarrhea as adverse drug reaction tended to occur in younger patients, we could not find any significant risk factors for diarrhea. [Conclusions] It was suggested that NTB more than or equal to 200 mg was effective for PF-ILD in reducing the markers of pulmonary fibrosis and sparing CS dose.

W54-3

A study of echocardiographic screening for collagenous pulmonary arterial hypertension in our clinic

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Conflict of interest: None

[Objective] CTD-PAH, especially SSc-PAH has the poorest prognosis. Recently, 2022 ESC/ERS Guidelines for pulmonary hypertension have

described the importance of risk assessment in SSc and revised the criteria for PH (mean PAP > 20 mmHg). In this study, we retrospectively reviewed the results of echocardiographic screening in patients with CTD. [Methods] Echocardiographic screening was performed in 234 patients with Sjögren's syndrome (SS), 182 with scleroderma (SSc), 111 with systemic lupus erythematosus (SLE), 26 with mixed connective tissue disease (MCTD) and 23 with poly- and dermatomyositis (PM/DM). [Results] A positive correlation was found between age and sPAP in SSc, and between age and PVR in SS. In the ROC analysis, the cut-off value of TRV for predicting PAH diagnosis was less than 3.1 m/s (AUC 0.891, sensitivity 57.1%, specificity 84.2%), and the cut-off value of the TAPSE/sPAP ratio was less than 0.5 mm/mmHg (AUC 0.870, sensitivity 71.4%, specificity 96.8%). [Conclusions] CTD-PAH has a poor prognosis and screening tests are important, and the combination of TRV and TAPSE/sPAP ratio may enable early diagnosis of PAH.

W54-4

Chest high resolution computed tomographic examination is useful to find concomitant lung cancer and coronary stenosis for the patients with immune-mediated inflammatory diseases

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Conflict of interest: None

[Objective] To evaluate the lung cancer (LC) and coronary insufficiency coincidentally found by chest CT in the screening for complicated lung diseases in the patients with immune-mediated inflammatory diseases (IMID). [Methods] CT images obtained in 1100 IMID patients from 2012 to 2022 were assessed. [Results] Eleven patients (7 females; mean age 67 years; 4 with RA; 2 with PsA; 2 with SLE; 1 with SSc; 1 with MCTD; 1 with Castleman disease; 4 with ILD) were diagnosed with LC. The histopathological findings included adenocarcinoma in 6, SCC in 4, and LC-NEC in 1 patient. For the treatment, surgical repair in 8 and chemotherapy in 2 patients were performed. Two patients died despite the treatment. Yet, thyroid cancers in 3, breast cancers in 2, and gastric cancers in 2 patients were also detected by CT. CAC in 70 asymptomatic patients were detected, and 13 of 70 needed surgery (Stent implantation in 9; CABG in 1). Aortic stenosis in 1 patient were treated with TAVI. Abdominal aortic aneurysm in 1 and superior mesenteric artery aneurysm in 1 patient were detected and treated. [Conclusions] The incidence of LC were higher in IMID (11/1100 patients) than in Japanese population (1/1000 population). CT examination is useful to find concomitant LC and coronary stenosis for IMID patients.

W54-5

Prognostic factors of interstitial lung disease: a 10-year longitudinal cohort analysis

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Conflict of interest: None

[Objective] This study aimed to analyze the prognostic factors in patients with connective tissue disease (CTD)-associated interstitial lung disease (ILD) and interstitial pneumonia with autoimmune features (IPAF) compared to other ILD (OILD) patients. [Method] We retrospectively collected data from 670 patients diagnosed as "interstitial pneumonia" or "pulmonary fibrosis" between 2011 and 2021 at Tomakomai City Hospital. We classified ILD patients into 3 groups of CTD-ILD, IPAF, and OILD. Mortality and prognostic factors were assessed using Kaplan-Meier methods and Cox proportional hazards respectively. [Results] The prognosis of OILD group was significantly worse than CTD-ILD and IPAF group (adjusted $p<0.001$, <0.01, respectively), but that of CTD-ILD and IPAF was similar (adjusted $p=1.0$). Multivariate analysis revealed the ILD classification ($p=0.11$, Hazard ratio (HR) 0.85 [0.70-1.04]) was not independent prognostic factor. However, age ($p<0.001$, HR1.03 [1.02-1.05]), man sex ($p<0.001$, HR 2.08 [1.51-2.87]), initial CT patterns as usual interstitial pneumonia (UIP) ($p<0.01$, HR 2.68 [1.27-5.67]) and diffuse alveolar damage (DAD) ($p<0.001$, HR 7.99 [3.85-16.60]) were independent prognostic factors. [Conclusion] Presence of autoimmune features was not a prognostic factor of ILD.

W54-6

Massive renal AA-amyloidosis: a histologically and biochemically distinctive subtype of SAA protein in reactive systemic amyloidosis

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Conflict of interest: None

[Case Report] A 50-year-old woman had been diagnosed as having RA at the age of 22, and revealed reactive AA amyloidosis at the age of 35. She died 3 months after admission. Autopsy revealed AA amyloidosis including the kidneys. Amyloid fibril proteins were investigated biochemically by predicted reaction monitoring with LC-MS/MS. Imaging MS was also used to confirm the location of SAA polymorphisms. Renal amyloid deposits were analyzed. LC-MS/MS revealed SAA isoforms 1.1, 1.3, 1.4, and 1.5. SAA 1.1 and 1.3 showed strong signals in both the cortex and medulla; SAA 1.4 and 1.5 were also present in both the cortex and medulla, but the signal was weaker in the former than in the latter. Merged images of the SAA 1.1 and 1.3 isoforms showed a similar distribution in the cortex, but SAA1.1 was more strongly deposited than SAA1.3 around interlobar arteries in the medulla. Merged images of the SAA 1.1 and 1.4 isoforms also showed a different distribution. LC-MS/MS detected SAA subtypes 1.1, 1.3, 1.4, and 1.5 in the renal tissue of this patient with AA amyloidosis associated with RA. Among the SAA isoforms, SAA1.1, 1.3, 1.4 and 1.5 were deposited in both the medulla and cortex of the kidney, but each of these samples showed different signal strengths and distributions.

W55-1

Impact of concomitant methotrexate and glucocorticoid on drug retention of biologics and JAK inhibitors: the ANSWER cohort study

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Conflict of interest: Yes

[Objective] To clarify the impact of concomitant methotrexate (MTX) and glucocorticoid (PSL) on drug retention of biologics (Bio) and JAK inhibitors (JAKi) in RA patients. [Methods] Following treatment courses were included. [TNF inhibitors (TNFi) =2704, anti-IL-6 receptor antibody (aIL-6R) =1218, CTLA4-Ig=903, JAKi=487; Bio/JAK naive cases 50.4%, age 60.1y, female 83.6%, disease duration 10.3y, DAS28-ESR 4.3, combined MTX dose 7.2 mg/week (52.0%), and combined PSL dose 5.3 mg/day (36.6%)] in this multi-center, retrospective study. Reasons of discontinuation was classified into 4 major categories. Data was adjusted by potent confounders with a Cox proportional hazards model and evaluated at

36 months. [Results] Discontinuation rate due to ineffectiveness was aIL-6R=24.2%, CTLA4-Ig=33.9%, JAKi=36.2%, and TNFi=40.3%. In TNFi group, MTX significantly improved (Hazard Ratio [HR] =0.75; P<0.001), while PSL significantly worsened (HR=1.21; P=0.0045) the discontinuation rate. Discontinuation rate due to toxic adverse events was CTLA4-Ig=13.4%, TNFi=14.9%, aIL-6R=15.1%, and JAKi=17.7%. PSL significantly worsened the discontinuation rate of TNFi (HR=1.31; P=0.013) and JAKi (HR=2.05; P=0.0061). [Conclusions] Impact of MTX and PSL on drug retention of Bio and JAKi differed between the agents.

W55-2

Effectiveness of tsDMARDs vs bDMARDs on non-inflammatory pain in patients with rheumatoid arthritis -ANSWER longitudinal cohort study-

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Conflict of interest: Yes

[Objective] Non-inflammatory pain (NIP) is one of the remaining issues in rheumatoid arthritis (RA). The aim of this study is to investigate whether targeted synthetic (ts) DMARDs decrease NIP compared to biological (b) DMARDs in RA patients in a longitudinal multicenter cohort study. [Methods] We examined the association between the choice of b- or tsDMARDs and the persistence of NIP (defined as swollen joint count=0 and CRP<0.5 mg/dL and patient VAS>40 mm) at week 52 using multivariable logistic regression model. Confounding factors (age, sex, disease duration, smoking status, stage, class, titer of RF and ACPA, dose of MTX and PSL, the use of six painkillers including NSAIDs, and disease activity at baseline) were adjusted with inverse probability of treatment weighting estimated by generalized propensity score. [Results] In the treatment courses (TCs) in which patients continued b/tsDMARDs for 12 months (b: n=4067, ts: n=379), NIP was observed in 749 TCs (18%) of bDMARDs, 88 TCs (23%) of tsDMARDs. In TCs which achieved swollen joint count=0 and CRP<0.5 mg/dL, there was no statistically significant difference in NIP between bDMARDs and tsDMARDs [adjusted OR=0.95 (95%CI: 0.87-1.03, p=0.23)]. [Conclusions] bDMARDs and tsDMARDs are comparable to control NIP in RA patients.

W55-3

Assessing the Effect of JAK Inhibitors on Interstitial Lung Disease in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Background] Rheumatoid arthritis (RA) frequently involves interstitial lung disease (ILD). JAK2 signaling was found to be critical for lung fibrosis. [Objectives] We aimed to evaluate the effect of JAK inhibitors on ILD and assess the differences in effect by JAK selectivity. [Methods] We extracted the RA patients with ILD who received JAK inhibitors from October 2021 to September 2022 at our department. Disease activity, blood tests, respiratory symptoms, and imaging tests have been retrospectively reviewed to evaluate the disease activities of arthritis and ILD. [Results] Eleven cases were extracted. ACPA was positive in 9 patients and RF in 10. Autoimmune phenotypes were ARS-positive, Sjögren's syndrome, and rheumatoid vasculitis in 2, 3, and 2 cases, respectively. ILD patterns were UIP, NSIP, and OP in 3, 5, and 3 patients. In one case, arthritis was uncontrolled, and ILD progressed. Meanwhile, ILD improved in one case treated with baricitinib (BAR), which blocks JAK2 signaling, and worsened after switching from BAR in another patient. In the other cases, ILD did not change with JAK inhibitors. [Conclusion] JAK inhibitors can be safely used in RA without worsening the outcome of ILD. Further case series are needed to verify the difference in JAK selectivity.

W55-4

The difference of creatine kinase change by IL-6 inhibitors and JAK inhibitors in rheumatoid arthritis

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Conflict of interest: None

[Object] Creatine Kinase (CK) was sometimes elevated by JAK inhibitors (JAKi) in RA patients. We examined whether the CK elevation is specific to JAKi or similar to IL-6 inhibitors (IL-6i). [Methods] We use the multicenter database of IL-6i (n=113) and JAKi (n=168). 71 cases each were extracted by propensity score matching (using age, sex, BMI, and CK at 0 week (W)). The difference of CK change and the outlier rate were compared by IL-6i and JAKi. The relative factors of elevated CK at 24 W were investigated from background by univariate analysis. [Results] Median age was 66 years, CK at 0 W was 57 IU/L, and mean BMI was 22.5 kg/m^2. CK at 4 W in JAKi was significantly higher than that in IL-6i (83 vs 72 IU/L, P=0,018). There was same tendency at 12 W and 24 W. The outlier rate of JAKi significantly increased (0 W: 4.2%, 4 W: 18.1%, 12 W: 21.7%, 24 W: 18.3%, P=0.015). That of IL-6i slightly incased (0 W: 5.6%, 4 W: 9.2%, 12 W: 8.6%, 24 W: 8.5%, P=0.745). There were significantly differences between groups (P=0,035). The relative factors of elevated CK significantly correlated with men, CK, and Cr, positively, and stage, class, mHAQ, eGFR, and PSL dosage, negatively. [Conclusions] The CK of JAKi elevated at 4 W and maintained until 24 W compared that of IL-6i. The CK elevation might be specific to JAKi.

W55-5

Effects of JAK inhibitors on lipid metabolism

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Conflict of interest: None

[Objective] There are reports of increased serum LDL-C and HDL-C with JAK inhibitors used for rheumatoid arthritis (RA). We investigated changes in serum lipids in RA patients treated with JAK inhibitors. [Methods] Changes in LDL-C, HDL-C, and LDL-C/HDL-C ratio (L/H ratio) were evaluated for each JAK inhibitor before and 3 months after administration in patients receiving JAK inhibitors. [Results] Sixty-one patients were enrolled. The JAK inhibitors included baricitinib (BAR) in 23, filgotinib (FIL) in 12, tofacitinib (TOF) in 11, peficitinib (PEF) in 10, and upa-

dacitinib (UPA) in 5. The mean differences in LDH-C, HDL-C, and L/H ratio after 3 months of treatment from those before treatment were, respectively, BAR: 13.2 ± 3.8 mg/dL, 11.4 ± 4.1 mg/dL, 0.01 ± 0.08; FIL: 3.8 ± 6.0 mg/dL, 9.1 ± 2.6 mg/dL, -0.24 ± 0.11; PEF: 6.9 ± 8.0 mg/dL, 7.5 ± 4.6 mg/dL, -0.16 ± 0.09; TOF: 6.7 ± 5.0 mg/dL, 9.4 ± 3.6 mg/dL, -0.09 ± 0.15; UPA: -0.80 ± 8.8 mg/dL, 3.0 ± 10.0 mg/dL, -0.02 ± 0.21. There were no significant differences in LDL-C, HDL-C, or L/H ratio among the drug groups. The L/H ratio increased slightly after 3 months of treatment with BAR, but decreased with the other drugs. [Conclusions] There were no significant differences among the drugs, and the L/H ratio worsened in BAR but improved in the other groups.

W55-6

Can JAK inhibitors replace MTX as an anchor drug for the treatment of rheumatoid arthritis?

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Conflict of interest: None

[Objective] This study investigated the potential of JAK inhibitor (JAK-i) as an anchor drug for substituting methotrexate (MTX) by comparing efficacy and safety between the two drugs. [Methods] Patients with rheumatoid arthritis (RA) who have initiated treatment with MTX or JAK-i since September 2014 were picked up. Mean values of the simplified disease activity index, health assessment questionnaire disability index, pain score with a visual analog scale, and EuroQol 5th-dimension (EQ5D) were compared at the initiation of treatment (BL) to three years after, were compared between the two drug groups. The two groups' survival and discontinuation due to adverse event (AE) ratio were compared. [Results] A total of 305 in the MTX group and 86 in the JAK-i group joined. All clinical parameters at any period and the AE ratio showed no significant difference. The survival ratio in the JAK-i group showed significantly inferior to those in the MTX group, however, improvement of EQ5D after BL of the high disease activity at BL showed significantly superior to those in the MTX group. [Conclusion] No superior results in the JAK-i group were demonstrated in both efficacy and safety than in the MTX group. Therefore, JAK-i is superior and valuable when limited usage such as in high disease activity.

W56-1

Safety of peficitinib (PEFI) in patients with rheumatoid arthritis (RA): Interim report of all-case surveillance

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Conflict of interest: Yes

[Objective] To investigate the safety of PEFI in real-world clinical practice. [Methods] Subjects are all patients who received PEFI after its launch. The outcome includes the incidences of adverse event (AE) of special interest such as serious infections and malignancy for 52 weeks or 3 years after the start of PEFI therapy. In the annual congress, we will report interim result in patients with fixed survey data up to 24 weeks as of September 2022. [Results] As of March 2022, the safety analysis set included 1668 patients with mean age of 68 years (57 years in PEFI phase 3 study of RAJ4). Pre-treatment test for tuberculosis, hepatitis B and C was undergone in 92%, 92% and 86%, respectively. The incidence of AE of special interest (≧1%) was 5% in neutropenia, lymphopenia and haemoglobin decreased, 3% in herpes zoster, 2% in serious infections, 2% in hepatic function abnormal and 1% in malignancy. Twenty-three patients (1%) died. [Conclusions] In real-world clinical practice, PEFI was used in older patients compared with the patients in the clinical trial. No new safety concern was identified in this interim report. The survey is continued collecting more patients' information, and we plan to examine the long-term safety and background factors affecting safety of PEFI.

W56-2

24-week, post-marketing surveillance (PMS) analysis of Upadacitinib (UPA) in Japanese patients with rheumatoid arthritis (RA)

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Conflict of interest: Yes

Objective: To evaluate safety of UPA in RA pts in all-case PMS in 24wk. Methods: All pts who received UPA were included in PMS, which started in April 2020. Pts background and the incidence of AE were evaluated in pts who completed 24wk observation period or discontinued treatment. Results: As of May 2022, 1660pts were included in safety analysis set (Mean age=65.4y, over 65y=59%, female=81%, mean RA duration =12.3y). 81% continued treatment for 24wk. 20.2%, 69.0%, and 10.6% were treated with UPA 7.5, 15, and 7.5 or 15 mg/day. At the entry, 46 and 42% received MTX and glucocorticoid, 21% had mild renal failure or more. AE and SAE occurred in 368/522 and 85/112 pts/events; 9 deaths were reported (2 COVID-19, 2 lung tumor, 2 subarachnoid hemorrhage, organizing pneumonia, bacterial pneumonia, unknown). As event count: 39 serious infection (SI) (8 PCP, 5 pneumonias, 4 urinary tract infections, 3 COVID-19), 63 HZ (56 non-serious and 7 serious), 19 CK elevation, 35 liver dysfunction, 4 neutropenia, 7 lymphopenia, 3 anemia, 4 renal dysfunction, 13 malignancy (3 lung tumor, 2 lymphoma), 5 MACE, 1 VTE, 1 interstitial lung disease. Conclusions: Most pts receiving UPA are over 65yr. Though AE included SI were reported, safety profile was consistent with RCTs with no new safety signals identified.

W56-3

Risk factor analyses for herpes zoster (HZ) and serious infection (SI) in patients (pts) with rheumatoid arthritis (RA) treated with baricitinib (Bari) by multivariate Cox model: All-case Post Marketing Surveillance Study (PMSS)

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Conflict of interest: None

Purpose: Bari was approved (Jul 2017) for RA pts who have inadequate response to other treatments. In an ongoing PMSS, we examined the risk factors for SI and HZ during the 24-wk follow-up period under Bari administration. **Methods:** We used multivariate Cox model and selected pts background, diabetic complications, and concomitant medications at baseline (BL) as common factors for SI and HZ. In addition, respiratory complications for SI and HZ history for HZ were selected as risk factors.

Missing values were imputed by the multiple imputation. **Results:** Of 4731 pts, the mean age: 64; female 80%; the mean disease duration: 12 years; and incidence rate of SI and HZ were 4.9 and 8.0/100 PY. Factors with high hazard ratios (95% CI) by multivariate analysis were; SI: steroids use at BL [2.4 (1.6-3.7)], presence of respiratory complications [2.1 (1.2-3.7)], ≧75 yr (vs <65) [1.9 (1.1-3.2)]; and for HZ history of HZ [3.2 (1.7-5.9)], initial dose 4 mg (vs 2 mg) [1.8 (1.2-2.6)], ≧75 yr (vs <65) [1.5 (1.0-2.4)], and steroid use at BL [1.3 (1.0-1.9)]. **Conclusions:** No new risk factors for SI and HZ were identified, but older age and steroid use at BL as common factors, respiratory complications for SI, and HZ history and initial Bari dose for HZ may be risk factors under Bari administration.

W56-4

An observational study on the incidence of herpes zoster with Janus kinase inhibitors at our Rheumatology Center

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Conflict of interest: None

[Objective] Clinical trials of JAK inhibitors have shown an increased incidence of herpes zoster (HZ), particularly in Asian populations. In this study, we investigated the HZ incidence of JAK inhibitors at our rheumatology center. [Methods] Patients who were prescribed JAK inhibitors at our rheumatology center between August 2017 and June 2022 were selected to investigate the incidence of HZ. HZ onset was determined by the history of antiviral drug administration. [Results] Ninety-seven patients (161 cases) were prescribed JAK inhibitors during the above period. The mean age of the patients was 64.7 years, the proportion of women was 89%, the mean duration of illness was 12.3 years, and the mean observation period was 59.5 weeks. Twenty patients (20.6% incidence) developed HZ during the observation period, with an incidence rate of 13.6/100 person-years. The highest incidence rate per drug was 21.07/100 person-years for upadacitinib. [Conclusions] The highest incidence of HZ among Asians in clinical trials of JAK inhibitors was 11.1/100 person-years for upadacitinib 15 mg/day, and even taking into account the short observation period, the incidence of HZ with JAK inhibitors may be higher in Japanese patients in actual clinical practice.

W56-5

Analysis of discontinuation of JAK inhibitors due adverse events in elderly patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] JAK inhibitors (JAKi) are as effective as biologics for rheumatoid arthritis (RA), and the opportunities to prescribe JAKi for elderly patients are increasing. This study aims to investigate the safety of JAKi for elderly patients. [Methods] Patients prescribed JAKi were enrolled. Adverse event-free survival for two years, and the reasons for discontinuation were retrospectively analyzed. The survival rates were compared between > 65-year-old and < 65-year-old patients using Kaplan-Meier methods. [Results] JAKi were prescribed in 195 patients (tofacitinib 67, baricitinib 64, peficitinib 4, upadacitinib 34, and filgotinib 21). The overall survival rate of JAKi was 51.9%. JAKi was discontinued due to inadequate response in 48, adverse events in 31, and other reasons in 9 cases. The adverse event-free survival rates were 79.6% for all patients, 72.3% for over 65 years old, and 86.3% for under 65 years old (over 65 vs. under 65, p = 0.349, log-rank test). The adverse events that caused discontinuation of JAKi were 17 (infection 6, cancer 3, and others) in over 65 years old, and 14 (infection 5, cancer 1, and others) in under 65 years old. [Conclusions] JAKi may be safely used for elderly patients, but it would be better to pay special attention for cancer and infection.

W56-6

Drug retention rates and safety of Janus kinase inhibitors in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To identify retention rate and safty of JAK inhibitors (JAKi) in elderly rheumatoid arthritis (RA) patients. [Methods] We analyzed retention rate of JAKi in 133 elderly RA patients (TOF 30, BAR 74, UPA 24, PEF 4, FIL 1) from 2015 june to 2021 july at our institution. [Results] Mean age 77.4 years, mean disease duration 8.4 years, 94 female patients, ACPA positive rate 63.8%, MTX concomitant rate 63.8%. In the Cox proportional hazards model, there was no effect of gender, MTX combination, or ACPA positivity, but age 75 years over (HR 0.36: 95%CI 0.13-0.96) was sigficantly associated with discontinuation due to inadequate response. Moreover, chronic lung disease (HR 2.37: 95%CI 1.06-5.32) and hypoalbuminemia (HR 3.37: 95%CI 1.41-8.06) were significantly associated with discontinuation due to adverse events. [Conclusions] In the treatment of JAKi in elderly RA, our results suggest that the discontinuation rate due to inadequate efficacy is low in the very elderly patients (≧75) and discontinuation rate due to adverse events is high in patients with chronic lung disease or low nutritional state.

W57-1

Status of use of Tocilizumab for rheumatoid arthritis in our hospital: From the NOSRAD registry

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Conflict of interest: None

[Objective] To examine the status of use of Tocilizumab for rheumatoid arthritis in our hospital with using the NOSRAD registry. [Methods] 371 patients of rheumatoid arthritis who introduced Tocilizumab before August 2021 were included in this study. The examination items consist of 1) Cumulative survival rate of Kaplan-Meier method 2) survival rate of each bio-naïve and switch cases 3) Reasons for discontinuation. [Results] Group of elderly patients with MTX treatment was higher rate of switch cases and lower rate of PSL treatment compared to other group. Survival rate of elderly patients with MTX treatment in Tocilizumab was significantly lower than Survival rate of young patients with or without MTX treatment in Tocilizumab. [Conclusions] Survival rate of elderly patients with MTX treatment in Tocilizumab was significantly lower than young patients with or without MTX treatment. Because of this, rate of Adverse event in group of elderly patients with MTX treatment was higher compared to other group.

W57-2

Factors Associated with Remission in RA Patients One Year After Tocilizumab Induction from multicenter Ultrasound Cohort Data in Kyushu, Japan

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Conflict of interest: None

[Objective] We are conducting a multicenter prospective RA musculoskeletal ultrasound (MSUS) cohort study (KUDOS) of RA patients starting biologic agents and JAK inhibitors at several hospitals in the Kyushu area. In this study, we examined factors associated with remission after 1 year of tocilizumab (TCZ) induction. [Methods] Using KUDOS data, 67 patients who were inducted with TCZ were included. Fifty-seven % of them were taking MTX. We analyzed by the LOCF method. Clinical characteristics of patients who achieved remission were examined. [Results] 1: CDAI improved significantly from 22.5 to 5.5. 2: US synovitis scores improved significantly from GS: 11 to 5 and PD: 7 to 1. 3: US strict remission rate (PD=0 and GS=0) was 13.4%. 4: Patients who achieved US strict remission had significantly shorter disease duration cases than those who achieved PD remission (PD=0) only. 5: Patients who achieved PD remission had significantly lower baseline disease activity and significantly lower PSL use. 6: Multivariate analysis showed that PD remission associated with PSL use (OR 0.191) and EGA (OR 0.957). [Conclusions] Patients using TCZ could be expected to achieve clinical remission at 1 year, even without MTX, but US remission was difficult to achieve with longer disease duration or with PSL.

W57-3

Comparison between sarilumab treatment and tocilizumab subcutaneous QW treatment in RA patients with an inadequate response to tocilizumab subcutaneous Q2W treatment

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Conflict of interest: None

[Object] To evaluate the efficacy of change of IL-6 inhibitor treatment in RA patients with an inadequate response to tocilizumab subcutaneous Q2W treatment. [Methods] 27 patients with RA who were treated with SAR and 26 patients with RA who were treated with tocilizumab subcutaneous QW were enrolled. [Results] In SAR group, the mean age was 62.7 years old and mean disease duration was 16.2 years. 12 patients (44.4%) were used MTX concomitantly. The mean CDAI decreased from 23.9 to 13.7 and the mean DAS-ESR decreased from 4.42 to 2.96 at 12 weeks. In TCZ-QW group, the mean CDAI and DAS-ESR values were 16.5 and 4.16 at baseline, respectively. The Δ values of CADI were -6.3 and that of DAS-ESR was -1.04. We next analyzed the difference of efficacy by body weight. The Δ values of CADI in patients with BW < 60 kg and over 60 kg were -12.7 and -6.5 in SAR group, -6.2/-5.7 in TCZ-QW group, respectively. [Conclusions] In RA patients with an inadequate response to tocilizumab subcutaneous Q2W treatment, both switching to SAR and the increase of interval of TCZ injection were effective. There was tendency that the physician chooses the increase of TCZ interval in patients with lower disease activity as compared with those of switching to SAR.

W57-4

Efficacy of switching from JAK inhibitor to tocilizumab in the patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Efficacy for switching between bDMARD and JAK inihibitor (JAK-I) in RA patients is unclear. Therefore, we evaluated eficcacy of tocilizumab (TCZ), swiching from JAK-I. [Methods] 23 patients who could not achieve CDAI remission with JAK-I and switch to TCZ 162 mg weekly subcutaneous injection were enrolled and the efficacy was prospectively observed up to 12 weeks. [Results] Mean age of patients was 62.5 ± 17.9 years, mean duration of disease was 8.6 ± 6.8 years, mean disease activity was DAS28ESR 4.1 ± 1.1, CDAI 14.9 ± 8.6, including moderate disease activity with relatively long duration of disease. JAK-I before TCZ administration were 18 baricitinib, 2 upadacitinib, and 3 filgotinib. 3 of the 23 patients progressed by the 4th week and discontinued the treatment, but others could continue up to week 12. The ACR20 response rate at week 12 was 54.5%. 11 of 23 patients (48%) achieved DAS28ESR remission and 3 (13%) achieved CDAI remission at week 12. Factors predicting ACR20 at week 12 were increased ESR, and neutropenia at week 0-4 (neutrophil count at week 4-week 0) by multivariate analysis. [Conclusions] TCZ administration is effective in JAK inhibitor-resistant patients, and neutropenia at 4 weeks suggests the possibility of predicting treatment response up to 12 weeks.

W57-5

The efficacy of inhibitors of interleukin-6 receptor, Sarilumab and Tocilizumab, in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the clinical efficacy of Sarilumab (SAR) and Tocilizumab (TCZ) in patients with rheumatoid arthritis (RA). [Methods] We evaluated the disease activities in RA patients for 52 weeks after starting administrations of SAR (N=29) and TCZ (N=143). [Results] The mean DAS28-CRP of SAR and TCZ groups were 4.41 and 4.48 at baseline (BL) (p=0.799), 2.96 and 3.38 at 4 weeks (W) (p=0.127), 2.37 and 2.83 at 12 W (p=0.079), 2.40 and 2.55 at 24 W (p=0.527), 2.49 and 2.51 at 36 W (p=0.934), 2.18 and 2.52 at 52 W (p=0.137), respectively. DAS28-CRP significantly decreased after 4 W from BL in both groups ($p<0.05$). When looking at the clinical courses in both groups in only using as second line biologic agents (Bio), the mean DAS28-CRP of SAR (N=11) and TCZ (N=50) groups were 4.02 and 4.56 at BL (p=0.192), 2.35 and 3.63 at 4 W (p=0.003), 1.58 and 3.07 at 12 W ($p<0.001$), 1.73 and 2.77 at 24 W ($p<0.001$), 1.69 and 2.62 at 36 W (p=0.001), 1.56 and 2.67 at 52 W ($p<0.001$), respectively. DAS28-CRP significantly decreased after 4 W from BL in both groups ($p<0.05$), however, DAS28-CRP after 4 W in SAR group were significantly lower than TCZ group. [Conclusions] Both of SAR and TCZ had good and quick clinical efficacy. However, SAR had stronger clinical efficacy than TCZ in using as second line Bio.

W57-6

Study on the relationship between tocilizumab and hypofibrinogenemia in patients with autoimmune diseases

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Conflict of interest: None

[Objective] We experienced hypofibrinogenemia and gastrointestinal bleeding during the use of tocilizumab (TCZ) for adult-onset Still disease (AOSD). Therefore, we investigated the relationship between TCZ and hypofibrinogenemia in patients with autoimmune diseases at our hospital. [Methods] We measured serum fibrinogen levels from February 2021 to September 2022 in 108 patients with autoimmune diseases who treated with TCZ, and investigated the relationship between treatment and fibrinogen levels. [Results] There were 91 rheumatoid arthritis, 2 polymyalgia rheumatica, 10 AOSD, 3 Takayasu arteritis, 2 giant cell arteritis, of the 108 patients who received TCZ (88 subcutaneous injections, 20 intravenous infusions). Fibrinogen levels after TCZ introduction were significantly lower than before TCZ (before: 434 (342-567) mg/dl, after: 218 (187-258) mg/dl, $p<0.005$). There were no significant differences in fibrinogen levels among patients due to body weight, BMI, dose interval, and dose frequency. There were 2 hypermenorrhea and 1 gastrointestinal bleeding during the use of TCZ, and fibrinogen levels decreased, and the bleeding improved after discontinuation of TCZ. [Conclusions] If bleeding is observed while using TCZ, it is necessary to check the fibrinogen level and consider stopping TCZ.

W58-1

A case of calcium pyrophosphate crystal arthritis that developed after initiating treatment with immune checkpoint inhibitor

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Conflict of interest: None

Case: A 71-year-old man was diagnosed with stage IV lung squamous cell carcinoma and treated with pembrolizumab (anti-PD-1 antibody; ICI), nab-paclitaxel, and carboplatin. After 6 months of chemotherapy, he developed acute tubular necrosis. In addition, he developed arthralgia in his left ankle, which was considered pseudogout and treated with NSAIDs. Pembrolizumab was discontinued for a potential diagnosis of immune-related adverse event (irAE), and prednisolone 20 mg/day was started. His symptoms improved, and prednisolone was tapered off in 3 months. Pembrolizumab was resumed 1 month after prednisolone discontinuation; however, left ankle arthralgia recurred, and he was referred to our department. Ultrasound showed high-echoic depositions on the hyaline cartilage. Arthrocentesis revealed CPP crystal in synovial fluid, and we made a diagnosis of CPP arthritis. Intraarticular injection of triamcinolone improved arthritis, and there has been no recurrence for 1 year. Discussion: Recently, crystal arthritis has been reported as an irAE. Our case was also considered CPP arthritis induced by ICI. Crystal arthritis should be considered under treatment with ICI because the clinical course and optimal treatment for crystal arthritis can differ from those for non-crystal arthritis.

W58-2

A comparative analysis of microscopic techniques for crystal in joint fluid in the diagnosis of crystal induced arthritis

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Conflict of interest: Yes

[Objective] The detection of crystals in joint fluid was covered by insurance in 2021, but no comparative study of identification methods has been reported. [Methods] Crystals were detected by 3 microscopic methods using 30 joint fluid samples from the patients with crystal induced arthritis suspected at our department from February 2020 to March 2021. A technician evaluated the sediment after centrifugation (CG) using U-GAN®. Furthermore, the remaining specimens before CG were evaluated within 48 hours by several rheumatologists in the order of (A) no polarization, (B) U-GAN and (C) polarized compensated microscope. The results of technician's evaluation were defined as reference. [Results] In the sediment after CG, 15 were crystal-positive (11 for CPP and 4 for MSU) and 15 were crystal-negative. Before CG, the crystals were detected with a sensitivity (Sens) of 66.7% (10/15; Sens of 72.7% (8/11) for CPP and 50% (2/4) for MSU) in (A), with a Sens of 80% (12/15; Sens of 81.8% (9/11) and 75% (3/4)) in (B). The results were in perfect agreement in (C) and U-GAN by technician. In all 3 methods, a specificity was 100% (15/15). [Conclusions] Crystals can be detected without CG. Although identification is possible without polarization, the evaluation using (C) may be more sensitive.

W58-3

Diagnostic biomarkers identified by metabolomic analysis in patients with pseudogout

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Conflict of interest: None

[Objective] To examine the characteristics of the metabolites in synovium fluid (SF) of pseudogout patients. To identify serum diagnostic biomarkers using the results of metabolomic analysis of serum samples compared with that of SF. [Methods] We collected serum and SF of 18 pseudogout and 12 rheumatoid arthritis (RA) patients who showed acute arthritis. We also collected serum of five pseudogout patients after improving arthritis. We performed metabolomic analysis of the samples using GC-TOFMS. The metabolic profiles were compared using multivariate statistical analysis. We compared pseudogout with RA, and pseudogout showing arthritis with not showing arthritis using the results of metabolomics profiles. [Results] A total of 123 metabolites from SF and 101 metabolites from serum were identified. By using OPSL-DA, twelve metabolites from SF and 15 metabolites from serum were different between pseudogout and RA. Twelve metabolites from serum were different between pseudogout showing arthritis and not showing arthritis. As a results, we identified two metabolites which elevating both in serum and SF seen in pseudogout with arthritis. [Conclusions] We identified two metabolites which may lead to elucidate the pathology and be the potential biomarkers for pseudogout.

W58-4

Comparative study of knee joint ultrasonographic findings in rheumatoid arthritis and gout

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Conflict of interest: None

[Objective] The mechanisms of inflammation in rheumatoid arthritis (RA) and gout are thought to be different. We investigated the characteristics of knee arthritis in these diseases. [Methods] Sixty-one cases diagnosed with RA and 79 cases diagnosed with gout were examined. [Results] There was no significant difference in joint synovitis in 36% of the RA group and 41% of the gout group. Suprapatellar bursitis was not significantly different in 61% of the RA group and 51% of the gout group. There was no significant difference in quadriceps tendon enthesitis in 41% of the RA group and 42% of the gout group. Quadriceps tendon enthesis bone formation was significantly higher in the gout group, with 47% of the RA group and 72% of the gout group ($p=0.0018$). There was no significant difference in enthesitis of the patellar ligament in 30% of the RA group and

37% of the gout group. Patellar ligament enthesis bone formation was significantly higher in the gout group, with 15% of the RA group and 37% of the gout group (p=0.0041). [Conclusions] No difference was observed between the RA group and the gout group in the findings of knee joint inflammation, but bone formation at the enthesis was significantly higher in the gout group, suggesting that gout inflammation promotes bone formation.

W58-5

Investigation of bone formation in gouty ankle arthritis using HR-pQCT images

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Conflict of interest: None

[Purpose] In this study, the ankle joints of patients with ankle gout were imaged by HR-pQCT and osteophytes or extra bones were examined. [Methods] Thirty male subjects underwent HR-pQCT scans of their ankles. 27 gouty joints (gouty group) and 32 non-gouty joints (nongouty group) were examined by HR-pQCT. Extra bone was defined as a normal bone structure found apart from the native bone. [Results] There was no significant difference in Achilles tendon enthesis osteophytes between 18 joints in the non-gout group and 21 joints in the gout group (p=0.1028). There was no significant difference in other osteophytes between 1 joint in the non-gout group and 5 joints in the gout group (p=0.0840). There was no significant difference in subfibular extra bone between 0 joints in the non-gout group and 4 joints in the gout group (p=0.4136). The number of subtibial extra bones was significantly higher in 10 joints in the gout group compared to 1 joint in the non-gout group (p=0.0015). The number of other extra bones was significantly higher in 12 joints in the gout group compared to 3 joints in the non-gout group (p=0.0028). [Conclusions] In gouty ankle joints, significantly more extra bones were observed than in non-gouty joints, and it was thought that bone formation were accelerated.

W58-6

Comparative study of pseudogout using plain X-ray, ultrasonography, and HR-pQCT images

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Conflict of interest: None

[Objective] Knees, shoulders, elbows, and wrists were the most common sites of pseudogout. In this study, we performed HR-pQCT in a case of wrist joint pseudogout, and compared the calcification findings between plain X-P (XP) and ultrasonography (US). [Methods] Subjects were 19 women (38 joints) who were diagnosed with pseudogout by confirming the calcification of the wrist joints by HR-pQCT findings. [Results] The calcification was observed in 37 joints (97%) by HR-pQCT, 25/37 joints (68%) by XP, and 29/37 joints (78%) by US. HR-pQCT showed the triangular fibrocartilage calcification in 33/37 joints (89%), the navicular lunate ligament calcification in 36/37 joints (97%), the triangular lunate ligament calcification in 33/37 joints (89%), and the thumb CM joint calcification in 24/37 joints (63%). Some cases had extensive calcification around the hamate and capitate bones. XP and US showed only the triangular fibrocartilage calcification. [Conclusions] In the HR-pQCT examination, calcification was observed in 37 out of 38 joints. The detection rate was higher with US than with XP, and all calcifications observed with XP were visualized with US. XP and US detected only triangular fibrocartilage calcification, but HR-pQCT showed extensive calcification.

W59-1

Comparison of suppression of neutrophil activation between C5a receptor (C5aR) antagonists and neutrophil elastase (NE) inhibitors

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Conflict of interest: Yes

[Objective] MPO-ANCA-induced neutrophil extracellular traps (NETs) are critically involved in MPO-ANCA-associated vasculitis (MPO-AAV). Cell swelling occurs during NET formation. Complement C5a primes neutrophils by binding to C5aR on the neutrophil surface and plays an important role upstream in pathogenesis. In contrast, NE promotes NET formation downstream of pathogenesis by participating in histone degradation (chromatin decondensation) and plasma membrane pore formation (DNA release). This study compared the effects of the C5aR antagonist avacopan and the NE inhibitor sivelestat on neutrophils. [Methods] Neutrophils isolated from human peripheral blood were pretreated with avacopan or sivelestat, primed by C5a or TNF-α, and then stimulated by MPO-ANCA immune complexes. Thereafter, cell swelling rate was evaluated by flow cytometry. [Results] Regarding MPO-ANCA-induced neutrophil activation, avacopan significantly suppressed cell swelling of C5a-primed neutrophils, whereas sivelestat significantly suppressed neutrophil swelling under both C5a and TNF-α priming. [Conclusions] Sivelestat, which acts downstream of MPO-AAV pathogenesis, may have a broader inhibitory effect on neutrophil activation, including NET formation, than avacopan, which acts upstream of pathogenesis.

W59-2

Suppression of neutrophil extracellular trap (NET) formation by inhibiting cathepsin C (CatC)

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Conflict of interest: Yes

[Objective] MPO-ANCA-induced NETs are critically involved in MPO-ANCA-associated vasculitis (MPO-AAV). CatC activates neutrophil serine proteases, including neutrophil elastase (NE), which is essential for NET formation, during neutrophil maturation. Previous study showed that a CatC inhibitor MOD06051 improved MPO-AAV in rats. This study aimed to show the inhibitory effects of MOD06051 on NE activity and NET formation. [Methods] Human bone marrow (BM)-derived hematopoietic stem cells were cultured with G-CSF to differentiate into neutrophils under the presence of MOD06051 (0-10 μM). Eight days later, the NE activity was measured. Male SD rats were orally administered with MOD06051 (0, 0.3, 3, or 10 mg/kg, bid) for 2 weeks and the NE activity in neutrophil fraction was determined. Rats were orally administered with vehicle or MOD06051 (3 mg/kg, bid) for 2 weeks. Neutrophils were primed with C5a or TNF-α, stimulated with MPO-ANCA immune complexes, and subjected for flow cytometry to detect NETs. [Results] MOD06051 suppressed NE activity both in vitro and in vivo. MPO-ANCA-induced NET formation in neutrophils derived from MOD06051-administered rats was reduced compared with vehicle controls regardless of priming factors. [Conclusion] MOD06051 suppressed NE activity and NET formation.

W59-3

Identification of proteins that confer DNase I resistance to neutrophil extracellular traps

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Conflict of interest: Yes

[Purpose] Neutrophil extracellular traps (NETs) play important roles in innate immunity. NETs are degraded by DNase I because excessive NET formation results in tissue damage and autoantibody production. The deposition of DNase I-resistant NETs in the lesions has been reported in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). This study aimed to identify the proteins that confer DNase I resistance to NETs. [Methods] DNase I-resistant NETs (AAV) and DNase I-sensitive NETs (tuberculosis) were compared by proteomic analysis. Proteins highly expressed in DNase I-resistant NETs or novel antibodies against these proteins were added during NET induction, and the effects on NET formation were analyzed morphologically and by flow cytometry. [Results] Addition of five proteins extracted by proteomic analysis during NET induction increased abnormal NETs, which morphological feature linked with DNase I resistance. Some newly generated antibodies against protein No. 5-2, one of the five proteins, suppressed the formation of abnormal and normal NETs. [Conclusion] No. 5-2 conferred DNase I resistance to NETs. Anti-No. 5-2 antibodies inhibited NET formation and might be applicable to the treatment of diseases involving DNase I-resistant NETs, such as AAV.

W59-4

Efficacy of avacopan in Three Patients with Microscopic Polyangiitis in Clinical Practice Setting

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Conflict of interest: None

[Background] Avacopan (AVC) has been available for the treatment of microscopic polyangiitis since June 7, 2022 in Japan, but its use in clinical practice has not been established. [Case 1] An 80-year-old woman with interstitial pneumonia (IP), elevated MPO-ANCA and worsening neuropathy in the right deep peroneal nerve area was treated with PSL 30 mg, RTX and AVC after mPSL pulse and PSL was reduced to 7.5 mg/day in 4 weeks. [Case 2] A 90-year-old woman. She was admitted to the hospital and started treatment with PSL 15 mg/day, AVC, and RTX. The dose was reduced to PSL 10 mg/day in 1 week and the patient was discharged from the hospital. [Case 3] An 82-year-old woman with IP and elevated MPO-ANCA for 3 years, started treatment with mPSL pulse and 3 RTX courses 3 months ago, and her PSL was reduced to 7.5 mg/day. CRP was elevated, AVC was started and the 4th RTX was performed, AVC was finished in total 6 weeks, CRP became negative. [Clinical Significance] Case 1 was in the induction phase of remission, and rapid PSL reduction was possible. Case 2 had delirium, but was discharged early after achieving induction of remission with a very low dose of PSL. In case 3, a short course of AVC before and after RTX avoided an increase in PSL at recurrence.

W59-5

Two cases of granulomatosis with polyangiitis in which ACTH stimulation test was useful in deciding to discontinue glucocorticoids at the start of avacopan

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Conflict of interest: None

[Introduction] In the ADVOCATE trial, patients with ANCA-associated vasculitis (AAV) receiving glucocorticoids were to discontinue it within 28 days of study entry [N Engl J Med 384:599]. We describe two cases of granulomatosis with polyangiitis (GPA) in which glucocorticoids were discontinued with reference to an ACTH stimulation test at the start of avacopan. [Case 1] A 60-year-old man, newly diagnosed with GPA, was treated with methyl-prednisolone pulse therapy (mPSL, 0.5 g, 3 days) and prednisolone (PSL, 60 mg/day, 1 week). On the second day for PSL 30 mg, ACTH stimulation test showed the 60-min values of 19.0 μg/dL, suggesting a normal adrenal function. Next day, PSL was stopped and avacopan was started. Since then, no symptoms due to adrenal insufficiency have been observed. [Case 2] A 70-year-old woman, newly diagnosed with GPA, was treated with mPSL pulse therapy, followed by PSL. Two months previously, she was also treated with PSL for 12 days. ACTH stimulation test was performed on day 6 of PSL 50 mg/day. The 60 min values was 19.0 μg/dL, and PSL was stopped next day at the start of avacopan. [Clinical Significance] an ACTH stimulation test was useful in deciding whether to reduce or discontinue glucocorticoids when avacopan was started.

W59-6

Systematic review for 2023 clinical practice guidelines of the management of ANCA-associated vasculitis

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Conflict of interest: None

[Objective] This systematic review (SR) was conducted by the Japan Research Committee for Intractable Vasculitis for the revision of the clinical practice guidelines (CPG) of the management of ANCA-associated vasculitis (AAV). This presentation focuses on the changes from the SR for the 2017 CPG. [Methods] MEDLINE, CENTRAL, and the Japan Medical Abstracts Society databases were searched for articles published from 2015 to 2020 to update the SR for four CQs, while EMBASE was added into those databases for articles published from 2000 to 2020 to conduct a SR for six newly developed CQs. [Results] Addition of plasma exchange to remission induction therapy did not reduce the risk of death, end-stage kidney disease, or relapse, while the risk of end-stage kidney disease was reduced in the previous SR. For remission induction, when used with cyclophosphamide (CY) or rituximab (RTX), reduced-dose glucocorticoid (GC) lowered the risk of serious adverse events compared to standard-dose GC. Avacopan improved sustained remission at 12 months compared to high-dose GC. For remission maintenance, long-term RTX or AZA reduced the risk of relapse compared to short-term RTX or AZA, respectively. [Conclusions] The results of this SR will be used for the 2023 CPG of the management of AAV.

W60-1

Prognostic impact of bronchiectasis on microscopic polyangiitis: a historical cohort study using J-CANVAS registry data

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Conflict of interest: None

Objective: To clarify the prognostic impact of bronchiectasis in microscopic polyangiitis (MPA). Methods: The J-CANVAS registry, which is being established at 25 sites in Japan, enrolls patients with new-onset or severe relapse of AAV between January, 2017 and June, 2020. The effect of bronchiectasis at diagnosis for the development of severe infection (including death from infection) and relapse of vasculitis (severe or mild relapse and death due to active vasculitis) up to 48 weeks after treatment was analyzed for eligible patients. The Cox regression model was used to adjust for age, gender, ANCA type, creatinine at diagnosis, severity of vasculitis (presence of each organ involvement), initial steroid dose, steroid pulse therapy, rituximab, and cyclophosphamide as adjustment factors. Results: A total of 408 patients were included in the study, and bronchiectasis was present in 43 patients (10.5%). By the 48th week after treatment, 82 patients (20.1%) had developed severe infections and 47 patients (11.5%) had relapses. The adjusted hazard ratios of bronchiectasis for severe infection and relapses were 2.64 (95%CI: 1.38-5.08, p=0.004) and 0.67 (95%CI: 0.20-2.19, p=0.503), respectively. Conclusions: In MPA, bronchiectasis was associated with the development of severe infections.

W60-2

Risk factors for serious infection in patients with microscopic polyangiitis: the REVEAL cohort study

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Conflict of interest: None

[Objective] Risk factors of serious infections in patients with microscopic polyangiitis in Japan were examined. We also focused on the pace of corticosteroids (CS) reduction. [Methods] 181 MPA patients hospitalized for induction therapy and followed for at least three months were recruited from REVEAL cohort, a multicenter cohort in Kansai. Patients were divided according to the presence of infections requiring hospitalization (serious infections: SI), and unvariate analysis and COX regression analysis were performed. In addition, patients were divided according to the median of the statistically significant variable among CS doses at each point and the ratios to the outset, and the cumulative incidence of SI was compared. [Results] There were 115 and 66 patients in the SI (-) and (+) group. Univariate analysis showed that age, smoking index, CRP, and CS dose ratio (3 months/outset) were associated with SI. COX regression analysis extracted age, CRP, and CS dose ratio (3 months/outset) (p values are <0.005, <0.005, and 0.04, respectively). The group with CS dose ratio (3 months/outset) >0.4 had significantly higher cumulative incidence of SI than the other (p=0.037). [Conclusion] Age, CRP, and CS dose ratio (3 months/outset) were suggested as risk factors for SI in MPA patients.

W60-3

Clinical differences according to serum MPO-ANCA titers at diagnosis in microscopic polyangiitis: the REVEAL cohort study

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Conflict of interest: None

[Objective] To determine whether clinical characteristics such as relapse and mortality rates and disease severity differ according to MPO-ANCA titers at diagnosis in microscopic polyangiitis (MPA). [Methods] 142 patients with newly diagnosed MPA who were hospitalized for induction therapy after December 2012 were recruited from the REVEAL cohort. Patients were divided into two groups according to the median MPO-ANCA titer at diagnosis. The background, clinical data, treatment details and relapse and mortality rates of the two groups were compared retrospectively. [Results] The median MPO-ANCA titer was 124 U/ml, and 71 patients were in both the high and low titer groups. The BVAS was significantly higher in the high titer group (12 vs. 15 points, P=0.022), with more frequent renal involvement (60% vs. 85.9%, P=0.001). There was no significant difference in the initial steroids dose, but intravenous cyclophosphamide was used significantly more frequently in the high titer group (28.4% vs. 55.4%, P=0.003). There were no significant differences in relapse and mortality rate between the two groups. [Conclusions] In MPA, patients with high MPO-ANCA titer at diagnosis had higher disease activity than those with low titer, but the relapse and mortality rates were not different.

W60-4

Stratification based on clinical characteristics of patients with microscopic polyangiitis (MPA); The REVEAL cohort study

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Conflict of interest: None

[Objective] To stratify patients with microscopic polyangiitis (MPA) based on the clinical characteristics using the database of the Kansai multicenter REVEAL cohort. [Methods] Two hundred eleven patients with MPA were enrolled from the REVEAL cohort. Clinical characteristics (sex, interstitial lung disease (ILD), prevalence of systemic organ lesions, age, CRP, serum Cre level) were extracted. Principal component analysis and cluster analysis were performed to stratify patients into subgroups. [Results] These patients were divided into three groups: cluster 1 (80 patients), cluster 2 (52 patients), and cluster 3 (79 patients). Cluster 1 was older (median age 77.7 years) and had a higher proportion of women (86.3%) and ILD (64%). Cluster 2 had a higher proportion of men (98.1%), smoking (91.8%), and ILD. Cluster 3 had the lowest age (median age 69.9 years) and less frequent ILD but renal dysfunction was severe (median serum Cre levels: 1.89 mg/dL), and BVAS was the highest between them. There were significant differences in respiratory and respiratory infection deaths between them. [Conclusions] Stratifications based on the clinical background of MPA patients are useful to understand differential phenotypic characterizations between subgroups and predict the prognosis.

W60-5

Prognostic factors affecting death in patients with microscopic polyangiitis: the REVEAL cohort study

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Conflict of interest: Yes

[Objective] To examine clinical factors related to prognosis in Japanese microscopic polyangiitis (MPA) patients in the real world. [Methods] The subjects were 194 MPA patients (median age 73.3 years, female 55%, median observation period 3.8 years) extracted from the database of the Kansai multicenter REVEAL cohort from 2005 to 2021. [Results] Of 60 deaths, 15 died due to MPA and 30 died due to infection. Patients' background factors that showed significant differences in the survival group and death group (univariate analysis) were age, serum Alb levels, serum CRP levels, BVAS, Five Factor Score (FFS), and EUVAS (p=0.0001, 0.025, 0,031, 0.004, 0.012, and 0.044, respectively). In multivariate analysis (cox proportional hazards model), older age was significantly associated with mortality (HR 1.052, 95%CI 1.016-1.091, p=0.004). The cut-off value for predicting survival by ROC analysis was 79.1 years old (AUC 0.73, sensitivity 60%, specificity 87%). High BVAS and FFS 2 were significantly associated with mortality in the <80 years group, and early systemic and severe of EUVAS in the ≧80 years group. [Conclusions] Older age over 80 years was a risk factor associated with mortality in MPA patients. BVAS, FFS, and EUVAS may be useful as age-stratified prognostic indicators.

W60-6

Examination of clinical factors affecting mortality from microscopic polyangiitis: the REVEAL cohort study

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Conflict of interest: Yes

[Objective] To examine the clinical factors associated with death from microscopic polyangiitis (MPA) in the real world of Japan. [Methods] The subjects were 194 MPA patients (median age 73.3 years, female 55%, median observation period 3.8 years) extracted from the database of the Kansai multicenter REVEAL cohort from 2005 to 2021. [Results] Of the total 60 deaths, 15 died due to MPA. Compared to the survival group (134 patients), the MPA death group (15 patients) was significantly older, had a higher peripheral white blood cell count (WBC), a higher BVAS, and a higher proportion of severe EUVAS (p=0.003, 0.020, 0,001, and 0.011, respectively). The cut-off values for predicting survival by ROC analysis were 79.1 years old (AUC 0.73, sensitivity 60%, specificity 87%), WBC 16520/μL (AUC 0.68, sensitivity 63%, specificity 90%), and BVAS 20 (AUC 0.76, sensitivity 60%, specificity 79%). The 2-year survival rates were significantly lower in the ≧80 years old and WBC ≧16520/μL groups compared with the respective control groups (p=0.004 and 0.002, respectively; log-rank test). [Conclusions] In Japanese MPA patients, being over 80 years old and having a high WBC level may be risk factors associated with MPA-related mortality.

W61-1

Fluctuation in anti-cyclic citrullinated protein antibody level determines the retention rate of TNF inhibitors in rheumatoid arthritis

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Conflict of interest: Yes

Purpose: The presence of anti-citrullinated protein/peptide antibody (ACPA) is a useful diagnostic and prognostic marker for rheumatoid arthritis (RA), but its titer fluctuation is still unclear. We previously reported that the patients with fluctuating ACPA antibody titers are more likely to relapse from remission. In this study, we will examine the effect of b/tsDMARDs on ACPA antibody titers and the effect of fluctuating ACPA antibody titers on drug retention rates. Methods: We included 459 patients with RA who had ACPA antibody titers measured multiple times and were positive at least once in the KURAMA cohort at the Kyoto University. Results: Positive conversion of ACPA was observed in 3.7%, 5.0%, 1.1%, and 12.5% of ACPA-negative patients, respectively. No drug showed a significant decrease in ACPA antibody titer during the 5-year observation period, although 23.8%, 29.4%, 26.3%, and 16.7% of patients showed a 3-fold or greater change in antibody titer, respectively. The probability of drug discontinuation due to ineffectiveness was higher for TNF inhibitors in patients with ACPA fluctuating more than 3-fold. Conclusions: b/tsDMARDs do not decrease ACPA antibody titers, and patients with fluctuating ACPA antibody titers are less likely to continue TNF inhibitors.

W61-2

A study of negative conversions of anti-CCP antibodies and anti-mutated citrullinated vimentin antibodies in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: In rheumatoid arthritis (RA), anti-citrullinated protein antibodies (ACPA) rarely become negative during the course of disease. In this study, we examined the clinical characteristics of cases in which anti-mutated citrullinated vimentin (MCV) and anti-CCP antibodies (Abs), had negative conversion. **Methods:** 1) We retrospectively examined anti-CCP and MCV Ab titers measured by ELISA (Anti-MCV®, ORIGENTEC) in 438 RA patients, whose sera were obtained for at least 2 points. 2) The frequency of cases that turned negative during the disease course and clinical characteristics before and after conversion were compared. 3) Changes of disease activity and laboratory tests after conversion were compared. **Results:** 1) 12 patients (2.7%) with anti-CCP and 57 (13.0%) with anti-MCV Abs turned to negative. 2) Before conversion, HAQ was higher in the anti-CCP negative conversion group (P<0.01), and anti-CCP Ab was higher in the anti-MCV negative conversion group (P<0.0005). 3) Only in the anti-MCV negative conversion group, there was a significant decrease in DAS28, SDAI, IgG and CRP. **Conclusion:** The anti-MCV negative conversion group shows different clinical characteristics from the anti-CCP negative conversion group.

W61-3

mCRP and autoimmune diseases

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Conflict of interest: None

Objective: C-reactive protein (CRP) is a dynamic protein that undergoes conformational changes between circulating native pentameric CRP (pCRP) and monomeric CRP (mCRP) forms. mCRP exhibits strong pro-inflammatory activity and activates platelets, leukocytes, and endothelial cells. Although pCRP is typically quantified rather than mCRP for clinical purposes, mCRP may be a more appropriate disease marker of inflammatory diseases. Therefore, simple methods for quantifying mCRP are needed. **Methods:** We developed a specific enzyme-linked immunosor-

bent assay (ELISA) to measure plasma levels of mCRP. Plasma mCRP concentration was measured in patients with adult-onset Still's disease (AOSD), polymyalgia rheumatica (PMR), rheumatoid arthritis (RA), infection and in control subjects. **Results:** We demonstrated that mCRP is elevated in some inflammatory autoimmune diseases, particularly AOSD. The mCRP concentration was also significantly higher among AOSD patients than RA, PMR patients and controls. **Conclusions:** The plasma mCRP levels are elevated in some autoimmune diseases, particularly AOSD. The plasma mCRP levels may therefore be a potentially useful biomarker for AOSD.

W61-4

Serum levels of caspase-cleaved cytokeratin-18 in interstitial lung disease associated with rheumatoid arthritis, dermatomyositis, and polymyositis

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Conflict of interest: None

[Objective] Although the detailed pathogenesis of interstitial lung disease (ILD) is unknown, the involvement of apoptosis has been suggested. We investigated whether the apoptosis marker in serum can be a marker of disease activity, to examine the involvement of apoptosis in the pathology of ILD associated with connective tissue disease (CTD). [Methods] We analyzed serum levels of caspase-cleaved cytokeratin-18 (M30) in 87 patients, consisting of 52 patients with rheumatoid arthritis (RA) and 35 with polymyositis or dermatomyositis (PM/DM), using enzyme-linked immunosorbent assays. [Results] The median (interquartile range) serum level of M30 was 283.2 (153.9-340.6) U/L in the patients with ILD associated with RA and PM/DM (RA-ILD, and PM/DM-ILD), and 143.4 (108.5-176.2) U/L in the patient without ILD. Serum level of M30 was significantly higher in patients with RA-ILD than those with RA without ILD. Furthermore, serum level of M30 was significantly higher in patients with PM/DM-ILD than those with PM/DM without ILD. Serum M30 levels were negatively correlated with percent-predicted forced vital capacity. [Conclusions] Lung apoptosis is suggested to be involved in the fibrosis of CTD-ILD. The serum M30 level can be useful as a detection and activity marker for CTD-ILD.

W61-5

Clinical Evaluation of Bone Marrow Suppression Caused by Methotrexate in Patients with Rheumatic Diseases

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Conflict of interest: None

{Objective} Methotrexate (MTX) has immunosuppressive effects by inhibiting the folic acid metabolism and it is widely used as a first-line medication for rheumatoid arthritis (RA). The purpose of this study was to investigate the patients with rheumatic diseases who had bone marrow suppression by receiving MTX, and to clarify their characteristics. {Methods} Twenty-one patients who were admitted due to bone marrow suppression by MTX between 2005 and 2022 were selected. The background, accompanied symptoms, laboratory findings, and treatment course of these patients were reviewed and analyzed from medical records. {Results} The background: 19 females, age 37-91 (mean 69). Disease: 20 RA, 1 Mixed Connective Tissue Disease. Treatment: MTX dose 4-12 (mean 5.8) mg/week, MTX duration 2-157 weeks. Folic acid was administered to only 6 patients. Complications: stomatitis; 11 (52%), Outcome: 18 recovered, 3 died. Cause of death; 3 infection. eGFR < 50 ml/min/1.73 m^2; 16, eGFR < 30; 9, hemodialysis patients 3. It took an average of 8.2 days to recover leukocytopenia. {Conclusion} Stomatitis was often accompanied with bone marrow suppression by MTX. Renal dysfunction and old-age were high risks of bone marrow suppression by MTX. When MTX is given in high-risk patients, folate should be used.

W62-1

The level of RF or anti-CCP antibody affect ultrasound findings in patients with rheumatoid arthritis?

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Conflict of interest: None

[Objective] Positive for auto-antibodies such as rheumatoid factor (RF) and anti-citrullinated peptide antibodies (CCP) or having high autoantibody titers is associated with the progression of joint destruction in patients with rheumatoid arthritis (RA). Therefore, we evaluated the relationship between ultrasound synovitis and RF or CCP levels. [Methods] A total of 750 RA patients who underwent ultrasoud of MCP joints, PIP joints, wrists and MTP joints were included. Patients were classified into a negative group and a positive group according to RF and CCP titers, and the positive group was further classified into quartiles (Q1-Q4) according to that levels, and disease activity and ultrasound synovial findings were compared. [Results] There was no difference in disease duration or disease activity both in the RF and CCP positive group and the negative group, but the ultrasound finding was significantly worse in both grayscale and power Doppler findings in positive groups. There was no significant difference in ultrasound findings between antibody titers in the RF-positive group and CCP positive group. [Conclusions] Ultrasound synovial findings were significantly worse in positive group than negative group on both RF and anti-CCP antibodies, regardless of disease activity.

W62-2

Does concomitant/non-concomitant use of MTX affect intra-articular synovitis findings under the use of biologics and JAK inhibitors?

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Conflict of interest: None

[Objective] Biological DMARDs (BIO) and JAK inhibitors (JAK) are generally more effective with methotrexate (MTX). However, there are few reports evaluating intra-articular synovitis with and without MTX. [Methods] A total of 750 rheumatoid arthritis (RA) patients who underwent ultrasoud of MCP joints, PIP joints, wrists and MTP joints were included. Of these, 517 patients (68.9%) who used BIO/JAK were evaluated for propensity adjusted for age, sex, duration of RA, disease activity (CDAI), CRP level, and MMP-3 level with or without MTX. The total score of grayscale (GS) and power Doppler (PD) findings (GSUS/PDUS) were compared. [Results] There were 358 (69.2%) patients with MTX and 159 (30.8%) patients without MTX. The mean dose of MTX was 8.8 ± 3.5 mg/week. Ultrasound synovial findings were significantly suppressed in the MTX combined group, GSUS 11.6 ± 11.8 vs 8.5 ± 8.0 ($p = 0.009$) and PDUS 8.3 ± 9.9 vs 5.5 ± 6.2 ($p = 0.004$). Notably, ultrasound findings were worse in non-TNF inhibitor users without MTX. [Conclusions] Ultrasound synovial findings in patients with BIO/JAK was more suppressed with MTX. It was considered necessary to keep in mind that synovitis may persist in patients who are not concomitant with MTX and are using non-TNF inhibitors.

W62-3

Analysis of ultrasound findings in patients with difficult to treat rheumatoid arthritis

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Conflict of interest: None

[Objective] In recent years, the concept of D2TRA (difficult-to-treat rheumatoid arthritis) has become widespread, and D2TRA patients are defined as a state in which activity cannot be controlled even with the use of various molecular-targeted drugs. In this study, we investigated the ultrasound synovial findings in D2TRA patients. [Methods] 517 RA patients with biological DMARDs who underwent MCP joints, PIP joints, wrists and MTP joints were included. Ultrasound findings and background factors in D2TRA cases and non-D2TRA cases were compared. [Results] There were 40 D2TRA patients and 477 non-D2TRA patients. Mean age was 61.2 vs. 65.0 years in the order of D2TRA and non-D2TRA, mean duration of RA was 17.6 vs. 14.9 years, CDAI was 12.6 vs. 9.8, and CRP level was 0.8 vs. 0.3 mg/dl, MMP-3 level was 295.6 vs 10.8 ng/ml, which was significantly higher in the D2TRA group. In the D2TRA group, the rate of concomitant use of MTX was low, but there was no difference in the average amount of steroid use. Regarding ultrasound findings, the mean of GSUS was 16.2 vs 9.5, and the mean of PDUS was 11.0 vs 6.4, both of which were significantly higher in the D2TRA group. [Conclusions] Ultrasound finding was not suppressed in patients with D2TRA.

W62-4

Damage progression of finger joint cartilage evaluated by semiquantitative ultrasound score in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] Previously, we have examined damage progression of finger joint cartilage using joint cartilage thickness (CT) evaluation by ultrasound (US) in patients with RA. We aimed to examine the temporal changes of semiquantitative US score in RA patients. [Methods] We enrolled 53 RA patients in whom the cartilage of finger joints was examined at baseline and 1-year later. The recorded images were scored semiquantitatively and were measured the CT. In addition, the joint space narrowing (JSN) was scored with a hand X-ray. DAS28-CRP was used to compare patients with persistent moderate to high disease activity (active patients) and other inactive patients from baseline to 1 year. [Results] The sum of total semiquantitative score from 16 joints per patient ranged from 0 to 22 (median 5) at baseline, and it was significantly correlated with CT (rho=-0.54, p>0.001) and JSN score (rho=0.67, p>0.001). Comparing the active patients group (10 patients) to the inactive patients group (43 patients), total CT was significantly reduced (-6.2% vs. -1.2%, p=0.004), but there was no significant worsening in the semiquantitative score (+16.6% vs. +21.6%, p=0.742). [Conclusions] This pilot study did not demonstrate the progression of cartilage damage by semiquantitative US score in patients with RA.

W62-5

Research on knee joint synovitis in rheumatoid arthritis after total knee arthroplasty using musculoskeletal ultrasonography

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Conflict of interest: None

Objective: The purpose of this study was to clarify the recurrence of synovitis after TKA in rheumatoid RA patients. Methods: This study was a retrospective cross-sectional study. Subjects were patients who met the 2010 ACR/EULAR RA classification criteria and underwent TKA at the Tokyo Metropolitan Tama General Medical Center. Synovitis was assessed by MSUS. RESULTS: Forty-five patients with RA after TKA underwent MSUS, with a total of 71 knee joints (38 right, 33 left). Patient background: age (years) 74.4±10.0, disease duration (years) 20.6±10.4, DAS28 (CRP) 2.50±0.87, csDMARDs users 87%, BioDMARDs users 44%, TKA postoperative period (years) 5.7±4.0. The number of GS and PD signals (number of joints (%)) of Grade 2 or higher was as follows. Suprapatellar bursa (GS/PD): 23 (32.4%)/4 (5.6%), medial recess: 32 (45.1)/9 (12.7), lateral recess: 48 (67.6)/13 (18.3), patellar tendon: 10 (14.1)/4 (5.6), medial knee joint: 12 (16.9)/7 (9.9), lateral knee joint: 13 (18.3)/10 (14.1), popliteal tendon: NA/13 (18.3), lateral collateral ligament: NA/8 (11.3). [Conclusion] A small proportion of RA knees after TKA had recurrence of synovitis mainly in the lateral recess of patellofemoral joint and popliteal tendon of the knee joint.

W62-6

Evaluation of the forefoot bursae using ultrasonography in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We examined the relation between Intermetatarsal bursitis (IMB) and submetatarsal bursitis (SMB) in RA patients and nonRA patients (other rheumatic disease) and evaluated. [Methods] 53 patients who had clinical symptom on the forefoot were studied. (RA: 48 patients, nonRA: 5 patients) We evaluated bursitis (IMB and SMB), synovitis, tendonitis, tenosynovitis using B-mode (GS) and Power Doppler (PD) ultrasound (US) from dorsal and palmar. [Results] 1) We detected IMB only: 14.6%, SMB only: 41.7%, Both: 43.8% in 48 RA patients. And in nonRA patients, IMB only: 60.0%, SMB only: 20.0%, Both: 20.0%. 2) IMB was frequently found among 2-3 MTP, and SMB was under 5 MTP. 3) When IMB was found, there was no synovitis in neighbouring MTPs in 68.5%. 4) All patients in nonRA had only effusion in bursitis, but many RA patients had GS positive or PD positive area in bursitis statistically. 5) The size of bursitis in RA was larger than in nonRA statistically. [Conclusions] Forefoot bursitis was sometime found without synovitis and tenosynovitis in neighbouring MTPs. The percentage of SMB was higher than IMB in RA, and sometimes we detected only SMB. It is important to examine not only dorsal side but also palmar side in RA.

W63-1

A case of chronic eosinophilic pneumonia (CEP) with rheumatoid arthritis (RA) who achieved steroid-free remission after administration of Baricitinib (Bari)

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Conflict of interest: None

56-year-old female. She suffered from RA at the age of 19. She first treated with gold. At the age of 42, she developed eosinophilic pneumonia, which resolved with glucocorticoid maintenance. Abatacept was introduced for RA in 2014, but the joint deformity progressed. After concomitant of tacrolimus and PSL dosage reduction from 3.5 to 3 mg, the peripheral blood eosinophil count and KL-6 levels got worth. CT showed multiple ground-glass opacities in both peripheral lung fields. Since other causes were ruled out, PSL was increased to 15 mg, and she recovered quickly. In 2019, after reducing the dose of PSL to 5 mg, recurrence of arthritis was observed. Though ABT was resumed, eosinophilia with arthritis was continued. And then switching to Bari4 mg with MTX, both arthritis and eosinophilia improved, and steroid-free remission was

achieved. CEP is relatively responsive to steroid therapy, but relapses after discontinuation are repeated, and adverse events due to long-term steroid administration become a problem. In Japan, Bari also used for atopic dermatitis, and it has been reported that it may suppress the differentiation and proliferation of eosinophils by inhibiting IL-5 signaling via JAK2, and is expected to be effective for CEP with RA.

W63-2

Clinical presentation of rheumatoid arthritis patients with anti-ARS antibodies

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Conflict of interest: None

[Objective] Anti-aminoacyl-tRNA synthetase (ARS) antibodies are specific autoantibodies found in polymyositis/dermatomyositis (PM/DM), but have been detected in some rheumatoid arthritis (RA) patients and reportedly more frequently in patients with interstitial lung disease (ILD) complications. The purpose of this presentation is to characterize the clinical features of anti-ARS antibody-positive RA patients. [Methods] We reviewed the clinical profile of seven patients experienced at our hospital and associated hospitals. [Results] Six of the seven patients were women, and RF/ACPA was positive in almost all of them. ILD appeared during the course of treatment after the diagnosis of RA in all cases. CK elevation was observed in 3 patients, dermatomyositis-like skin rash in 3 patients, and 2 patients were diagnosed as PM/DM (1 PM, 1 DM). Anti-ARS antibodies were anti-PL-12 antibodies in 4 cases, and anti-PL-7, anti-Jo-1, and anti-KS (suspected) antibodies in 1 case each. [Conclusions] In all cases, the diagnosis of RA was preceded by the development of ILD, which was then found to be positive for anti-ARS antibodies; we need to consider the association with anti-ARS antibodies when a new appearance of ILD occurs during the course of RA treatment.

W63-3

Risk factors associated with conversion from polymyalgia rheumatica to rheumatoid arthritis

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Conflict of interest: None

[Objective] Polymyalgia rheumatoid arthritis (PMR) cases sometimes undergo conversion to rheumatoid arthritis (RA). This study aimed to identify the clinical risk factors associated with the conversion from PMR to RA. [Methods] The subjects were 64 PMR patients who were diagnosed based on the EULAR/ACR PMR classification criteria from April 2017 to April 2022. During the course of treatment for PMR, conversion from PMR to RA were detected and clinical risk factors associated with this conversion were examined. [Results] The average age of the subjected patients was 78.6 years, 60% of the patients were female, and all of them were treated with glucocorticoids (GC). Of these PMR cases, 13 cases (80.2 years old) had converted to RA. All of the cases were anti-CCP antibody negative. The average period from PMR onset to RA conversion was 1.2 years, CRP level at conversion was 3.21 mg/dl, MMP-3 level was 286 ng/dl, and GC dose was PSL 7.6 mg. RF level at PMR onset, presence of joint symptoms at PMR onset, and CRP level at 3 months after starting PMR treatment were identified as risk factors associated with the conversion. [Conclusions] PMR patients with high RF titer, joint symptoms, and high CRP levels at 3 months after treatment are at risk of developing RA.

W63-4

A Case of Adult-Onset Still's Disease with Skin Manifestation Resembling Heliotrope Rash in Dermatomyositis

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Conflict of interest: None

Case A 72-year-old woman presented to our hospital with high fever, headache and malaise. She appeared erythematous rash on upper eyelids and her serum ferritin level was extremely elevated (23,373 ng/mL). A diagnosis of Adult-onset Still's disease (AOSD) was made. Treatment was initiated with 50 mg of prednisolone (PSL) but condition didn't improve. We add on weekly intravenous tocilizumab (TCZ). Once she achieved remission but relapsed after tapering of PSL at 10 mg. From the elevation of serum ferritin level (14038 ng/mL), thrombocytopenia (36000 /μL) and hemophagocytosis in bone marrow examination, we diagnosed her with macrophage activation syndrome (MAS). We administered 1000 mg of methylprednisolone for 3 consecutive days and weekly TCZ and she achieved re-remission. Discussion AOSD shows various cutaneous manifestations including ones resemble heliotrope rash or Gottron papules in dermatomyositis (DM). Ikeda et al. reviewed the literatures of AOSD with DM-like skin rash and reported multiple cases accompanying with MAS or disseminated intravascular coagulation (DIC). Our case also shows skin manifestation resembling heliotrope rash and relapsed with MAS. We should recognize that AOSD can present with a DM-like rash and such case may be more likey to be severe.

W63-5

Risk factors for adverse drug reactions to trimethoprim-sulfamethoxazole in Adult onset Still's disease

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Conflict of interest: None

[Objective] We investigated the risk factors for adverse drug reactions (ADRs) to trimethoprim-sulfamethoxazole (TMP-SMX) in AOSD. [Methods] 31 patients with AOSD treated at our department between April 2010 and August 2022 were included in this study. Baseline characteristics, comorbid organ damage, and blood test data were retrospectively examined, and patients were divided into ADR-positive and ADR-negative group, and were copared. [Results] Of the 31 patients, 15 were ADR-positive and 16 were ADR-negative with a median age of 38 years/54.5 years and 86.7%/68.8% female. There were no significant differences in baseline characteristics or complications between the two groups, but there was a significant difference in CRP levels within one week prior to the introduction of the TMP-SMX (median 1.55 vs 0.11, $p = 0.048$). There was no significant difference in the presence of skin rash at the time of TMP-SMX use, but skin rash was seen in 7/13 in the ADR-positive group, compared with 3/15 in the ADR-negative group ($p = 0.11$). [Conclusions] It is better to refrain from TMP-SMX use in AOSD with elevated CRP levels within 1 week. ADRs caused by TMP-SMX tended to occur more frequently in AOSD with skin rash, and avoidance of administration should be considered.

W63-6

Significance of early introduction of Tocilizumab in Adult-onset Still's disease

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Conflict of interest: None

[Background] We aggregated patients with Adult-onset Still disease (AOSD) received in our hospital for the previous 10 years, examined and reported on the clinical characteristics of cases requiring hospitalization, and herein report our findings. [Method] In addition to 36 previously reported cases, 7 cases with AOSD (5 females and 2 males) who required inpatient treatment between July 2020 and August 2022 were aggregated, with a particular focus on cases of TCZ introduction. [Results] The number of cases in which TCZ was introduced which was only 4 cases of recurrence in the aggregation until June 2020, increased to 9 cases. All the additional 5 cases had TCZ introduced at the time of the first onset. Of these, 3 cases had good treatment response, but 2 cases developed macro-

phage activation syndrome (MAS). Corticosteroid tapering progresses in many patients due to the introduction of TCZ, which facilitates future withdrawal and leads to improvement in long-term prognosis for patients with AOSD. However, MAS should be considered. [Conclusion] As described in previous reports, it was reconfirmed that MAS may develop after cytokine inhibition therapy in AOSD. However, TCZ is a valuable treatment option for AOSD; hence, further accumulation of cases is desired in the future.

W64-1

A case of TAFRO syndrome-like symptoms in patients with systemic lupus erythematosus successfully treated with the combination of belimumab and cyclosporin

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Conflict of interest: None

Case: A 53-years-old man was consulted to our department for evaluation of acute kidney injury, thrombocytopenia, and edema in the extremities. CT showed a large amount of pleural and abdominal effusion with splenomegaly. A test for antinuclear antibodies was positive at a titer of 1:640 with a speckled pattern with hypocomplementemia. Bone marrow biopsy showed reticulin fibrosis. A lymph node biopsy revealed pathological findings consistent with Castleman disease. He was diagnosed with TAFRO-like syndrome with systemic lupus erythematosus (SLE), and high-dose glucocorticoids with intravenous tocilizumab were initiated. At week 4 of initial treatment, he suffered from septic shock due to necrotizing fasciitis. We started cyclosporin at week 7 of the initial treatment, followed by intravenous belimumab. In the next two months, anasarca, thrombocytopenia, and renal insufficiency gradually improved. At week 24 of initial treatment, he was discharged and subsequently does not experience evident disease flares. There is no report that TAFRO-like syndrome with SLE can be treated with cyclosporin and belimumab. We investigated the association between clinical course and trends of biomarkers, including B cell-associated cytokines, and reported this case with some literature reviews.

W64-2

A 31-year-old Man with monarthritis suspected malignant lymphoma and diagnosis with PAPA syndrome

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Conflict of interest: None

[Case] A month before visiting our department, right knee pain and swelling developed and he visited orthopedics. Contrast-enhanced MRI was performed and malignant lymphoma or Cystic Ganglionosis could be considered. He consulted to the other clinic and open biopsy was performed. Histologic examination showed only inflammatory granulation and bacterial cultures were negative, non-malignancy. No diagnosis was made and he was referred to our department. We found that the cysts and articular cavity were connected and considered synovial cystitis from the MRI image. We picked up acnes on his chest, and we got that his identical twin had similar arthritis and treated seronegative rheumatoid arthritis (RA). We considered pyogenic arthritis, pyoderma gangrenosum and acne (PAPA) syndrome and performed genetic test. The gene mutation was detected at PSTPIP1 gene and we diagnosed the case as PAPA syndrome. [Discussion] PAPA syndrome is an extremely rare, autosomal-dominant, hereditary auto-inflammatory disease. Because of the rarity, the diagnosis is difficult without the suspicion. We shouldn't diagnosis seronegative or atypical course arthritis as RA. PAPA syndrome should be considered to patients with refractory acne or family history of refractory arthritis.

W64-3

A case of Schnitzler syndrome mimicking IgG4-related disease

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Conflict of interest: None

[Case] A 60-year-old man was referred to our hospital for a 10-year-history of spontaneously regressing urticarial rash and joint pain resistant to prednisolone. He had edematous erythema on his extremities and trunk. The laboratory findings were significant for leukocytosis with marked neutrophilia (WBC 15600/μL, neutrophils 68.4%), elevated serum C-reactive protein (6.86 mg/dL) and IgM (460 mg/dL) with IgM-kappa monoclonal protein, suggesting Schnitzler syndrome. On the other hand, IgG4-related disease was also suggested from elevated serum IgG4 (344 mg/dL), submandibular gland enlargement, abdominal lymph nodes swelling and wall thickening of gallbladder and bile duct revealed by computed tomography and magnetic resonance imaging. Endoscopic ultrasonography showed gallbladder cholesterolosis and no bile duct wall thickening. Biopsies of submandibular gland, lymph node and bone marrow revealed no abnormal findings suggesting IgG4-related disease, while skin biopsy showed urticarial dermatitis with perivascular neutrophil infiltration in dermis. A diagnosis of Schnitzler syndrome was finally confirmed. [Conclusion] Because Schnitzler syndrome is a rare entity, its pathogenesis remains unknown. There are cases that must be differentiated from IgG4-related disease.

W64-4

A case of Löfgren syndrome during follow-up of mass-type muscular sarcoidosis

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Conflict of interest: None

A 55-year-old man initially palpated a mass in the left gastrocnemius muscle. Histopathological examination of the resected specimen showed non-caseating epithelioid granuloma. Erythema nodosum-like eruption on the face and deposits on the posterior corneal surface of the right eye confirmed the diagnosis of mass-type muscular sarcoidosis. There were no active lesions and he was followed up without treatment. Two years later, he developed a fever, polyarthritis and erythema nodosum-like eruption. A CT scan showed nodular shadows in the lung fields, bilateral hilar lymphadenopathy, multiple nodules in the kidney and spleen, and splenomegaly. A diagnosis of Löfgren syndrome was made. NSAIDs were poorly effective, so administration of PSL 30 mg/day was started. The fever quickly subsided and arthritis and eruption improved. One year later, PSL was gradually reduced to 3 mg/day without recurrence. Acute sarcoidosis with three cardinal symptoms of polyarthritis, erythema nodosum and BHL is called Löfgren syndrome. Löfgren syndrome is a very rare disease among Japanese and this is the second case of Löfgren syndrome with mass-type muscular sarcoidosis in Japan. The relationship between the clinical prognosis and HLA has been pointed out. We also report the HLA results of this case.

W64-5

A case of suspected chronic sarcoid myopathy presenting only muscle symptoms

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Conflict of interest: None

A 64-years-old male had proximal muscle weakness in his upper and lower limbs for about 4-5 years. Laboratory tests at a previous hospital showed levels of ACE, 65.3 IU/L; sIL-2R, 5580 U/mL; and lysozyme, 33.9 μg/mL. PET-CT in April X showed accumulation in the muscles of the whole body. Based on these results, Sarcoidosis was most suspected. His muscle symptoms worsened during followed up without treatment. PET-CT in September of the same year also showed exacerbation of accumulation in the muscles. He was referred to our department in October for diagnosis and treatment. The upper extremity coronal MRI with fat-suppressed T2-weighted images showed an inner stripe of decreased signal intensity with outer stripes of increased signal intensity, so-called three stripes sign. Muscle biopsy were performed from this site. No other lesions (lung, lymph node, eye, heart, skin, joint) of characteristic of sarcoidosis were present. Based on these laboratory findings, we diagnosed chronic sarcoid myopathy and started treatment with prednisolone.

W64-6

A case of sarcoidosis requiring differentiation from cholangiocarcinoma due to bile duct stricture

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Conflict of interest: None

[Case] A 78-year-old female was incidentally pointed out enlarged common hepatic artery lymph nodes in CT, of which size has been unchanged for follow-up four years. Because of lower bile duct wall thickening with contrast enhancement, bile and pancreatic duct dilation, and systemic lymphadenopathy in contrast CT, PET-CT was performed under suspicion of bile duct cancer. It showed abnormal FDG-uptakes in the common bile duct wall and multiple intra-abdominal and mediastinal lymph nodes. A bile duct stent was placed for prevention of cholangitis or pancreatitis. Whereas brush cytology and bile duct biopsies during ERCP showed no findings of malignancy, EUS-FNA of hilar lymph node indicated histological pattern of non-caseating necrotizing granulomas. By these clinical course and elevation of serum lysozyme and sIL-2R (12.2 μg/mL and 746 U/mL respectively), bile duct lesions and lymphadenopathy due to sarcoidosis were supposed to lead bile duct stenosis. 30 mg of prednisolone (PSL) therapy reduced lesions of bile duct and lymph nodes. No sign of relapsing has been observed after PSL tapering and removal of bile duct stent. [Clinical Significance] We report a rare case of sarcoidosis with bile duct stenosis by bile duct lesions and swollen surrounding lymph nodes.

W65-1

The clinical profiles and relapse rate of dermatomyositis with anti-TIF1gamma antibody

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Conflict of interest: None

[Objects] In this study we analyzed the clinical profiles of polymyositis/dermatomyositis with anti-TIF-1γ antibody (TIF), therapeutic drugs and relapse rate in comparison with anti ARS antibody (ARS). [Methods] TIF diagnosed after 2016 and ARS diagnosed after 2014 in our department were included. Clniclal symptoms, blood examination, therapy and course were retrospectively extracted. [Results] Twenty cases of TIF and 44 cases of ARS were included. The rates of Gottron's sign (100% vs 57%), heliotrope rash (60% vs 16%), muscle symptom (95% vs 64%), dysphagia (57% vs 10%), interstitial pneumonia (10% vs 100%), malignancy (60% vs 7%) were significantly different ($p < 0.05$). Malignancies were diagnosed with 12 cases of TIF (lung cancer 6, malignant lymphomas 2, others 4). 90% of TIF were treated with prednisolone (1 mg/kg). Though the usage of immunosuppressive drugs for TIF were significantly lower than ARS (20% vs 98%), there were no significant differences in relapse rates. The relapse rate of TIF without malignancy were significantly lower than with malignancy ($p < 0.05$). [Conclusions] The relapse rates were comparable between TIF and ARS. We should take the higher relapse rate of TIF with malignances into account in decreasing steroids.

W65-2

Clinical features and prognosis of patients with anti-Ku antibody: A retrospective study

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Conflict of interest: None

Objective: Anti-Ku antibody has been associated with overlap of systemic autoimmune diseases such as polymyositis (PM)/dermatomyositis (DM), systemic sclerosis (SSc) or systemic lupus erythematosus (SLE). However, the clinical features and prognosis of anti-Ku-(+) patients have not been fully elucidated due to the low frequency and technical difficulties in antibody detection. Therefore, we reviewed the anti-Ku-(+) cases experienced at Kyoto University hospital to analyze their clinical characteristics and prognosis. **Methods:** Clinical data from 12 patients from 1994 to 2022 were retrospectively examined. Anti-Ku antibody was detected by protein-immunoprecipitation. **Results:** 10 patients were female, and the onset age was 43 years (range, 14-82 years). 7 had PM/DM, 1 had SLE, 1 had overlap of PM and SSc, 1 had discoid lupus erythematosus (DLE), 1 had fibromyalgia, and 1 had myocarditis. ILD was found in 5 patients; 1 had NSIP, and 4 had unclassifiable ILD. Cardiac involvements were seen in 3. There were 4 deaths during the entire observational period (median length: 6.24 years (range, 0.852-20.4 years)), 3 of which had PM/DM with ILD. All of the patients with cardiac involvements died. **Conclusion:** ILD and cardiac involvements might be associated with prognosis of anti-Ku-(+) patients.

W65-3

Characteristics of anti-Ro-52 antibody-positive myositis

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Conflict of interest: None

[Objective] Anti-Ro-52 antibody-positive myositis is often complicated with interstitial lung disease (ILD) and have poor prognosis. We investigated the impact of anti-Ro-52 antibody in patients with dermatomyositis (DM)/polymyositis (PM) complicated with ILD. [Methods] Between November 2018 and September 2022, 12 cases with DM/PM measured anti-Ro-52 antibody were included. We compared patients between in the anti-Ro-52 antibody-positive group and -negative group. [Results] The mean age was 60.8 ± 10.4 years, 8 patients were female and 4 were male. In the anti-Ro-52 antibody-positive group, 3, 2, and 1 patients had complications with systemic scleroderma, Sjögren's syndrome, and rheumatoid arthritis, while there were no other connective tissue diseases in the negative group. There were no significant differences in ferritin, KL-6, LD, or CK except for IgG. Oxygen administration was required for 3 patients in the positive group. During the study period, 2 patients died only in the positive group, but there was not significant difference between the two groups. [Conclusions] Anti-Ro-52 antibody-positive myositis was associated with other connective tissue diseases, oxygen administration and high

IgG level. To evaluate the prognosis of anti-Ro-52 antibody, further investigation is needed.

W65-4

Clinical features of anti-Ro52 antibody-positive polymyositis (PM) and dermatomyositis (DM)

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Conflict of interest: None

[Objective] To clarify clinical features of anti-Ro52 antibody (Ab)-positive PM/DM. [Methods] For 35 patients diagnosed with PM/DM between Jan 2019 and Jun 2022, we performed 1) evaluation of clinical background, and 2) comparison of clinical features between anti-Ro52 Ab positive (n=20) and negative group (n=15), retrospectively. [Results] 1) Age at diagnosis was 57.5±14.0 years, 32 cases were female. 20 cases were PM and 15 cases were DM (including 4 CADM). 20 cases were positive for anti-Ro52 Ab, 13 for anti-ARS Ab, and 4 for anti-MDA5 Ab. ILD was detected in 25 cases, 6 of which were rapidly progressive. Steroid-resistant cardiomyopathy was detected in 5 cases, malignancy in one case, and Sjögren's syndrome (SS) in 3 cases. 2) The frequencies of anti-ARS Ab positivity (65.0% vs. 0%), ILD (95.0% vs. 40.0%), and concomitant use of immunosuppressants (100.0% vs. 57.1%) were significantly higher in the anti-Ro52 positive group ($p<0.05$). Steroid-resistant cardiomyopathy tended to be more common in positive group (25.0% vs 0%, $p=0.057$). The frequencies of PM/DM, positivity of anti-MDA5 Ab, malignancies, and SS were comparable between groups. [Conclusion] Anti-Ro52 Ab-positive PM/DM had significantly higher rates of anti-ARS Ab positivity and ILD, and concomitant use of immunosuppressants.

W65-5

Analysis of Clinical Significance of negative conversion of anti-ARS antibodies

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Conflict of interest: None

[Objective] No established evidence exists regarding the clinical significance of anti-ARS antibody (aARS) titers. We evaluated the relationship between changes in antibody titer and the clinical course. [Methods] Cases with positive aARS were included and divided into two groups: negative conversion (N group) and continuously positive (P group). We compared antibody titers and their trends, the organs affected, and clinical improvement and prognosis. [Results] Twenty-four subjects were included. Five patients showed negative conversion. Three patients in the N group and 14 patients in the P group were treated, and no significant difference in initial antibody titers is detected between two groups [N; 101 (37.6-108.0), P; 126.0 (60.25-163.0)]. Four patients in the N group had interstitial lung disease (ILD), but all responded well to treatment and progressed without apparent progression on CT. Two patients with severe ILD showed negative conversion after 18 and 24 weeks with marked improvement of ILD. The other patient in the N group showed arthritis and enthesitis, but the clinical symptoms improved, and the antibody titer became negative. [Conclusion] Negative conversion of aARS may have clinical significance with a favorable prognosis and suggest achieving immunological remission.

W65-6

A case of rheumatoid arthritis with anti-SRP antibody-positive immune-mediated necrotizing myopathy and trigeminal nerve lesions after vaccination for novel coronavirus

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Conflict of interest: None

[Case] A 42-year-old female with rheumatoid arthritis (RA) had been treated by adalimumab for 11 years. She developed trigeminal neuralgia 12 days after receiving the third vaccination for novel coronavirus. At 14 day after vaccination, serum creatin kinase (CK) level was 1,137 U/L, although at 49 day before vaccination it was 120 U/L. Two months after the vaccination, she developed myalgia in the proximal muscles, and serum CK level was 4,092 U/L. Myalgia in the proximal muscles, high serum CK level, and positive anti-SRP antibody were observed. A muscle biopsy from quadriceps was consistent with immune-mediated necrotizing myopathy (IMNM). Brain MRI on STIR showed high signal in the trigeminal region. The patient was treated with 1 mg/kg/day of prednisolone, tacrolimus, and high-dose intravenous gamma globulin. The myositis improved, however, the trigeminal neuralgia persisted. [Discussion] An immunostimulatory action of the vaccination for novel coronavirus may be related to the onset of IMNM and trigeminal nerve lesion. A long history of TNF inhibitor administration for RA might have been involved in the pathogenesis. [Conclusion] We reported a case of anti-SRP antibody-positive IMNM and trigeminal nerve lesion after vaccination for novel coronavirus.

W66-1

Recovery time from dysphagia in patients with inflammatory myopathies

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Conflict of interest: None

[Objective] The dysphagia in patients with IIM recovery period after treatment is not clear. The aim of this study was to clarify the degree of dysphagia in patients with IIM and the recovery period. [Methods] Of 188 adult primary myositis patients, 32 with dysphagia were included in this study. The mean age was 60.4 years, and the mean disease duration was 3.0 months. Survey items included myositis-specific antibody, initial and final swallowing evaluation by DSS table. Presence or absence of aspiration (DSS: 1 to 4 points is defined as aspiration), and the recovery time to normal oral food intake after treatment when patients started having difficulty in ingesting normal food due to aspiration (DSS: 6 or higher). [Results] Antibody distribution were: Anti-TIF1 antibody i was the most common autoantibody, with 14 cases. Of the 19 patients who had difficulty in ingesting a normal diet due to aspiration, 2 patients were excluded due to death after complications from malignant tumors, and 17 patients were able to ingest a normal diet for an average of 112.6 days and the median was 55 days after treatment. [Conclusions] Dysphagia was observed in 32 out of 187 adult patients with IIM. Recovery after treatment took an average of 112.6 days and a median of 55 days.

W66-2

Dysphagia in patients with idiopathic inflammatory myopathy: Clinical features and prognosis

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Conflict of interest: None

[Objective] To clarify the characteristics and prognosis of idiopathic inflammatory myopathy (IIM) associated with dysphagia. [Methods] We enrolled patients with IIM who had been admitted to our department since January 2003. Univariate and multivariate analyses were performed using

the Cox proportional hazards model, with the outcome defined as severe relapse (requiring prednisolone (PSL) 30 mg or more or hospitalization). [Results] Of the 124 patients, 10 (8.1%) had dysphagia and 19 (15.3%) had malignancies. Patients with dysphagia were significantly more likely to have malignancy (50.0% vs. 12.3%). During a median observation period of 43.5 months (6-232), 31 (25.0%) had a severe relapse, and dysphagia was associated with severe relapse (hazard ratio: HR 3.40, 95%CI 1.02-11.4). Multivariate analysis (age, sex, anti-TIF1-γ antibody (Ab), and dysphagia) showed that dysphagia was associated with severe relapse independently of anti-TIF1-γ Ab with HR 8.33 (1.6-44.2). When malignancy and interstitial lung disease were added as variables, dysphagia was also associated with severe relapse independently of malignancy (HR 6.0, 1.3-27.7). [Conclusion] In patients with IIM, dysphagia is associated with severe relapse even in those without anti-TIF1-γ Ab or malignancy.

W66-3

Analysis of skeletal muscle MRI in anti-MDA5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objective] We analyzed skeletal muscle Magnetic Resonance Imaging (MRI) findings in anti-MDA5 antibody-positive dermatomyositis and clarified its relationship with the prognosis of rapidly progressive interstitial pneumonia. [Methods] Among anti-MDA5 antibody-positive dermatomyositis patients who were treated between January 1, 2008 and March 31, 2022 at the Department of Rheumatology and Collagen Diseases of the Jikei University Hospital or Kashiwa Hospital, 29 patients who underwent upper arm or thigh MRI were analyzed. Perifascial lesions and intramuscular lesions in the left and right biceps, triceps, deltoids, quadriceps, hamstrings, and gluteus maximus were assessed by STIR or enhanced TI. [Results] Patients with intramuscular lesions in MRI at any of the 9 proximal muscles had significantly lower 6 month mortality rate than those without intramuscular lesions. In addition, the extensity of the lung lesions on chest CT at the time of diagnosis was significantly narrower in patients with intramuscular lesions. Further, the spread of lesions on chest CT was inversely correlated with myopathy findings. [Conclusions] In anti-MDA5 antibody-positive dermatomyositis, myopathy findings on skeletal muscle MRI may be a good prognostic factor for rapidly progressive interstitial pneumonia.

W66-4

Locations of leukocyte infiltration in myositis shape distinct radiographic patterns in muscle MRI

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Conflict of interest: None

[Objective] In recent years, the muscle pathology of idiopathic inflammatory myopathies (IIMs) has been better comprehended and classified into more distinct subsets. This study aimed to clarify whether skeletal muscle MRI can predict muscle pathology, myositis-specific autoantibodies (MSAs), and clinical manifestations in each IIMs subset. [Methods] This cross-sectional study included a cohort of consecutive patients with new-onset IIMs. The association between distribution of infiltrating leukocytes (i.e. endomysium, perimysium, fascia) in the biopsied muscle and MRI findings at the biopsied site was evaluated. Clinical data were assessed based on chart review. [Results] Of 86 patients with IIMs, 57 underwent a muscle biopsy. Foggy, honeycomb, and fascial patterns found in MRI images were associated with leukocyte infiltration in the endomysium, the perimysium, and the fascia, respectively (odds ratio 13.1, 5.9, 19.4; $p < 0.05$). In addition, MRI analysis in 86 patients revealed characteristic findings in each subgroup, and specific MRI findings were correlated with clinical manifestations including muscle weakness, dysphagia, or occurrence of malignancies. [Conclusions] Muscle MRI is a useful tool for predicting muscle pathology, disease subtypes, and clinical manifestations in IIMs.

W66-5

Clinical features in 14 patients with immune-mediated necrotizing myopathy

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Conflict of interest: None

[Objective] To investigate clinical features of immune-mediated necrotizing myopathy (IMNM). [Method] We retrospectively surveyed clinical Information via clinical records of patients who were diagnosed with IMNM based on the histological findings of biopsied muscle. [Result] Fourteen patients (10 women; mean age 56 years) had clinical profiles, including statin therapy, malignancy, or cutaneous lesion in one patient each, and myocardial disorder, interstitial lung disease, or arthritis in 4 patients each. Musculoskeletal manifestations involved dysphagia in 5, muscular atrophy in 7, neck weakness in 9, and proximal limb weakness in 11 patients, as well as increased serum CK levels (4556.6 U/L). Positivity for myositis-specific antibodies, including anti-SRP antibody (Ab) in 5, anti-HMGCR Ab in 3, anti-ARS Ab in one, and both anti-ARS and anti-SRP Abs in one patient, were identified. Prednisolone at a mean dosage of 0.84 mg/kg/day was administered; besides, concomitant agents were tacrolimus in 12 and high-dose intravenous immunoglobulin therapy in 8 patients. Recurrence was observed in 4 patients (mean observation period 35.9 months). [Conclusion] Histopathological examination is necessary for the diagnosis of IMNM, leading to determining a therapeutic strategy.

W66-6

Immune checkpoint inhibitor (ICI)-induced radiation recall myositis (RRM)

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Conflict of interest: None

[Case] A-70-year-old man with persistent hematuria was diagnosed with bladder cancer (stage IIIA). Two months later, he refused a total bladder resection. Then, chemotherapy with gemcitabine and carboplatin was initiated; however, his condition progressed to advanced stage (stage IV). Twelve months later, the patient was additionally treated with radiation therapy. However, no notable change in tumor diameter was observed. Fourteen months later, anti-PD-L1 antibody was administered. At a subsequent follow-up, the patient presented with muscle weakness in the gluteal region, laboratory tests revealed high levels of CPK. MRI revealed high-intensity areas in the bilateral gluteus maximus and rectus abdominis muscles, etc, and FDG-PET revealed high FDG uptake in the same areas. These inflammatory findings were localized to the irradiated areas. The biopsy specimen indicated myositis. Overall, these findings led to the possible diagnosis of ICI-induced RRM. Finally, steroid therapy improved the muscle symptoms, CPK level and imaging findings of myositis. [Conclusions] Although RRM is rarely encountered in clinical settings, its diagnosis should be considered while continuing treatment with not only chemotherapeutic agents but also ICIs in patients with a history of radiation therapy.

W67-1

AI-assisted diagnostic system for osteoporosis using the chest X-ray images-Accuracy evaluation using test data for use in health checkups

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Conflict of interest: Yes

[Objective] We evaluated the accuracy of BMD estimates for the L-spine (Group L) and proximal femur (Group H) when calculated from AP chest X-ray images alone on our AI-assisted diagnostic system for osteoporosis using test data that mimic the YAM distribution in the general population. [Methods] Test data were generated by imitating the YAM distribution of measured DXA values in a large-scale cohort study of residents. The study/test data included 4217/207 cases in Group L and 5047/207 cases in Group H. BMD estimates were calculated by inputting only the AP chest X-ray images from the test data after training the AI with the measured DXA values and AP chest X-ray images from the training data. [Results] The absolute error between the measured and estimated values and the correlation coefficient was 8.3%/0.79 for Group L and 9.2%/0.77for Group H. The AUC to discriminate YAM <80% and YAM≦70% was 0.95/0.93 for Group L and 0.91/0.94 for Group H, indicating high accuracy. [Conclusions] The practical application of this system, which outputs highly accurate BMD estimates of the lumbar spine and proximal femur from only one image, is expected to lead potential patients, estimated to be more than 10 million in Japan, to early treatment and prevent fragility fractures.

W67-2

Rheumatoid arthritis is no longer a risk factor for osteoporotic fractures -Cohort analysis considering time-dependent covariates, TOMORROW study-

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Conflict of interest: None

Background: RA is considered to have a high fracture risk. But with advances in RA treatment, is the concept still valid? Objectives/Methods: To evaluate fracture risk in RA patients, age-gender-matched 208 RA patients and 205 volunteers (Vo) (84.5% female, age 60.2 years, BMI 22.4, history of fracture 32.7%, ThBMD (thoracic spine bone density) 0.72 g/cm^2) were followed for 10 years. Since treatment content and internal factors change over 10 years, we attempted to identify fracture risk factors using the Cox proportional hazards model with time-dependent covariates. Results: There were 42 and 15 major fractures in the RA and Vo groups, respectively, with significantly more cases in the RA group (log-rank test, p=0.001). However, age (HR 1.047, 95%CI 1.020, 1.070, p=0.001), history of fracture (HR 1.843, 95%CI 1.004, 3.380, p=0.049), and homocysteine level (HR 1.205, 95%CI 1.023, 1.420, p=0.026) were the only significant fracture risk factors. RA per se was not a significant risk factor (HR 1.876, 95% CI 0.918, 3.830, p=0.085). Discussion: The median disease duration of RA patients participating in the TOMORROW study, which started in 2010, was 10.3 years. RA is no longer a risk factor for osteoporotic fractures, although it is likely to be a trailing effect of the past.

W67-3

Verification of the actual situation and safety of bisphosphonate drug withdrawal in glucocorticoid-induced osteoporosis -a 10-year observational study in patients with autoimmune inflammatory rheumatic diseases-

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Conflict of interest: None

[Objectives] An approach to discontinue bisphosphonate (BP) in postmenopausal osteoporosis patients has been proposed. But, there are insufficient studies in glucocorticoid (GC)-induced osteoporosis (GIOP). [Methods] A total of 121 patients were enrolled, using BP and GC at the initial examination. Osteoporotic fractures (OF) and avascular necrosis of the femoral head (AVN) were determined from medical records and X-ray data. [Results] Age at the first examination was 55 (42-64) years old, 89% of females, PSL 10 (8-12) mg/day, duration of BP use 5.0 (3.0-6.3) years, and the observation period 9.0 (6.2-9.4) years. BP was discontinued in 57 patients, 35 of whom (D-group) were followed up with active vitamin D preparation or no treatment. BP was continued in 64 patients (C-group). New OF were 0 in D-group vs. 10 (16%) in C-group (p=0.013), and new AVN occurred in 3 (9%) vs. 0 (p=0.042), but D-group showed a lower age and serum NTX concentration, and higher bone mineral density than C-group. After adjusting for age and sex, BP discontinuation did not increase the risk of both. [Conclusions] BP withdrawal was continued in patients who were young, had a low risk of OF, and no new OF occurred. It was considered that there are cases in which BP discontinuation can be considered even in GIOP.

W67-4

Examination of osteoporosis treatment in Autoimmune disease patients with anti-resorptive agent-related osteonecrosis of the jaw

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Conflict of interest: None

[Objective] Bone resorption inhibitors are often used in autoimmune diseases. We summarize the progress of patients with anti-resorptive agent-related osteonecrosis of the jaw (ARONJ), and examine the improvement of osteoporosis treatment after ARONJ. [Methods] We will retrospectively examine patients who received bone resorption inhibitors and were diagnosed and treated for ARONJ while attending our immunology department from January 2016 to October 2022. [Results] Ten patients were included in the study. ARONJ was classified into stages 0-3, including 2 patients with stage 1, 3 patients with stage 2, and 5 patients with stage 3 ARONJ. Nine patients were off bone resorption inhibitors. Three patients in stages 1 and 2 resumed bone resorption inhibitors after sequestrectomy, and one patient in stage 3 resumed them under the observation of an dental surgeon. Three patients in stages 1 and 2 did not have exacerbation of ARONJ after resumption, but one patient in stage 3 had exacerbation. Four of the stage 3 cases were not resumed due to treatment of ARONJ. [Conclusion] It is suggested that bone resorption inhibitors can be resumed in patients with stage 1 or 2 ARONJ, but close collaboration with dental surgeons is necessary.

W67-5

Increasing mHAQ predicts fracture incidence in the next year

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Conflict of interest: None

[Objective] To explore an factor predicting fracture incidence on RA

patients. [Methods] Using NinJa database, we extracted RA patients who were registered for hospitalization or surgery due to fracture from 2008 to 2020 as fracture patients, and targeted patients who were registered consecutively up to 4 years prior to the year of fracture, disease activity (DAS28), Changes in ADL (mHAQ) and oral steroid dose were analyzed for each year from 4 years before the fracture to the year the fracture occurred. Patients with multiple fractures were eligible for the first fracture. [Results] 653 patients were included, with an age at onset of fracture of 74.0±8.5 years, and disease duration of 21.2±11.8 years. DAS28: 3.67±1.23, 3.60±1.21, 3.67±1.24, 3.55±1.19, 3.48±1.15, mHAQ: 0.767±0.696, 0.775± 0.715, 0.814±0.730, 0.906±0.793, 1.037±0.814, Number of patients taking oral steroids and daily dose (PSL conversion): 437 cases 4.5±2.8 mg, 432 cases 4.4±2.4 mg, 429 cases 4.4±2.5 mg, 420 cases 4.4±2.3 mg, 432 cases were 4.5 mg ± 2.3 mg. Comparison of each index between years by a paired t-test showed that mHAQ significantly increase from 2 years before fracture to year before fracture (p=0.0004). [Conclusions] Increase of mHAQ may be a predictor of fracture development in the following year.

W67-6

Characteristics of rheumatoid arthritis patients experiencing fragility fractures

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is known to cause osteoporotic complications. Even when RA patients undergo regular bone density testing and are appropriately treated for osteoporosis, they frequently sustain fragility fractures. In this study, we investigated the characteristics of RA patients with fragility fractures. [Methods] Subjects were 44 female RA patients with fragility fractures and 130 female non-RA patients with fragility fractures. The primary endpoints were lumbar spine YAM (Young Adult Mean) and femoral YAM. Secondary endpoints included analysis of fracture site and cause of injury in RA patients. [Results] The RA group was younger than the non-RA group and had significantly higher lumbar spine YAM. Age-adjusted comparisons also showed significant differences only in lumbar spine YAM. Fracture site was spine in 45%, femur in 18%, and other in 36%. Only one fragile spine fracture was due to a fall. [Conclusions] This study found that RA patients who experienced fragility fractures had higher lumbar spine bone density than non-RA patients, which may be related to bone quality deterioration in RA patients. It is important to incorporate occupational therapy in addition to physical therapy in the treatment of RA patients with spinal fractures.

W68-1

Therapeutic effect of zoledronic acid on severe osteoporosis in real clinical practice

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Conflict of interest: None

[Objective] Investigation of the effect of zoledronic acid (ZOL) on severe osteoporosis in real clinical practice. [Method] 40 cases of severe osteoporosis who started ZOL treatment from February 2017 to June 2021. We investigated the patient's background and the primary endpoint [rate of change in bone mineral density (BMD) in the lumbar spine and proximal femur, and rate of change in bone metabolic markers at 12 months]. [Result] 34 patients were female, with an average age of 75.7 years, and the average T-scores were -2.7 at the lumbar spine and the proximal femur. Bisphosphonates were used in 16 cases, no medication in 9 cases, romosozumab in 6 cases, denosumab in 4 cases, active vitamin D monotherapy 3 cases, selective estrogen receptor modulators and teriparatide accounted for 1 case each. The percent change in lumbar spine BMD (g/cm^2) was +3.9% and +3.6% at 6 and 12 months, respectively ($p<0.05$). Femoral BMD was +1.6% ($p<0.05$) and +0.3% ($p=0.258$). Changes in bone turnover markers were BAP -31.9% and -10.6% ($p<0.05$), P1NP -39.2% ($p<0.05$) and -11.9% ($P=0.18$), NTX -18.8% and 10.4% ($p<0.05$), Tracp-5b 28.5% and -10.7% ($p<0.05$). [Conclusion] ZOL is expected to be effective in increasing lumbar bone density in patients with severe osteoporosis 6 to 12 months after initiation.

W68-2

Comparative study of Romosozumab therapeutic effect between rheumatoid arthritis and non-rheumatoid arthritis patients

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Conflict of interest: None

[Objective] We compared the therapeutic effect of Romosozumab (ROMO) in rheumatoid arthritis (RA) and non-RA arthritis patients, and investigated the influence of RA on therapeutic effect. [Methods] This study enrolled 36 RA patients and 49 non-RA patients who treated with ROMO for 12 months at our clinic. We investigated 28 patients in each group matched by propensity score. [Results] Back ground of Matched RA patients at baseline were mean duration of disease 9.2 years, CRP 1.5 mg/dl, DAS28-CRP 3.2, prednisolone usage 0%, and biologics usage 32.1%. The age was 77.3 in RA, 76.2 in non-RA, BMI was 20.0 in RA, 19.8 in non-RA, serum Alb was 4.0 in RA, 4.3 in non-RA (P=0.002) at baseline. Change of Lumbar spine BMD at 12 months was 9.3% in RA, 14.4% in non-RA (P=0.02), there was significant differences. There were no significant differences in change of serum TRACP-5b at 1 month, 6 months and 12 months, change of serum P1NP at 1 month, 6 months and 12 months, change of Lumbar spine BMD at 6 months, change of total hip BMD at 6 months and 12 months, and change of femoral neck BMD at 6 months and 12 months. [Conclusions] The therapeutic effect of ROMO may be attenuated in RA patients.

W68-3

The Effect of Romosozumab Treatment on Bone Quality

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Conflict of interest: None

[Objective] In this study, we investigated the effect of ROMO on bone quality during ROMO treatment. [Methods] Bone mass was measured by lumbar spine and femoral neck bone mineral density (DEXA method), structural bone quality by Trabecular bone score (TBS), material quality by blood pentosidine, and TRACP-5b, P1NP, and ucOC were measured for bone metabolism. [Results] The mean age was 81 years. Bone mineral density change rate was Δ5.8 (5.6~18)% to 9.5 (7.3~30)% at the lumbar spine, Δ2.9 (1.1~29)% to 1.9 (3.1~28)% at the femoral neck, and Δ1.03 (1.2~16)% to 1.86 (1.3~24)% at the TBS, with significant increase only at the lumbar spine. There was no relationship between bone mineral density and the rate of change in TBS. Blood pentosidine was 0.0569→0.0509→0.0586 μg/mL, and ucOC was 5.78→12.1→7.4 ng/ml, showing significant change only in ucOC, The significant changes at 1 month of treatment were confirmed in P1NP 67→122→75→55 ng/ml, TRACP-5b 414→329→348→322 mU/dL. [Conclusions] Bone strength changes due to ROMO treatment gave the impression of a significant effect of bone mass increase. The bone metabolism responded significantly in the early period after ROMO administration, and the bone quality and bone mass increase effect of ROMO treatment seemed to vary from case to case.

W68-4

Identification of morphological new vertebral fracture risk factors in osteoporotic patients treated by denosumab

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Conflict of interest: None

[Objective] Denosumab has been proven to increase bone mass and prevent fractures in the treatment of osteoporosis. However, vertebral fractures did occur, and we aimed to identify the risk factors for vertebral fractures. [Methods] The number of 248 patients started denosumab treatment for osteoporosis at our hospital. The Total Genant Score (TGS) was calculated on lateral spine radiographs (Th5 to L5) at the beginning of treatment and every six months. The increase of 1 TGS point or more was defined as a new vertebral fracture. The Cox proportional Hazard model was used to identify risk factors with the occurrence of a new vertebral fracture. [Results] New vertebral fractures occurred in 54 patients during follow-up of 1526±843 days. Baseline TGS was 3.26. Cox proportional hazards analysis using age, sex, BMI, baseline TGS, and baseline femoral total BMD as explanatory variables showed that only femoral total BMD was a significant as inhibitor of new vertebral fractures (HR 0.011, 95%CI 0.000-0.319, P=0.009). 91 rheumatoid arthritis (RA) patients were included, but no difference between the RA and non-RA groups. [Conclusions] At baseline, TGS and total femoral BMD had a significant negative correlation (r=-0.307. P<0.025), and vertebral fractures were more common with low BMD.

W68-5

Treatment for atypical femoral fractures patients with rheumatoid arthritis

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Conflict of interest: None

(Objective) In patients with rheumatoid arthritis (RA), there are some cases of using osteoporosis drugs for a long time. We should take care of get atypical femoral fractures (AFF) in RA patients. This is the 5 cases report of treatment for RA patients diagnosed as AFF. (Methods) 1 male and 4 females, average age of 72.2 years and an average duration of RA of 15.6 years. All patients had subtrochanteric fractures. 3 patients had complete fractures, 2 patients had incomplete fractures. In this study, we investigated patients' medications, bone density, bone metabolism, length of hospital stay, and walking style before and after surgery. (Results) All patients used antiresorptive drugs of bisphosphonate (BP) and 4 patients used PSL. Bone density values were preserved. Bone formation markers were suppressed. Bone resorption markers were maintained. In patients with complete fractures, the average of hospital stay was 85.3 days, and walking styles were worsened. In patients with incomplete fractures, the average hospital stay was 8 days, and walking styles were maintained. (Conclusions) In this study, all patients used BP, and 4 patients used PSL. Bone formation markers were suppressed. Patients with incomplete fractures had short hospital stay and walking style were maintained.

W68-6

The association with CKD in patients with osteoporosis and risk assessment by FRAX®

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Conflict of interest: None

[Objective] The rate of chronic kidney disease (CKD) patients with osteoporosis (OP), and bone mineral density (BMD) and fracture risk using the Fracture Risk Assessment Tool (FRAX®) were evaluated and compared them between CKD and non-CKD patients. [Methods] Of 254 patients diagnosed with OP, 136 (53.5%) in the CKD group with eGFR<60 and 118 (46.5%) in the non-CKD group with eGFR≧60 were compared. T-scores in the lumbar spine (L), total hip (TH), and femoral neck (FN), and fracture probability by FRAX® were investigated in each patient. Mean age, T-score, and risk of fracture by FRAX® were investigated and compared between the two groups. [Results] The mean age of the CKD group (81±7 years) was older than that of the non-CKD group (75±9 years) (p<0.01). T-scores in the CKD and non-CKD groups were -0.1±2.6 and -0.5±2.8 (p=0.27) for L, -2.2±1.0 and -2.2±1.0 (p=0.90) for TH, and -3.2±0.7 and -3.0±0.8 (p=0.04) for FN. The risk of fracture due to FRAX® was 29±13% and 24±11% for major fractures (p=0.01) and 14±11% and 11±8% for hip fractures (p=0.01) in the CKD and non-CKD groups, respectively. [Conclusions] The CKD group was older than the non-CKD group, and BMD was lower in the femoral neck.

W69-1

Elucidation of the cause of stomatitis in Behçet's disease

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Conflict of interest: None

[Object] Behçet's disease (BD) is an intractable disease characterized by recurring stomatitis, but the cause of stomatitis is largely unknown. It has been reported that the ability of saliva to induce neutrophil extracellular traps (NETs) is reduced in BD patients. In this study, we investigated whether the decreased NET induction activity in BD saliva was involved in the development of stomatitis. [Methods] We compared NET induction activity, myeloperoxidase (MPO)-DNA complex levels, and sialyl Lewis X (SLX; NET-inducible substance in saliva) levels in healthy subjects and BD saliva, including BD suspicious cases. Proteomics analysis compared BD saliva before and after treatment whose NET induction activity was restored by treatment. [Results] NET induction activity was decreased in BD saliva, but there was no relationship between stomatitis and NET induction activity. SLX levels decreased in BD saliva, especially those with stomatitis. Serpin B10 was extracted by proteomics analysis and was decreased in BD saliva with stomatitis. Binary logistic regression analysis showed that NET induction ability and lower serpin B10 level in saliva were associated with BD stomatitis. [Conclusion] The occurrence of BD stomatitis is related to NET induction ability and serpin B10 in saliva.

W69-2

Efficacy and safety of the SARS-CoV-2 mRNA vaccines in Behçet's disease patients

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of the SARS-CoV-2 vaccine (VC) for Behçet's disease (BD) patients. [Methods] Among BD patients in our hospital, we investigated the history of SARS-CoV-2 VC, its adverse reactions, and the incidence of COVID-19. The SARS-CoV-2 spike protein (SP) antibody and SARS-CoV-2-specific T cell count were also measured for immune response analysis. [Results] 124 of 141 BD patients had received SARS-CoV-2 VC. Seven patients were affected by COVID-19, and one patient died of severe pneumonia. Multivariate analysis showed significantly less VC in affected cases (p=0.031). No case of severe adverse reactions after VC was observed during the observation period. SP antibody titers 6 weeks after VC did not differ by the drug in multivariate analysis among BD patients. However, antibody titers were lower in BD patients compared to healthy controls (p=0.05). They were significantly lower in healthy controls and BD patients receiving TNF in-

hibitors (p=0.007). SARS-CoV-2 specific T cell count 6 months after VC did not differ by patient background or treatment. However, there was a significant correlation with SP antibody titer. [Conclusions] SARS-CoV-2 VC effectively prevented the development of COVID-19 in BD patients.

W69-3

Clinical features of our patients with Behcet's disease with arthritis

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Conflict of interest: None

[Objective] Arthritis with Behcet's disease (BD) is important in diagnosis and severity criteria. We clarify the clinical features in 247 patients (pts) with BD. [Methods] We compared the clinical features in our pts, diagnosed according to the MHLW BD criteria (2003), with arthritis (n=111) or without arthritis (n=136). [Results] Uveitis were less (22.5 vs 41.9%, p=0.001), tendency for women, intestinal ulcers and nodular erythema were common (70.3 vs 57.4%, p=0.036/40.5 vs 26.4%, p=0.019/44.1 vs 30.2%, p=0.023) in pts with arthritis. In pts with arthritis, positivity of HLA-B51, HLA-26 and RF were 36.5, 22.5 and 15.3%, respectively, mean CRP was 1.72 mg/dl. The test values had no different in each pts group. TJC was 3.2 and SJC was 1.2 (Large joints were 55.1 and small joints were 47.7%). The HAQ score was 0.76, walking (0.90), reach (1.19) and usual activities (1.05) were high. Colchicine (76.6%), MTX (47.7%), anti-TNF-Ab (40.5%) and GCs (26.1%) were used. In 79 pts followed over a year, TJC (3.2→0.5) and SJC (1.4→0.1) were decreased. [Conclusions] Frequency of uveitis, gender, intestinal ulcers and nodular erythema in pts with arthritis differ from pts of without arthritis. Pts with arthritis had more large-joint and severe impairments in ADL. Colchicine, MTX and anti-TNF Ab were used than GCs.

W69-4

Increased intrathecal production of IL-6 in chronic progressive Nemuro-Behecet's disease

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Conflict of interest: None

[Objective] The present study was designed to elucidate the mechanism of the elevation of cerebrospinal fluid (CSF) IL-6 in chronic progressive neuro-Behcet's disease (CPNB). [Methods] Paired serum and CSF samples were obtained from 5 patients with CPNB who were treated with infliximab and followed up thereafter. The levels of albumin and IL-6 in CSF and sera were measured by ELISA. [Results] Serum IL-6 and CSF IL-6 were elevated in CPNB compared with control patients with non-inflammatory neurological diseases. Treatment with infliximab dramatically decreased CSF IL-6 in the next day, but not serum IL-6 or Q albumin (CSF/serum albumin quotient). Of note, CSF IL-6 indices were dramatically decreased on the next day of treatment with infliximab in 5 patients with CPNB. [Conclusions] These results indicate that serum IL-6 as well as CSF IL-6 is involved in the pathogenesis of CPNB. In addition, it is suggested that the elevation of CSF IL-6 might not be caused by BBB breakdown, but by its intrathecal production in CPNB. Further studies to delineate the role of serum IL-6 would be important.

W69-5

Characteristics of patients with Behcet's disease with joint involvement at our institution

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Conflict of interest: None

[Objective] We explore the clinical characteristics of Behcet's disease (BD) in our hospital and clarify the effects of arthritis. [Methods] BD patients visiting our hospital from January 2020 to October 2022 were included. Clinical features, BD activity index and arthritis activity were evaluated to characterize patients with residual joint disease. [Results] Sixty-four patients with BD were included in the study. Past lesions included oral ulcers in 64 patients, genital ulcers in 51 patients, skin lesions in 54 patients, eye lesions in 17 patients, arthralgia in 54 patients and arthritis in 49 patients. The mean arthritis activity was SDAI 6.87 and DAS-28-CRP 2.37. The 21 patients free of arthritis and the 28 patients with arthritis were compared. The mean activity in the arthritic group was SDAI 8.76, DAS 28-CRP 2.73, patient VAS 55, physician VAS 10, 2 tender joints and 1 swollen joint. In the group with arthritis, the number of cases with oral ulcers was significantly higher (p=0.016), and the VAS of oral ulcers tended to be higher. BDCAF was also significantly higher in the group with arthritis (p=0.003). [Conclusions] It was suggested that BD activity is high in patients with residual arthritis activity, which is likely to interfere with daily life.

W69-6

Association between disease activity and major organ involvement as discovered from the Behcet's Disease Registry Study

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Conflict of interest: None

[Objective] Treatment to target (T2T) for Behcet's disease (BD) has not been established. We conducted the survey to examine the association between the Behçet's Disease Current Activity Form (BDCAF), an overall disease activity index and major organ involvement. [Methods] From a multicenter BD registry we selected patients who were "18 years or older", "met the MHLW diagnostic criteria", and "had disease for at least 6 months". Patients were followed up prospectively at 1 and 2 years after registration, and the incidence and relapse of major organ involvement were investigated. [Results] A total of 262 consecutive cases were extracted. The median BDCAF score was 2.0 [IQR 1.0-4.0] for both Yokohama city university and other institutions. BDCAF scores were available for 173 patients at 1-year follow-up, and 135 patients at 2-year, with median scores of 2.0 [IQR 1.0-3.0] and 1.0 [IQR 0.0-2.0], respectively. Relapse of ocular, intestinal, and neurological lesions was observed in 11, 3, and 1 patients at the 1-year follow-up, and in 9, 2, and 1 patient at the 2-year. There was no relapse of major organ involvement until 52 weeks after the survey in the group with a BDCAF score of 0. [Conclusions] The results suggest an association between BDCAF score and relapse of major organ involvement.

W70-1

Usefulness of HScore in the diagnosis of macrophage activation syndrome associated with adult Still's disease

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Conflict of interest: None

[Objective] We will examine the utility of HScore as a diagnostic criterion for macrophage activation syndrome (MAS), a complication of

adult Still's disease (ASD), in comparison with HLH-2004 diagnostic criteria (modified HLH-04). [Methods] 115 patients with active ASD diagnosed according to Yamaguchi criteria at our hospital (2004-2022), Kindai University Nara Hospital (2010-2022), and Izumi City General Hospital (2018-2022) were included. The MAS+ group was defined as patients "with hemophagocytosis confirmed by bone marrow puncture" [Results] Sixty patients were enrolled in MAS- group and 23 in MAS+ group. MAS+ group had significantly higher levels of Ferritin, sIL-2R, LDH, AST, and Trig, and significantly lower ESR, PLT, and Fib. The median HScore was significantly higher in MAS+ group: 234 (IQR: 210-261) than in MAS- group: 129 (IQR: 102-167). The optimal cutofff values for ROC analysis were 192 for HScore (AUC: 0.99, 95%CI: 0.97-1.00, sensitivity: 95.7%, specificity: 96.7%) and 4/7 for modified HLH-04 (AUC: 0.95, 95%CI: 0.89-1.00, sensitivity: 87.0%, specificity: 91.7%) was calculated. Only HScore was extracted in multivariate analysis (OR: 1.27, 95%CI: 1.01-1.60, p<0.0001). [Conclusion] HScore may be a more useful criterion than modified HLH-04 for the diagnosis of ASD-MAS.

W70-2

Decreased production of complement in adult-onset Still's disease patients with hypocomplementemia

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Conflict of interest: None

[Objective] We evaluated the etiology of adult-onset Still's disease (AOSD) with hypocomplementemia. [Methods] Ninety-nine patients with AOSD who were admitted to our hospital from 2011 to 2020 were included. They were divided into low CH50 and low C4 (low complement group; LCG) and high CH50 and high C4 (high complement group; HCG). We evaluated the laboratory findings, cytokine and complement profile, and treatments. [Results] Seven patients were classified into LCG. C3 was significantly lower in LCG (104.5 vs 150.3 mg/dL, p=0.005). Ferritin titers (19990 vs 3348 ng/mL, p=0.043) and IL-18 titers (191239 vs 117404 pg/mL, p=0.043) were higher in LCG. AOSD with hypocomplementemia had higher disease activity. Meanwhile, C5a was lower in LCG (26.7 vs 49.4 ng/mL, p=0.036). The relative complement activity was lower in LCG. The relative complement activity was 58.6 (24.1-76.2) vs 79.5 (76.5-83.0) % (p=0.028) in classical pathway and 65.7 (30.8-74.9) vs 91.4 (59.5-100.0) % (p=0.028) in alternative pathway. No evidence of complement pathway activation was found in AOSD with hypocomplementemia. [Conclusions] Relative hypocomplementemia in patients with AOSD was thought to be due to decreased production of complement, but not to activation of complement pathway.

W70-3

A case of ankylosing spondylitis developed IL-17 inhibitor-induced Behçet's disease-like lesions

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Conflict of interest: None

<Case> A 53-year-old woman with ankylosing spondylitis (AS) had been treated with secukinumab since February 20XX, and her axial symptoms was improved. Then, stomatitis started to appear, therefore, she was switched from secukinumab to adalimumab. However, her stomatitis did not improve. Upper gastrointestinal endoscopy revealed laryngeal edema and multiple aphthae/ulcer lesions from the oral cavity to the gastroduodenum. Several viral infection tests were negative. Ulcerative lesions were also observed on her vulva, and she was diagnosed with IL-17 inhibitor-induced Behçet's disease-like lesions. She was treated with intravenous prednisolone (PSL) 50 mg daily. Then, her symptoms remitted and PSL was tapered. After 5 months, upadacitinib was initiated due to exacerbation of her axial symptoms. Then, AS was maintained remission without flare of. IL-17 inhibitor-induced Behçet's disease-like symptoms. <Conclusions> IL-17 inhibitor-induced Behçet's disease-like lesions has been reported rarely, and we would like to discuss about our case including the mechanism with literature review.

W70-4

Clinical enthesitis in patients with Behcet's disease

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Conflict of interest: None

[Objective] Behcet's disease (BD) is one of the diseases that can cause clinical enthesitis, but its details are unknown. The purpose of this study was to clarify the characteristics of clinical enthesitis in BD patients. [Methods] Cases of enthesitis were retrospectively identified from the medical records of BD patients attending our outpatient, and their clinical characteristics were analyzed. [Results] Fifteen patients with BD had clinical enthesitis. The mean age at BD onset was 34.4±7.3 years. HLA-B51 was positive in 5 of 10 patients. The sites of enthesitis were achilles tendonitis in 14 patients, pes anserinus in 2 patients, and plantar fasciitis in 2 patients. Sacroiliitis was present in 2 cases. Folliculitis was present in 11 cases, erythema nodosum in 9 cases, genital ulcer in 11 cases, uveitis in 6 cases, and epididymitis in 2 cases. CRP at the time of enthesitis was positive in 8 cases. Colchicine was administered in 12 patients and non-steroidal anti-Inflammatory drugs in 8 patients. [Conclusions] Clinical enthesitis was the most common form of achilles tendonitis in patients with BD, and all patients had concomitant arthritis.

W70-5

Significance of HLA-A26 positivity in HLA-B51 positive Behçet's disease patients

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Conflict of interest: None

[Objective] Behçet's disease (BD) is an inflammatory disease characterized by recurrent oral aphthous ulcers and various other manifestations. Although HLA is one of the genetic factors in BD, the clinical importance of HLA-A26 is poorly recognized. This study aimed to examine the association between HLA-A26, HLA-B51, clinical manifestations, and disease severity. [Methods] This study was a cross-sectional observational study and enrolled BD patients who were treated at Kyoto University Hospital and Kurashiki Central Hospital from 2006 to 2021. Disease severity was evaluated using Krause score reflecting the entire spectrum of disease manifestations. [Results] In total, 204 patients were enrolled in this study. HLA-B51 was positive in 53 of 110, HLA-A26 in 25 of 92, and both HLA-B51 and HLA-A26 in 6 of 92 patients. HLA-B51 was associated with uveitis, neuro-involvement, and disease severity; however, HLA-A26 showed no significant association independently. In HLA-B51 positive patients, uveitis was more frequent (frequency: 100% vs. 48.5%, $p = 0.027$), and Krause scores were higher (median: 7.5 vs. 5.0, $p < 0.01$) when HLA-A26 was also positive. [Conclusions] Our study demonstrated the importance of confirming both HLA-A and HLA-B haplotype for disease activities in BD patients.

W70-6

A case of macrophage activation syndrome with elderly-onset still's disease under tocilizumab treatment

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Conflict of interest: None

An 87-year-old Japanese woman with no medical treatment. She had a sore, a sore throat, fatigue, and loss of appetite for a few days and gradually difficulty walking. On examination, fever and erythema were observed on the buttocks and extremities. Laboratory tests revealed WBC 9690/μL, Neut 85%, CRP 13.3 mg/dL and ferritin 14448 ng/ml. Enhanced CT scan revealed no abnormalities and antimicrobial therapy was initiated to treat but her fever did not resolve. On day 7, Prednisolone (PDN) 40 mg/day was started as elderly onset adult still disease (EOSD) in the absence of obvious infection or malignancy. On day 20, CRP improved to 7 mg/dL, but the patient developed fever again, so steroid pulse therapy was started. The fever resolved and the CRP decreased to 1 mg/dL but did not turn negative. On day 35, the patient became febrile, so tocilizumab (TCZ) 320 mg was introduced, and PDN was tapered off. On day 43, she tested positive for cytomegalovirus antigenemia and recovered on ganciclovir. On day 70, fever, low WBC, high LDH, and hemophagocytosis on bone marrow examination led to the diagnosis of macrophage activation syndrome (MAS). On day 165, she was discharged from the hospital. The use of TCZs during the remission induction phase for EOSD may lead to MAS.

W71-1

Concomitant fatty liver in patients with rheumatoid arthritis: with a focus on long-term follow-up data

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Conflict of interest: None

[Objective] We aimed to investigate the association of fatty liver with RA. [Methods] 571 patients with RA were followed up for 1 year or longer at our institution between September 2010 and September 2022. 77 patients who were followed up for 5 years or longer were included in our study. Fatty liver was diagnosed mainly using abdominal ultrasonography, and changes over time were assessed using the Fib-4 score. After January 2014, treatment interventions were performed. [Results] In the 77 patients, the mean Fib-4 score gradually worsened. All patients received weight-loss guidance and 26 patients successfully lost weight. Of these 26 patients, only four showed improved Fib-4 scores. [Discussion] When we evaluated the 77 patients who were followed up for 5 years or longer, the mean Fib-4 score gradually worsened, with Fib-4 score improvement observed in four patients only. Fib-4 scores improved only in 15.4% of patients who received weight-loss guidance. Although fatty liver showed no marked improvement with the treatment interventions used, the Fib-4 score improved in the patients whose grip strength increased by >50 mg. [Conclusion] The results of our study indicate the need to implement preventive measures against fatty liver in patients with RA in the future.

W71-2

Treatment course after development of lymphoproliferative disease in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the course of OIIA-LPD and disease activity in the patients with RA after the onset of OIIA-LPD. [Methods] Fourteen RA patients with OIIA-LPD were included. The patients background, LPD types, treatment for LPD, recurrence of LPD, and the changes in RA treatment and disease activity after the onset of LPD were retrospectively investigated. [Results] The average age was 64.4 years old (2 males, 12 females) and the duration of illness was average 12.4 years. MTX in 12 patients, tacrolimus (TAC) in 7 patients bDMARDs in 5 patients, prednisolone (PSL) in 3 patients were used. The types of LPD were MTX-LPD in 5 cases, DLBCL in 7 cases, and Hodgkin lymphoma in 2 cases. Eight patients were treated only with MTX or bDMARDs withdrawal, and six patients were treated with chemotherapy. The mean follow-up period was 4.8 years and no recurrence of LPD was observed. RA treatment after the onset included TAC in 8 patients, PSL in 7 patients, bDMARDs in 3 patients, and JAK inhibitor use in 2 patients. Disease activity (DAS28-CRP/CDAI, /SDAI) was 2.3/4.1/4.7 before onset, and 2.3/5.3/6.5 at the last follow-up. [Conclusions] Although there was no marked worsening of disease activity of RA and recurrence of LPD, careful follow-up is still needed.

W71-3

Results of upper gastrointestinal biopsy screening for AA amyloidosis in RA patients during last three decades

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Conflict of interest: None

[Objective] To investigate transitions of the incidence, clinical features and prognosis of AA amyloidosis complicating RA (AA) during last 3 decades. [Methods] We divided the 399 AA patients into 3 decade interval group (1900,2000,2010) by the year of the AA diagnosis and compared the incidence, clinical features and prognosis of each group. [Results] 1. 399 of 7046 RA patients were diagnosed with AA by upper GI screening. 2. Incidence of AA was significantly decreased in recent onset groups ($p<0.0001$). 3. Interval from onset of RA to AA diagnosis was prolonged in recent onset groups ($p=0.0073$). 4. CRP values were decreased significantly by the lapse of the time ($p<0.0001$). 5. Manifestation of AA symptoms were decreased significantly in recent decade group ($p=0.0006$). 6. Prognosis (5 year survival rate) improved significantly in recent decade group (Log rank test $p<0.0001$). [Conclusions] Decreased incidence and improved prognosis of AA were demonstrated during last three decades.

W71-4

Differences and similarities in cytokine profiles of macrophage activation syndrome in systemic lupus erythematosus and adult onset Still's disease

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Conflict of interest: None

[Objective] To clarify the differences and similarities in the cytokine profiles of macrophage activating syndrome (MAS) between systemic lupus erythematosus (SLE) and adult-onset Still's disease (AOSD) [Methods] The study participants included 9 patients with MAS-SLE, 22 with non-MAS-SLE, 9 with MAS-AOSD, and 13 with non-MAS-AOSD. Serum cytokine levels were measured using a multiplex bead assay. Moreover, cytokine patterns were examined using principal component analysis (PCA). [Results] IL-6, IL-8, IL-18, and TNF-α levels were elevated in patients with SLE and AOSD. IFN-α levels were elevated in SLE, whereas IL-1β and IL-18 levels were elevated in AOSD. In SLE, IFN-α and IL-10 levels were higher in MAS than in non-MAS and controls. PCA revealed distinctive cytokine patterns in SLE and AOSD, enhanced cytokine production in MAS, especially in SLE. PCA showed no differences in cytokine patterns between the MAS and non-MAS groups. [Conclusions] Cytokine profiles differed between SLE and AOSD but not between MAS and non-MAS. MAS is induced by the enhancement of underlying cytokine abnormalities rather than by MAS-specific cytokine profiles. Type I IFN may be involved in MAS development in patients with SLE, whereas IL-1β and IL-18 may be involved with AOSD.

W71-5

Assessment of skeletal muscle mass in autoimmune disease patients treated with glucocorticoids using bioelectrical impedance analysis

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Conflict of interest: None

[Objective] Bioelectrical impedance analysis (BIA) is a simple and noninvasive method to measure skeletal muscle mass. We aimed to evaluate the validity of measuring skeletal muscle mass of autoimmune disease patients on glucocorticoids using BIA. [Methods] We recruited new-onset autoimmune disease patients who were admitted to our hospital from April 2021 to September 2022 and started 0.4 mg/kg or more of prednisolone (PSL). Skeletal muscle mass index (SMI) calculated by the BIA method and physical function were assessed every two weeks from the start of glucocorticoids until discharge. [Results] A total of 48 patients with a median age of 64 years were included in the study. The median initial PSL dose was 40 mg/day. Forty-six patients completed the set of assessments at two weeks, and twenty-four completed it at four weeks. SMI decreased over time, and change in SMI at four weeks was correlated with the circumference of the thigh and calf. In addition, the change in SMI at four weeks was negatively correlated with the initial dose and accumulated dose of PSL. [Conclusions] In autoimmune disease patients on glucocorticoids, the validity of measuring skeletal muscle mass by BIA was confirmed.

W71-6

Clinical features of pulmonary hypertension with anti-SS-A antibodies

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Conflict of interest: None

[Objective] To examine the clinical features of anti-SS-A antibody-positive pulmonary hypertension. [Methods] Twelve cases with pulmonary hypertension (PH) diagnosed by right heart catheterisation between April 2013 and September 2022 with a mean pulmonary artery pressure (mPAP) ≧25 mmHg and positive anti-SS-A antibody were included. [Results] Age 51.1±10.8 years, sex 91.7% (female), mPAP 37.1±13.5 mmHg, PVR 9.9± 6.2 WU. Of the 12 cases, 2 had SjS, 3 had SLE, 3 had SSC, 1 had MCTD and 3 undetermined diagnosis with only positive anti-SS-A antibody and no secretory disorders. Secondary SjS was present in three cases, two with SSC and one with MCTD. Interstitial pneumonia (IP) was a complication in four cases, with %VC>70% in all cases and PCWP > 15 mmHg in two cases. Both pulmonary vasodilators and immunosuppressive therapy (IST) were used in 11 cases, with a significant improvement in mPAP of 27.4± 10.4 mmHg after treatment (p=0.030). In one case of undetermined diagnosis, mPAP improved with IST. There were three deaths, one each from PH, IP and lung cancer. [Conclusions] IST is effective in some cases of PH with only anti-SS-A antibodies. Further cases are needed to determine predictors of response to treatment in patients with anti-SS-A antibodies.

W72-1

SARS-CoV-2 mRNA Vaccination Caused Flare of Rheumatoid Arthritis or Immune-Related Diseases

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Conflict of interest: None

[Purpose] It has been noticed that immune function is enhanced following COVID-19 mRNA vaccination, which induces immune-associated diseases (IADs). We investigated whether vaccination flares in RA patients, or whether IADs occurs in humans without immune disease. [Subjects and Methods] Primary survey: Adverse reactions seen after two vaccinations in 1,272 RA patients and 1,117 staffs. Secondary survey: Cases of IAD including RA were investigated as adverse reactions. [Results] 1. Staffs observed arthralgia in 0.9%, while RA patients had worsening arthralgia in 3.6%. 2. RA patients had 10 cases of transient worsening of arthralgia and 27 cases of RA relapse; 3 cases of acute exacerbation of interstitial pneumonia were observed during RA relapse. Hospitalization was required for 9 severe cases. (3) 3 cases of RA, 2 cases of SLE and 1 case of hemophagocytic lymphohistiocytosis (HLH) were observed in humans without IRDs. (4) We experienced one case of RA after COVID infection. [Discussion] RA patients may develop flare-ups after vaccination. The same disease may be caused after vaccination or by COVID infection itself. The high levels of IL-6 in serum suggest that IL-6 Amp causes Cytokine Release Syndrome, which leads to inflammation and disruption of immunological homeostasis.

W72-2

Experience with recombinant zoster vaccine (RZV) in rheumatoid arthritis patients on JAK inhibitors

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Conflict of interest: None

Objective: To evaluate the safety of RZV in Japanese patients with rheumatoid arthritis using JAK inhibitors and the number of patients who developed herpes zoster. Methods: To evaluate rheumatoid arthritis patients who received RZV and rheumatoid arthritis patients who did not receive RZV. Results] As of October 2022, 35 patients were vaccinated with RZV, the mean age was 71.37 years, the disease duration was 10 years, and there were 6 patients with a history of herpes zoster. JAK inhibitors were tofatinib in 4 patients, baricitinib in 15 patients, peficitinib in 4 patients, upadacitinib in 7 patients, and filgotinib in 5 patients. None of the patients in the RZV vaccination group had flare-ups of rheumatoid arthritis. Side effects were swelling and pain at the vaccination site in 3 cases. 116 patients were not vaccinated with RZV, mean age was 73.1 years, and disease duration was 10 years. Twenty patients had a history of herpes zoster. JAK inhibitors included tofatinib in 18 patients, baricitinib in 27, peficitinib in 4, upadacitinib in 28, and filgotinib in 39. Nineteen of the patients developed herpes zoster. Conclusion: Herpes zoster occurred in only one case after RZV vaccination. RZV was administered relatively safely, and no relapse of rheumatoid arthritis was observed.

W72-3

Restoration of low anti-SARS-CoV-2 antibody reactivity after the first set of vaccination by the booster in rheumatoid arthritis

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Conflict of interest: None

[Objective] This is the follow-up study of the last year's report at this meeting of the low reactivity against SARS-CoV-2 mRNA vaccines in rheumatoid arthritis (RA). Comparison of the antibody level among the same patient groups after the first booster is the objective this time. [Methods] Patients included in this study were those with RA (n=65), life-style related diseases (n=37), RA + life-style related diseases (n=51) of 30 years and older and these patient groups were compared with each other of antibody level. Antibody titer was measured using ARCHITECT SARS-CoV-2 IgG II Quant reagent developed by Abbott (normal < 50 U/ml, sensitivity 99.37%, specificity 99.55%). RA patients were grouped into 4 according to the medication used, a group on biologics (n=44), a group on methotrexate (n=58), a group on conventional DMARDs (n=12) and a group on steroids (n=13). [Results] Anti-SARS-CoV-2 Antibody level in RA patients, which was lower after the first set of doses, increased following the booster to the same level as that in those with life-style related diseases. [Conclusions] Patients with RA, who are considered immunocompromised, need at least one booster to mount antibody to the similar level to patients with life-style related diseases.

W72-4

The efficacy and safety of SARS-CoV-2 vaccine in Japanese patients with rheumatic diseases

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of SARS-CoV-2 mRNA vaccine in Japanese patients with rheumatic diseases (RD). [Methods] RD patients receiving glucocorticoids or immunosuppressants who were scheduled to receive vaccinations were included. Patients attending for diseases other than RD and malignancies were recruited as contols. Following the guidance of American College of Rheumatology, immunosuppressive drugs were withdrawn before and after vaccination. Blood samples were collected before vaccination and 1, 3, and 6 months after vaccination (M1, M3, and M6), and Spike-specific SARS-CoV-2 antibody titers were measured. [Results] There were 290 RD patients and 34 controls, with a mean age of 66.5 and 70.7 years, respectively. Compared by disease, antibody titers tended to be lower in vasculitis and dermatomyositis/polymyositis. Compared by treatment, antibody titers were significantly lower in the abatacept and rituximab groups in M1, M3, and M6. Factors influencing the amount of change in titer were older age, abatacept, TNF inhibitors, IL-6 inhibitors, and prednisolone. Adverse events were similar in both groups. [Conclusions] There may be differences in antibody acquisition and antibody titer over time in RD patients depending on the type of immunosuppressive drug.

W72-5

Safety of SARS-CoV-2 vaccines in patients with rheumatic disease

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Conflict of interest: None

[Objective] To assess adverse events (AE) and disease flare after SARS-CoV-2 vaccines in patients with rheumatic disease (RD). [Methods] Patients who received three doses vaccine (Pfizer or Moderna) were included, and those who were attending for diseases other than RD and malignancies were considered controls (C). We surveyed their treatment, changes in disease activity, and AE appeared after the first (D1), second (D2), and third (D3) dose of vaccine by referring to their clinical records. [Results] We collected information of 1317 patients. The largest group of patients received three doses of Pfizer's vaccine: 657 in RD group and 139 in C group. The mean (±SD) age was 66.5 ± 14.9 years and 70.7 ± 18.0 years, respectively, with a similar gender ratio. The most common AE was local pain (approximately 20% in RD group and 37% in C group) in both D1, D2, and D3, followed by fever, which increased with each dose (18% and 31% in D3, respectively). Exacerbation of RD was observed in 4 patients (0.6%), 2 of whom required intensified treatment. [Conclusions] The frequency of AE after SARS-CoV-2 vaccine in RD group was rather lower than in C group, and exacerbations of disease activity were infrequent, indicating safety in RD patients.

W72-6

Recombinant Zoster Vaccine (RZV) Does Not Cause Disease Relapse in Rheumatoid Arthritis

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Conflict of interest: None

[Objective] While rheumatoid arthritis patients are at high risk of developing herpes zoster (HZ), concerns have been raised that RZV may cause disease flares in immunocompromised rheumatoid patients. We investigated the safety of recombinant herpes zoster vaccine (RZV) in a Japanese population of rheumatoid arthritis patients. [Methods] Fifty-three RA patients who received two doses of ZRA at our hospital between October 2021 and October 2022 were analyzed retrospectively. The study protocol was approved by the Ethics Committee of the hospital (approval number R3-065). [Results] Of the 53 patients, 11 were males and 42 were females. The mean dose of biologics used was 3.9 mg. ESR, CDAI, SDAI, PtVAS, DrVAS) at 4, 8, 12, 24, and 52 weeks. Treatment was changed during the observation period in 17 patients, of which 2 patients had new or increased doses of drugs added as treatment intensification. No cases of herpes zoster occurred during the observation period. Adverse events included local site reactions in 29 patients and systemic symptoms such as fatigue and malaise in 8 patients, which resolved in an average of 3.4 ± 2.8 days. [Conclusions] RZV did not cause rheumatoid arthritis flares.

W76-1

Efficacy in patients with systemic lupus erythematosus treated with anifrolumab in maintenance therapy

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Conflict of interest: None

[Purpose] The purpose of this study is to examine the efficacy and safety of anifrolumab in combination with existing therapy, and to verify the status of achieving treatment goals. [Methods] Patients with SLE attending our hospital who had been receiving anifrolumab for at least 24 weeks were included in the study. The clinical symptoms such as musculoskeletal symptoms, general malaise, and glucocorticoid (GC) use were examined for 24 weeks before and after anifrolumab use, and the relationship with disease activity was verified. [Results] There were 7 patients with SLE who met the above criteria. All 7 patients were female and the median age was 39 years. 7 patients were induction in the remission maintenance phase, and all were switched from belimumab to anifrolumab. The treatment goal was to improve musculoskeletal system in 4 patients, to improve fatigue in 1 patient, to improve serology in 1 patient, and to reduce the steroid dose in 1 patient. LLDAS remission was achieved in 5 of 7 patients, while DORIS clinical remission (with treatment) was achieved in 1 patient (14%). [Conclusions] Previous reports have shown increased expression of type I IFN-induced genes in synovial tissue, which may be useful in SLE patients with residual musculoskeletal symptoms, as in this case.

W76-2

Background and clinical course of patients with systemic lupus erythematosus who were introduced to anifrolumab in our department

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Conflict of interest: None

[Background] Anifrolumab (ANF) is a new treatment for SLE, and we report 8 cases of patients who received ANF in our department. [Methods] We evaluated the background of the 8 patients and the change in each disease activity before and 12 weeks after the introduction of ANF. [Results] Six patients were female, age 45.9 (36-80) years [median (range)], and disease duration 10.5 (0.5-15) years. At diagnosis, all patients were positive for antinuclear antibody, 3 for anti-dsDNA antibody, 1 for anti-Sm antibody, and 3 for anti-RNP antibody. Prednisolone dose at ANF induction was 10.0 (5-22.5) mg, and 4 patients switched from belimumab. 3 patients had low complement at ANF induction, 1 patient was anti-dsDNA antibody positive, 5 patients had arthritis, 4 patients had skin rash. One case was discontinued due to herpes zoster. The changes in the endpoints before and 12 weeks after ANF introduction were SLEDAI-2K: 5.0 (2-8) to 1.0 (0-2)/p=0.01, SLE-DAS: 5.1 (1.12-10.63) to 1.6 (0.37-4.25)/p=0.03, PGA: 1.0 (0.60-1.65) to 0.8 (0.15-0.99)/p=0.03, Lupus Impact Tracker: 36.3 (15-72.5) to 33.8 (7.5-75)/ p=0.90, showing a significant decrease in

activity assessment. [Conclusion] Disease activity improved after the introduction of ANF, and ANF is expected to be a potential treatment for SLE in the future.

W76-3

Analysis of the efficacy of anifrolumab in Japanese patients with systemic lupus erythematosus (SLE) (Japanese subgroup analysis of the TULIP-2 study)

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Conflict of interest: Yes

[Objective] To analyze the efficacy of anifrolumab (ANI) in Japanese patients with SLE. [Method] We analyzed disease activity and glucocorticoid (GC) dose reduction in a Japanese subgroup within the TULIP-2 trial that showed the efficacy and safety of ANI vs placebo (PBO) in patients with moderate to severe active SLE. [Result] In the Japanese subgroup [ANI, n=24; PBO, n=19], who attained BICLA response at week 52 (primary endpoint) was ANI: 12/24 (50%); PBO: 3/19 (15.8%), nominal P=0.014, and attained BICLA response maintained it up to week 52 was higher in the ANI than PBO at all time points to week 52. At week 52, the LLDAS was achieved by ANI: 9/24 (37.5%); PBO: 3/19 (15.8%). ANI: 5/24 (20.8%) were in LLDAS for ≧50% of the observed time vs 0/19 (0%) of patients in PBO. At week 52, the percentage of improvement in BILAG organ domains for mucocutaneous and musculoskeletal was ANI: 54.5%; PBO: 22.2% and ANI: 57.9%; PBO: 18.8%, respectively. A flare during the study period was ANI: 16.7% compared PBO: 31.6%. The patients who tapered GC throughout the study period were ANI: 14/24 (58.3%); PBO: 6/19 (31.6%). [Conclusion] In the Japanese subgroup of the TULIP-2 trial, ANI showed improvement of disease activity and GC dose reduction, similar to that observed in the overall population.

W76-4

Clinical features in patients with systemic lupus erythematosus treated with Aniflorumab and its efficacy and safety

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Conflict of interest: None

[Objective] To examine the clinical features of patients treated with Anifrolumab and its efficacy in clinical practice. [Methods] We identified five cases of SLE treated with anifrolumab in University of Tsukuba Hospital, and retrospectively evaluated 1) their baseline characteristics, 2) treatment efficacy and safety profiles. [Results] 1) Gender was 4 females, 1 male. Mean age was 47.0±9.7 years old and mean disease duration was 12.4±10.2 years. Mean SLEDAI-2K was 5.8±3.5. Skin rash and arthralgia were presented in four and three cases, respectively. All cases were treated with prednisolone (PSL), and the mean of their dose was 9.9±4.2 mg/day. Hydroxychloroquine and immunosuppressive drugs were concomitantly used in five and four cases, respectively. 2) In two cases treated for more than three months, their symptoms disappeared and SLEDAI-2K was improved. PSL was reduced from 17.5 to 14 mg/day in one case. Anifrolumab was discontinued in one case due to fever and arthralgia. No adverse events were observed in the other four cases. [Conclusions] Patients treated with Aniflorumab were more likely to present cutaneous and musculoskeletal symptoms. Aniflorumab might be effective to control disease activity and to reduce PSL without notable safety concern in clinical practice.

W76-5

Three cases of using belimumab (BLM) in combination with steroids and other immunosuppressants for Neuropsychiatric Systemic Lupus Erythematosus (NPSLE)

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Conflict of interest: None

[Objective] There are few reports on the use of BLM for NPSLE. We report three NPSLE cases successful treated with BLM, which could lead to dose reduction of glucocorticoid (GC). [Case 1] A 18-year-old woman was diagnosed with SLE due to aseptic meningitis, high titers of anti-ds DNA. She was treated with high-dose GC, but she developed a non-traumatic subarachnoid hemorrhage after treatment. High-dose GC, IVCY, and plasma exchange were performed, which dramatically improved these symptoms, whereas inflammation in blood test is continued, BLM and azathioprine (AZA) were added 6 months after treatment, thereafter she had achieved Lupus Low Disease Activity Score (LLDAS). [Case 2] A 25-year-old woman was diagnosed with SLE due to alveolar hemorrhage, NPSLE (psychosis) and high titers of anti-ds DNA. These symptoms were improved after induction of remission with high-dose GC, IVCY. She had achieved LLDAS 5 months after treatment by addition of BLM and AZA. [Case 3] A 29-year-old woman was diagnosed with SLE when she presented lupus nephritis (class 4,5), NPSLE (microcerebral infarction), high titers of anti-ds DNA. These symptoms were improved after induction of remission with high-dose GC, MMF and BLM, thereafter GC has been gradually reduced to low dose.

W76-6

Belimumab for the treatment of lupus associated protein loosing gastroenteropathy

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Conflict of interest: None

A 69-year-old woman was diagnosed with systemic lupus erythematosus at another hospital in X-25 and started treatment with prednisolone 30 mg and azathioprine 75 mg. In X-6, she was referred to our hospital and stabilized on prednisolone 3 mg. In X-5, he showed a gradual decrease in albumin and weight gain, and was admitted to the hospital in X-4 for close examination and treatment. On admission, physical examination revealed edema in both lower legs, and blood tests showed albumin of 1.9 g/dL. After close examination, a protein leak scintigraphy was performed at another hospital, suspecting protein loosing gastroenteropathy, and showed accumulation in the small intestine and transverse colon. Prednisolone was not increased and berimumab 400 mg IV every 4 weeks was administered. Albumin recovered to 3.0 g/dL after 6 months of treatment and to 3.5 g/dL after 2 years of treatment, and protein leak scintigraphy showed decreased accumulation in the small intestine and transverse colon. Improvement of edema in both lower legs, elevated albumin, and improvement of protein leak scintigraphy were observed without increasing the steroid dose, suggesting the beneficial effect of belimumab.

W77-1

Association between hydroxychloroquine (HCQ)-induced adverse events (AEs) and clinical features in patients with systemic lupus erythematosus (SLE)

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Conflict of interest: None

[Objective] To clarify the risk factors of HCQ-induced AEs in SLE. [Methods] Cases of SLE treated with HCQ in our department between Sep 2015 and Jun 2022 were identified from electrical medical charts. We retrospectively analyzed their 1) baseline characteristics, 2) autoantibody (Ab) profiles, 3) AEs 4) risk factors for drug eruption. [Results] 1) There were 253 patients, mean age was 40.7±14.4 years, and 89.7% were female. For organ involvement, nephritis was identified in 41.5%, skin in 74%, joints in 80.6%, hematological disorders in 65.6%, and serositis in 22.5%, respectively. 2) Ab positivity was 126/245 (51.4%) for anti-SS-A, 18/208 (8.7%) for anti-SS-B, 87/229 (37.9%) for anti-U1-RNP, and 38/231 (16.5%) for anti-Sm. 3) AEs were observed in 57 cases (22.5%), including drug eruption in 19/57 (33.3%), gastrointestinal symptoms in 24/57 (42.1%), and ophthalmologic abnormalities in 9/57 (15.8%). 51 cases (20.2%) discontinued HCQ because of AEs, and the most frequent AEs causing drop out were drug eruption (18 cases). 4) Of the cases with drug eruptions, 14/19 (73.6%) were positive for anti-SS-A. The odds ratio of anti-SS-A positivity for drug eruption was 2.85 (95% CI: 1.05-7.36). [Conclusions] Anti-SS-A Ab was suggested to be a possible risk factor for HCQ-induced drug eruptions.

W77-2

The dose of hydroxychloroquine may be overdosed when adjusted to ideal body weight

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Conflict of interest: None

[Objective] The dose of hydroxychloroquine (HCQ) is adjusted to ideal body weight (iBW) calculated from height and sex in Japan. American Academy of Ophthalmology recommends HCQ dose of 5 or less mg/kg of real weight (rBW) to prevent HCQ retinopathy. We researched the ratio of patients with systemic lupus erythematosus (SLE) who received HCQ dose of over 5 mg/kg of rBW. [Methods] Patients prescribed HCQ for SLE between September 2015 and June 2022 were included. We retrospectively collected the data from medical records. [Results] Of 220 patients, females were 193 (87.7%) and the median age was 40 years old (IQR: 30-48). The median administration duration of HCQ was 2.2 years (IQR: 0.6-4.4). The number of patients with 5 or more years with HCQ treatment was 31 (14.1%). In 4 patients, HCQ was discontinued due to suspected retinopathy or ocular fundus lesion, but there was no patient with definite HCQ retinopathy. The median HCQ dose was 4.33 mg/kg of rBW (IQR: 3.77-5.26 mg/kg) and the ratio of patients who received 5 or more mg/kg of rBW was 30.5%. [Conclusions] The dose of HCQ may be overdosed when adjusted to iBW in Japan. In our hospital, 30.5% of patients were prescribed 5 or more mg/kg of rBW of HCQ. To prevent HCQ retinopathy, we should pay attention to rBW when we prescribe HCQ.

W77-3

Glucocorticoid doses and minimally important differences in emotional health of SLE patients: a 6-year longitudinal observational cohort study (the LUpus registry of NAtionwide institutions (LUNA))

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Conflict of interest: None

[Objectives] Glucocorticoid doses are associated with emotional health (EH) in patients with systemic lupus erythematosus (SLE). This study estimated the minimally important differences (MID) required to interpret the magnitude and calculated the glucocorticoid dose equivalent to achieve it. [Methods] This cohort study used data from the adult SLE patients' registry between 2016 and 2022. The outcome measure was the EH of the Japanese version of the Lupus Patient-Reported Outcome. The exposure was glucocorticoid doses (mg oral prednisolone or equivalent). We fitted linear models using the generalized estimating equations for repeated measures, and the estimated MID at 12 months by the anchor-based method was divided by coefficient β to calculate the GC equivalent. [Results] Overall, 1285 patients (median age: 47 years, interquartile range: 36-59; 87% female) were included. The glucocorticoid dose was significantly associated with the EH (per 1 mg increase, β= -0.73, [95%CI -1.08 to -0.39], $P < 0.01$). The MID for improvement was estimated at about 9.2 pt., and the average glucocorticoid dose equivalent to achieving it was about 12 mg. [Conclusions] This study result suggests that the achievement of MID for EH corresponds to approximately a mean 12 mg dose of glucocorticoid tapering.

W77-4

A retrospective observational study on the treatment and its transition of systemic lupus erythematosus

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Conflict of interest: None

[Objective] Recently, hydroxychloroquine (HCQ), mycophenolate mofetil, and biologics belimumab and anifrolumab have been newly approved for the treatment of SLE. The treatment of SLE has changed significantly in the last 10 years, including the development of guidelines and the widespread acceptance of Treat to target (T2T). We investigated the transition. [Methods] From January 2012 to October 2021, we collected

data from electronic medical record of 1356 SLE patients at Juntendo Hospital, Juntendo University School of Medicine, and retrospectively analyzed changes in patient profile, therapeutic drugs, glucocorticoid (GC) dose, anti-DNA antibody titers and complement level. [Results] The average age of patients continued rising. As the combinations of treatment with immunosuppressants, HCQ, and biologics were increasing, the proportion of GC monotherapy decreased from 30% to 16%, and the proportion of GC-free therapy increased from 9.9% to 14.6%. The average GC dose was decreased from 7.3 mg/day as prednisolone equivalent to 5.2 mg/day. The proportion of patients with hypocomplementemia and high anti-DNA antibody titer was decreased. [Conclusions] Although the dose of GC was decreased, the serological disease activity improved. We would control disease activity independently of GC.

W77-5

How does the increase in drug options in the treatment of SLE affect the clinical course of the SLE?

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multiple organ dysfunction associated with the production of a variety of autoantibodies. Recently, new therapeutic agents such as hydroxychloroquine (HCQ) and biologics have become available. [Objective] To determine whether the increased treatment options have changed disease activity and steroid dosage in patients with SLE at our hospital. [Subjects] SLE patients attending our outpatient hospital on October 1, 2017 and August 1, 2022 were included in the study. [Assessment] Patients' clinical information, treatment details, comorbidities and complications were assessed. [Results] Eighty-six patients with SLE in 2017 and 95 patients in 2022 were included in the study. HCQ use increased from 6% in the 2017 SLE group to 52% in the 2022 SLE group. Median PSL-equivalent steroid use was 7 mg in the 2017 SLE group and 6 mg in the 2022 SLE group, which were similar. Infectious complications were 27% in the 2017 SLE group and 19% in the 2022 SLE group, showing a decrease. [Conclusion] The 2022 SLE group had a higher rate of concomitant HCQ use. Steroid use did not change, but the frequency of infectious complications decreased, possibly due to the increased use of HCQ, an immunomodulator.

W77-6

Is S100 Protein Useful as a Therapeutic Index in SLE?

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Conflict of interest: None

[Objective] This study aims to analyze whether the S100 protein is a marker of therapeutic efficacy in SLE. [Methods] Patients with SLE had only received additional HCQ were included in the study, and comprehensive disease activity was assessed before and 3 and 6 months after HCQ treatment. Serum cytokines and S100A8 and S100A9 related to disease activity were measured. [Results] Of the 59 eligible patients, 36 patients maintained LLDAS and 23 patients did not maintain LLDAS at baseline, and SLE-DAS in both groups was significantly reduced after 3 months. Serum TNF-α, IL-6, IL-1ra, S100A8, and S100A9 levels also decreased significantly in both groups after 3 months, but there was no difference in change in cytokine levels between patients who achieved LLDAS after HCQ treatment and those who did not. Although there was no significant relationship between change in SLE-DAS and change in biomarkers in patients who did not maintain LLDAS at baseline, in patients who maintained LLDAS, S100A8 and S100A9 levels were higher at baseline in patients whose SLE-DAS improved significantly after HCQ treatment, and were negatively correlated with the amount of decrease in SLE-DAS. [Conclusions] S100 protein may need to be regulated in cases where LLDAS is achieved but disease activity remains.

W78-1

In adalimumab treatment, Remission induction and treatment continuation at 416 weeks in 230 patients

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Conflict of interest: Yes

[Object] Clinical usefulness and treatment continuation following 368 weeks of adalimumab (ADA) in rheumatoid arthritis (RA) patients were investigated. [Methods] Subjects were 186 analyzable patients introduced to ADA at the author's institution from May 2009 to Oct. 2014. Mean age was 54.3 years, mean duration of illness 6.5 years. 189 received MTX ≧10 mg/week (≧10 group) and 34 MTX<10 mg/week (<10 group). The course of DAS28 (ESR), HAQ and remission rate were analyzed. [Results] Overall DAS28 (ESR) remission rate showed clinical remission in 51% of patients from 12 weeks, and achieved 68% from 52 weeks, after that this condition continued. Overall HAQ remission rate at 416 weeks was 85%; treatment continuation rate was 51.3%., and those of≧10 group was 52.7%. [Conclusions] ADA plus an adequate dose of MTX with early escalation in early-stage RA and Bio Naïve patients is the best approach to maximally exploit the ADA potential.

W78-2

Current status of rheumatoid arthritis patients usingu certolizumab pegol as first Bio

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Conflict of interest: None

[Objective] We clarify the efficacy in rheumatoid arthritis (RA) to whom certolizumab pegol (CZP) were administrated as the first bio. [Methods] The subjects were RA patients with CZP administration in our institution. Age and reason of administration, methotrexate (MTX) use, and disease activity in bionaive cases were evaluated. [Results] There were 88 cases, and 55 had been administered as the first bio. The reasons were insufficient effect in 31 cases, hope for pregnancy in 22, and postpartum flare in 4. The age of administration was 46.5±16.7 years old, but those who hoped to pregnancy were 33.9±5.3, and those with postpartum flares were 35.0±3.4, which were lower than 57.0±15.9 for those with insufficient effect (P<0.01). MTX was used in 28 case, 2 of those hoping for pregnancy, and 26 with insufficient effect, which was higher (P<1.00). MTX dose was reduced or discontinued in 13 with insufficient effect and in all who hoped for pregnancy. Regarding disease activity (SDAI), 81.3% hoping for pregnancy achieved LDA at 4 weeks, while 67.8% with insufficient effect (P=0.30), and at 12 weeks 94.4% and 69.6% achieved (P=0.10), showing no significant difference. [Conclusions] In our institution, CZP was administrated to hope for pregnancy as the 1st bio, but it was equally effective.

W78-3

Prospective Prolonged Interval Trial of Biologic Agents in Rheumatoid Arthritis

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Conflict of interest: Yes

[Objective] In this study, we prospectively extended intervals accord-

ing to protocol in patients who remained in remission, and examined the relapse rate, relapse timing, and patient background of relapse/non-relapse cases. [Methods] 64 steroid-free patients (37 TNFi, 21 IL-6Ri, 6 CTLA4-Ig) who started biological agents (BIO), had DAS remission for at least 6 months were enrolled in the study. The extension protocol consisted of 1.5x, 2x, and withdrawal and DAS evaluation of the dosing interval as BIO standard dosage every 6 months, and extension if it was below the LDA. [Results] After the start of extension, 48.4% of the patients stopped dosing, 29.7% relapsed, and 21.9% were on extension. The mean dosing interval in relapse cases was 1.75x, and the mean relapse time was 3.8 months. There were no significant differences in patient background. In joint ultrasonography performed at the time of interval extension, there was no difference between the two groups in Power Doppler, but the Grey Scale was significantly lower in the non-relapse cases. [Conclusion] The Grey Scale at baseline was lower in patients who were able to extend the interval, suggesting that joint ultrasound evaluation prior to interval extension may be predictive of patients who are able to extend the interval.

W78-4

A study of nine patients with rheumatoid arthritis treated with ozoralizumab

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Conflict of interest: None

[Objective] To investigate the efficacy of Ozoralizumab (OZR), a humanized anti-TNFα NANOBODY® compound for RA. [Methods] In this study, we included 9 patients who entered in the multicenter, double-blind, parallel-group, placebo-controlled trial 3000-JA and in the multicenter randomized open-label clinical trial 3001-JA at our hospital. Patients' clinical data during 52-week observation period were analyzed. [Results] Nine patients were included: 7 in the OZR 30 mg group, 2 in the 80 mg group. The mean age was 56.0 years, the mean disease duration was 8.0 years. DAS-28CRP and SDAI at the start / 1 week / 4 weeks / 52 weeks of OZR were 4.76±0.90 / 3.63±1.00 / 2.93±0.85 / 1.93±0.76, and 29.24±9.92 / 17.66±10.47 / 12.14±6.96 / 6.04±5.19, respectively. Both scores were significantly decreased at 52 weeks (DAS28-CRP; $p<0.001$ and SDAI; $p<0.001$) as well as at 1 week compared with the start of OZR (DAS28-CRP; $p=0.004$, SDAI; $p=0.003$). HAQ-DI was also improved significantly from 0.72±0.36 at the start of OZR to 0.50±0.26 at 1 week ($p=0.029$). There were no cases of discontinuation due to adverse events or worsening of disease activity. [Conclusions] The efficacy of OZR was confirmed at 1 week post-treatment and was maintained during 52 weeks, suggesting the potential for immediate efficacy.

W78-5

Regulation of TNF-alpha signaling in a synovial cell by an affibody molecule

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Conflict of interest: None

[Objective] Affibody clones have been obtained from mutation libraries that are expected to be bound to inflammatory mediators and used as artificial antibodies. In addition to Ras which related in intracellular signaling pathway, TNF-α have been targeted by affibody molecules. In this study, inhibition of intracellular signaling pathway was investigated by using affibody molecules in synovial cell. Furthermore, an inhibitory effect by specific binding of an affibody molecule to TNF-α was also examined. [Methods] Affibody clons which can bind to Ras were introduced into synovial cell line by a plasmid vector. Then, TNF-α or S1P was added to the cell and its effect to proliferation was examined. While affibody clones which bind to TNF-α directly were produced in *Escherichia coli* and added into medium to inhibit function of TNF-α. [Results] The inhibitory effect of affibody molecules to cell proliferation and to production of inflammatory mediator such as IL-6 and PGE2 by synovial cells were observed. Furthermore, affibody molecules against TNF-α was able to inhibit proliferation of a synovial cell. [Conclusions] An inhibitory effect to signal transduction cascade of both affibody molecules was suggested by above experiments on inflammatory mediator production and cell proliferation.

W78-6

A case of rheumatoid arthritis with drug-induced lupus caused by golimumab and complicated by interstitial pneumonia

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Conflict of interest: None

[Case] 79-year-old woman. She had been treated with MTX, PSL, and AZA for rheumatoid arthritis (RA) complicated with Sjögren's syndrome before X-10, and after remission, she was changed to MTX and infliximab (IFX), and remission was maintained. In X-5, MTX and IFX was changed to GLM, and the disease activity improved to low. In X, She got a slime glass shadow at chest and high levels of anti-dsDNA antibody and KL-6. In addition to interstitial pneumonia due to RA, drug-induced interstitial pneumonia due to golimumab (GLM), GLM-induced lupus and interstitial pneumonia due to GLM were considered as possibilities, and the cough improved when GLM was discontinued. Since sputum cultures were negative, antimicrobial therapy was not performed. 1 month after discontinuation of GLM, anti-dsDNA antibody titer decreased, and the diagnosis of GLM-induced lupus and interstitial pneumonia caused by it was made. [Discussion] The onset of drug-induced lupus caused by GLM varies from 1 month to 4 years after the treatment, depending on the case. Most of the clinical changes are hypocomplementemia and skin manifestations, and interstitial pneumonia is rare. Interstitial pneumonia caused by anti-TNF antibody drugs should be investigated for drug-induced lupus by searching for anti-DNA antibodies.

W79-1

Relationship between histopathological findings and the 2-year therapeutic response in eosinophilic granulomatosis with polyangiitis (EGPA)

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Conflict of interest: None

[Objective] The manifestations of eosinophilic granulomatosis with polyangiitis (EGPA) vary widely among individuals. Eosinophilic infiltration and vasculitis are thought to coexist in the background of the disease, and pathological findings associated with these conditions are frequently encountered, but data on the relationship of these findings with the prognosis and treatment effect are scarce. The present study investigated the relationship between the pathological findings and therapeutic response in EGPA. [Methods] The subjects were patients with EGPA who underwent pathological analysis and were treated at our department for more than two years. Data related to EGPA were collected and analyzed, and the therapeutic responses were compared in light of the pathological findings. [Results] Twenty-six patients fulfilling the 2022 ACR/EULAR classification criteria for EGPA with a median age of 65 years and a median BVAS at onset of 21 were enrolled. A poor treatment response was associated with necrotizing vasculitis. [Conclusions] The pathological findings of necrotizing vasculitis in EGPA are not only important for diagnosis but may also be associated with the therapeutic response.

W79-2

Comprehensive analysis of renal pathology in ANCA-associated vasculitis

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Conflict of interest: None

[Objective] We examined the relationship between renal pathology and renal prognosis in Japanese cohort of patients with ANCA-associated vasculitis (AAV). [Methods] Patients were diagnosed with ANCA-associated vasculitis and underwent renal biopsy from 1996 to 2020. Renal pathology was newly evaluated by three nephrologists, mainly glomerular, tubular, interstitial, and vascular lesions. We applied the results of renal pathology to the glomerular classification by Berden et al. (J Am Soc Nephrol. 2010), chronicity score (Kidney International. 2017), and renal risk score (Kidney International. 2018) respectively and examined the association with renal prognosis. [Results] A total of 255 patients were included in the study. The mean number of glomeruli collected per patient was 23. According to Berden classification, 40 (16%) were Sclerotic, 66 (26%) Focal, 15 (6%) Crescentic, and 134 (53%) Mixed. In the chronicity score, 15 (6%) were minimal, 95 (37%) mild, 95 (37%) moderate, and 50 (20%) severe. In the renal risk score, 24 (9%) were low, 169 (66%) intermediate, and 62 (24%) high. [Conclusions] We found the distribution of previously reported scores in the Japanese cohort. We will report the relationship between these scores and renal prognosis.

W79-3

Analysis of renal histopathological findings of ANCA positive patients

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Conflict of interest: None

[Objective] A renal biopsy is often done in ANCA-associated vasculitis. However, it is not fully clear in which cases a renal biopsy should be performed. [Methods] MPO-ANCA or PR3-ANCA positive Patients (n = 29) who underwent renal biopsy from June 2014 to October 2022 were retrospectively evaluated. [Results] There were 19 cases of vasculitis (13 MPA, 3 GPA, 3 EGPA) and 10 non-vasculitis. Many Vasculitis cases had high CRP levels. Renal dysfunction was observed in 11 vascultis cases, urinary protein was observed in 13, and hematuria was observed in 15. Vasculitis (crescent formation, necrotizing glomerulonephritis, vasculitis, etc.) were observed in renal biopsy tissue in 17 vascultis cases. There was one vasculitis case without abnormal urinary findings or decreased renal function, but renal biopsy showed evidence of afferent arteritis. [Conclusions] In patients with ANCA-positive and high CRP levels, vasculitis may be diagnosed by renal biopsy.

W79-4

Investigation of clinical characteristics of patients with muscle lesions associated with ANCA-associated vasculitis (AAV)

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Conflict of interest: None

[Objective] To clarify the clinical characteristics of patients with muscle lesions associated with AAV. [Methods] From April 2016 to October 2022, we retrospectively examined the clinical characteristics of patients with muscle lesions from patients diagnosed with AAV at our hospital. [Results] Among 62 patients with AAV, 15 patients (5 males and 10 females) met the above criteria, and 24.2% of all AAV patients had muscle lesions. The median age at onset was 75.8±8.0 years. The median age at onset was 75.8±8.0 years. 14 patients had MPA, 1 had GPA, 9 had MPO-ANCA (138.1±99.7 U/mL), CRP 13.9±5.3 mg/dL, BVAS 8.1±7.1. Simple MRI of the lower extremities was performed in all patients, and findings of muscle vasculitis were observed in 14 patients. Muscle biopsy was performed in 12 patients, and 8 patients had findings of muscle vasculitis. The time from onset to diagnosis was 38.4±33.9 days and from onset to treatment was 51.8±42.9 days in 4 patients (6.5%) with AAV only for muscle vasculitis. [Conclusion] Muscle lesions associated with AAV can be a blind spot, but 6.5% of patients were found to have latent lesions. It took more than one month to diagnose the disease, suggesting that myopathological findings, MRI and biopsy of the same area are useful for early diagnosis.

W79-5

Efficacy of muscle biopsy for the diagnosis of anti-neutrophil cytoplasmic antibody-associated vasculitis

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Conflict of interest: None

[Objective] We aimed to examine the efficacy of muscle biopsy (MB) for the diagnosis of anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) and assess the factors related to MB positive. [Methods] We conducted a retrospective chart review of AAV patients who underwent MB from 2015 to 2022 at University of Yamanashi Hospital. Twenty-nine patients were identified. We collected patients' back ground, clinical symptoms and biological features. [Results] The median age was 76 years. 14 case was male (48%), 26 was MPA (90%). MRI of muscle were performed in 26 case (90%), and 9 case (31%) underwent renal biopsy. The duration from onset to diagnosis was longer in MB-positive patients than -negative (median 3 vs 2 months, $p<0.05$). The proportion of myalgia and renal involvement were higher in MB-positive (each 69 vs 31%, and 69 vs 31%, $p<0.05$). Crescent formation and fibrinoid necrosis in the histopathology from the kidney biopsy and the patients with histological diagnosis of AAV were more frequent in MB-positive group. [Conclusions] MB is efficient diagnostic tool for AAV. MB-positive may be associated with renal involvement, and should be considered in some conditions such as contraindication of kidney biopsy.

W79-6

Usefulness of serum sulfatide level as a biomarker for ANCA-associated vasculitis

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Conflict of interest: None

[Objective] Sulfatides are glycosphingolipids associated with coagulation and platelet aggregation. Since anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) stimulate coagulation and platelet aggregation, we examined whether serum sulfatide level could be a biomarker to predict disease activity in AAV patients. [Methods] We conducted a retrospective, single-center, observational study. We measured serum sulfatide levels in control (10 candidates for living-donor kidney transplantation) and 35 AAV patients, and compared the sulfatide levels among four classes (focal, crescentic, mixed, and sclerotic class) of glomerular lesions. [Results] Serum sulfatide levels in patients with AAV were significantly lower than those in the controls. Serum sulfatide levels were significantly different between the four classes, and serum sulfatide levels in the crescentic class were significantly lower than those in the other classes. Serum sulfatide levels were significantly correlated with albumin, cholesterol, C-reactive protein, and pentraxin 3. [Conclusions] Serum sulfatide levels are significantly correlated with crescentic glomerulonephritis, which is an active glomerular lesion in AAV patients. Serum sulfatide level may be a useful biomarker to predict AAV disease activity.

W80-1

Factors associated with glucocorticoid discontinuation in rheumatoid arthritis patients -T-FLAG study-

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Conflict of interest: None

[Objective] The 2020 update of clinical practice guidelines for the management of rheumatoid arthritis (RA) state that glucocorticoid (GC) should be used in the shortest possible time. However, in clinical practice, there are a certain number of RA patients who cannot stop GC. [Methods] Of the 538 RA patients (T-FLAG study) who visited us, 157 patients used GC. After 2 years of follow-up, we investigated the patients who discontinued GC. [Results] Of 157 patients (111 females, 70.7%), 24 patients (15.3%) discontinued GC within 2 years. The median age was 73/65 years old (GC continuation/discontinuation, $p<0.05$), disease duration was 8/7 years ($p=0.22$), CDAI was 6.3/3.1 ($p=0.35$), GC dose was 5/2.5 mg/day ($p<0.05$). In the ROC analysis, the cut-off values for GC discontinuation were 68 years old and 3 mg/day. In the Cox proportional hazards model, GC discontinuation was significantly associated with age (hazard ratio 0.96). [Conclusions] The subjects of this study were established RA patients. Considering that the GC discontinuation rate was 15.3%, it is difficult to discontinue GC for established RA. Furthermore, careful attention should be paid to GC use in elderly RA patients, and reducing GC dose to less than 3 mg/day as soon as possible may lead to GC discontinuation.

W80-2

Features of EORA in NinJa cohort

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Conflict of interest: None

[Background/Objective] Elderly onset RA (EORA) is attracting attention as the age of onset increases. NinJa database, a national cohort, was used to examine the characteristics of Japan EORA. [Patients] For 15553 RA cases listed in the NinJa database 2020, the age of onset 65 years or older were defied as EORA (E) and the following was YORA (Y), and the two groups were compared. And also the cases within 3 years of onset were examined. [Results] Number of cases E/Y 3774 (24.3%)/11179, mean duration of disease (y) 6.6/16.8, ACPA positivity rate (%) 61.5/78.1, RF positivity rate (%) 64.6/75.7, mean mHAQ 0.6/0.35, mean DAS28CRP 2.16/2.15, DAS28CRP remission rate (%) was 64.8/63.1, and there was a significant difference in antibody positivity rate and physical function. The cases within 3 years of onset, E/Y1226/1099 patients were DAS-CRP2.25/2.16 Remission rate (%) 62.7/64.9, and drug usage rate (%) was steroid 36/22.8, MTX 53.2/71.8, average dosage 7.9/9.1 mg/w, bio 11/13.6, JAKi 4.9/3.5. [Discussion/Conclusions] We evaluated the actual situation of EORA treatment in Japan using NinJa cohort. EORA had a low antibody positivity rate, as previously reported. MTX usage tended to be low while steroid usage tended to be high, but disease activity was controlled almost the same as YORA.

W80-3

Examination of factors related to functional impairment in elderly rheumatoid arthritis patients

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Conflict of interest: None

[Purpose] Elderly rheumatoid arthritis patients may have poor control of disease activity and their physical dysfunction may be exacerbated. [Methods] Patients aged 75 years or older were extracted from the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry, and the relationship between physical dysfunction and patient background factors was investigated. [Results] There were 750 (34.4%) patients aged 75 years or older in the entire AORA registry (2180 patients), including 159 males and 591 females, with an average age of 81 years. The HAQ-DI averaged 0.996. We showed the correlation between the HAQ-DI and age, patient/physician VAS, and each comprehensive disease activity index. HAQ-DI of 0.5 or less, which indicates functional remission, accounted for 27.6% of the total cases. No significant difference in HAQ-DI was observed regardless of MTX or PSL administration. [Conclusions] Elderly patients with rheumatoid arthritis had worsening physical function with age, and the HAQ-DI was higher in women and in patients with a history of brain disease. In order to improve the physical function of the elderly, orthopedic treatment and rehabilitation intervention are necessary from the viewpoint of total management, without relying on drugs.

W80-4

Efficacy and safety of hydroxychloroquine in Japanese patients with active rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To investigate the efficacy and safety of hydroxychloroquine (HCQ) in Japanese patients with rheumatoid arthritis (RA). [Methods] Patients with active RA, despite conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), were recruited. HCQ was administered for 24 weeks, in addition to prior treatment. The primary endpoint was the proportion of American College of Rheumatology (ACR) 20 achievement at week 24, compared to that of a propensity score matched historical control group. [Results] Sixty patients were enrolled and administered HCQ. We also identified 276 patients as candidates for the historical control group. Propensity score matching yielded 46 patients in each group. The proportion of ACR20 achievements at week 24 was significantly higher in the HCQ group than that in the control group (54.4% vs. 28.3%, $P = 0.007$). The proportion of ACR50 and ACR70 achievement at week 24 were also higher in the HCQ group than those in the control group (ACR50, 30.4% vs. 4.3%, $P = 0.006$; ACR70, 17.4% vs. 0%, $P = 0.005$). Neither hydroxychloroquine retinopathy nor any new safety signal was observed during the study. [Conclusions] The addition of HCQ to csDMARDs was effective, with no new safety signal in patients with RA.

W80-5

Efficacy and Safety of Generic Tacrolimus - Doubts about the efficacy and safety of the generic product-

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Conflict of interest: None

[Objectives] we report on the examined patients whose disease activity could not be suppressed with generic tacrolimus (Gen) but was suppressed after switching to original tacrolimus (Ori). [Methods] The following patient parameters were examined: VAS, ESR, CRP, MMP-3, RF,

tacrolimus trough, and SDAI. In principle, each value during the 3 months before and after the change was compared and examined for each month. [Results] Ori dose was reduced compared to Gen dose, and disease activity was suppressed in all nine patients. Improvement was observed in every parameter investigated after the change. Moreover, adverse reactions (rash, anorexia, renal impairment) disappeared or improved in three patients after the change. [Discussion] Although it is recommended to promote the use of generic drugs owing to soaring medical costs, there have occasionally been reports on concerns and doubts regarding the use of Gen in the field of transplantation. In the use of Gen for rheumatoid arthritis, our efficacy and safety results rationalize the need to switch to Ori. [Conclusion] We suggest that switching from generic tacrolimus to original tacrolimus is an option when generic tacrolimus is insufficiently effective or causes adverse reactions.

W80-6

Examining an impact of recent drug supply disruptions on rheumatoid arthritis drug prescription trends using a largescale claims database

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Conflict of interest: None

[Objective] The COVID-19 pandemic and scandals involving manufacturers in Japan caused drug supply disruptions. Rheumatoid arthritis (RA) drugs have been also affected, but no bird's-eye view data is shown. We investigated changes in prescription trends of RA drugs over time. [Methods] We used claim data owned by JMDC Inc. and patients treated for RA between April 2018 and March 2019 were eligible for inclusion. We traced until March 2022 and summarized RA drug prescriptions. Drugs which had been adjusted shipment were summarized by brand-name drugs or generic drugs. [Results] 14364 patients were eligible. Patients who used Iguratimod, Tocilizumab, Baricitinib were increased, Bucillamine, Infliximab were decreased. A percentage of patients whose prescription pattern changed from previous year were 37.6% in 2019, 34.7% in 2020 and 34.2% in 2021. However, in 2021, the percentage of patients who changed from generic drugs to brand-name drugs in the same ingredient from 2020 was increased. [Conclusions] In spite of supply disruptions, change of RA drug prescription trends were not large, and more than half of patients were treated in the same drugs. However, it was shown the number of patients who migrated to brand-name drugs was increased, affection of supply disruptions was revealed.

W81-1

Outcomes of Pregnancy with RA at showa maternity outpatient clinics

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Conflict of interest: None

[Objective] Pregnancy with RA (rheumatoid arthritis) is a risk factor for adverse pregnancy outcomes. In recent years, the spread of DMARDs that can be used even when a child is desired has made it possible to maintain remission during pregnancy. Therefore, we evaluated pregnancy outcomes and postpartum relapse in RA women. [Methods] From January 2018 to September 2022, 19 women who underwent RA treatment during pregnancy and one year after childbirth at our hospital were enrolled. Relapse of RA was defined as the need to restart treatment or change medication. Descriptive statistics were used. [Results] Of the 23 pregnancies in 19 women, the median age at pregnancy was 36 years, the disease duration was 4 years, and the pregnancy outcomes were spontaneous abortion in 3 cases (13%). All of the pregnancies except for miscarriage were full-term birth. There was one low birth weight infant (5%).14 had relapsed RA within one year after delivery, and 8 stopped taking biologics during pregnancy. The median time to relapse was 2 months. [Conclusions] Postpartum relapse occurs at a high rate and occurs relatively early, so it is essential to share treatment methods, including the resumption of biologics during pregnancy and parenting methods that are conscious of joint load with patients.

W81-2

The treatment for rheumatoid arthritis in interconceptional period in the collagen disease maternal outpatient clinic of our hospital

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Conflict of interest: None

[Objective] We examined the RA disease activity and treatment during the interconceptional period from the delivery of the previous child to the conception of the next child. [Methods] The subjects were RA patients who received management of two consecutive pregnancy at our maternal outpatient clinic from April 2013 to October 2022. We conducted a retrospective survey on RA disease activity, treatment, and obstetric outcomes. We investigated treatment during the interconceptional period. [Results] The subjects were 13 patients. The median age at delivery of previous child was 30 years, and disease duration was 4 years. The duration of interceptional period was 21 months, and 9 patients (69%) received additional treatment. Two cases (15%) were within 3 months after the delivery of previous child, and 7 cases (53%) were after 4 months. Details of additional treatment was start or modification of biologics in 3 cases (23%), start of salazosulfapyridine in 3 cases, and tacrolimus in 3 cases. There was no significant difference in RA disease activity between pregnancy of the previous child and next child. [Conclusions] In pregnancies of patients with RA, continuous adjustment of RA treatment during the interconceptional period is inportant.

W81-3

The current state of fertility treatment and pregnancy outcomes of women complicated with Rheumatoid arthritis in a single center

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Conflict of interest: None

[Objective] We analyzed pregnancies with rheumatoid arthritis (RA), and clarified the current state and issues of Fertility Treatment of women complicated with RA in our institution. [Methods] Patients with RA who were managed from pregnancy planning to delivery at Kagawa University Hospital from April 2007 to September 2022 were enrolled. We retrospectively investigated the patients' clinical background characteristics, disease activity, treatment agents and pregnancy outcomes. [Results] Thirty-two pregnancies in 23 women with RA were analyzed. Nine pregnancies were established through fertility treatment. The mean Time to Pregnancy was 10.4±10.9 months. Nine cases needed more than 12 months to pregnancy and 5 of them received fertility treatment. There was no significant difference in the patients' clinical background characteristics, disease activity, treatment agents and pregnancy outcomes between in Fertility treatment group and in Natural pregnancy group. [Conclusions] Any of the patients' clinical background characteristics, disease activity and treatment agents did not associated with having fertility treatment. Pregnancies with fertility treatment did not result in more adverse pregnancy outcomes.

W81-4

A cases of CHB (congenital heart block) with high titer of maternal serum IFN-a

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Conflict of interest: None

[Case] A 35-year-old woman. [Medical history] At X-4, she complained of joint pain, and diagnosed as rheumatoid arthritis (RA) with Sjögren's syndrome, therefore MTX was started. Because of hope for pregnancy, MTX was disucontinued at X-1, and she became pregnant at X year. She was referred to the perinatal department at 12 weeks, and referred to our department at 21 weeks. [Pregnancy history] 1 pregnancy and 1 delivery. [Clinical Course] At the time of referral, RA remained in remission, and there was no comorbidity. Anti-SS-A antibody was positive, and titer was 133.8 IU/ml. CHB was recognized at 22 weeks. Third-degree atrioventricular block was diagnosed, therefore dexamethasone was started, however, no improvement was observed. She was transferred to a specialized facility at 29 weeks, and delivered by caesarean section at 35 weeks. Her infant weighed 1840 g and was an indication for pacemaker implantation. Ro52 and Ro60 antibody titers in mother's serum were 178.5 IU/ml and 202.4 IU/ml, respectively. In addition, serum IFN-α was measurable, 332.2 pg/ml. [Discussion] It has been reported that serum IFN-α levels were higher in anti-SS-A antibody-positive mothers and infants. We report on the relationship between CHB and IFN-α by anti-SS-A antibody, adding literature review.

W81-5

Trends in the treatment of articular juvenile idiopathic arthritis and young rheumatoid arthritis using the epidemiological receipt database

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Conflict of interest: None

[Objective] To clarify the issues in treating articular juvenile idiopathic arthritis (aJIA) by comparing it with young rheumatoid arthritis (yRA) in Japan. [Methods] The subjects were selected aged 30 years or younger in the fiscal years 2011-2020 health insurance database established by JMDC, Inc. ICD10 codes were used for extraction. Disease definition was defined as cases with at least two prescriptions of disease-modifying anti-rheumatic drugs (DMARDs). The prescribing status of conventional synthetic (cs) DMARDs, biologic/molecularly targeted (b/ts) DMARDs, as well as the trends in medical costs, were evaluated. [Results] Among 5,109,040 insured patients aged 30 years or younger, 209 aJIA and 1,830 yRA patients were extracted. In aJIA, the b/tsDMARDs prescriptions increased from 35% to 50% from FY2016. The percentage of b/tsDMARDs prescribed as monotherapy increased to 15% in FY2020. The rate of prescribing b/tsDMARDs for yRA increased from 30% to 35%. The rate of prescribing csDMARDs as monotherapy did not change. The median annual medical cost per capita for aJIA nearly doubled in FY2020 compared to FY2016, equivalent to 2.5 times that of yRA. [Conclusions] aJIA b/tsDMARDs prescription rates are higher than yRA, revealing the reality of higher annual medical costs per capita.

W81-6

Independence after transfer from Tokyo Metropolitan Children's Medical Center to Department of Rheumatic Diseases, Tama Medical Center: Results of a questionnaire survey of 22 cases

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Conflict of interest: Yes

[Objective] To investigate independence after transition in cases with child-onset rheumatic diseases. [Methods] All cases transferred from the Children's Medical Center to Department of Rheumatic Diseases, Tama Medical Center, and visiting our department as of Sep 2022, were evaluated with a questionnaire about independence answered by the attending physicians. [Results] 22 cases were analyzed: 27.2 ± 7.5 (mean ± SD) years old (yo) on the last visit, 16 females (73%), all SLE except 1 male APS, age of onset 11.2 ± 2.8 yo, age at transition 21.6 ± 5.5 yo, disease duration at transition 10.4 ± 6.1 years, disease duration at last visit 16.0 ± 7.4 years, time after transition to the last visit 5.6 ± 3.2 years. The rates of "yes" or "rather yes" in female vs male for "(seems to) have talked to medical staff about pregnancy and childbirth" (Q7) were 75% vs 17% ($p = 0.02$) and for "seems to be able to manage their own medical record" 75% vs 0% ($p < 0.01$). The rate in the younger age group at transition (17.3 ± 2.0 yo) vs the older age group (25.8 ± 4.5 yo) for "seems like to know the effect of the medicine taken" were 64% vs 100% ($p = 0.045$) and for Q7 were 36% vs 82% ($p = 0.04$). [Conclusion] Independence after transition may be affected by gender and age at transition.

W82-1

Efficacy of salazosulfapyridine monotherapy in patients with rheumatoid arthritis who had factors associated with preference for salazosulfapyridine as the first-line drug

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Conflict of interest: None

[Objective] To analyze efficacy of salazosulfapyridine (SASP) monotherapy in patients with rheumatoid arthritis (RA). [Methods] 68 patients who were naïve to RA treatment and had been treated for at least 24 weeks were included. First, we analyzed the overall baseline data, the retention rate of monotherapy with SASP for 24 weeks, and the treatment outcome. Next, we compared the 24-week treatment outcomes of patients whose treatment was started with SASP due to the following factors: older (75 years or older), seronegative RA, moderate disease activity or better, lung disease, renal disease, and liver disease. [Results] Age was 67.8 years. 24 patients were 75 years or older. 42 were female. 75.0% were RF/ACPA positive, DAS28-CRP=4.2, and 54.4% had high disease activity. The 24-week retention rate of SASP monotherapy was 65.4%, and DAS28-CRP improved to 3.2. There was no significant difference in disease activity between the two groups in terms of seronegative RA, disease activity, lung disease, renal disease, or liver disease, either at baseline or at 24 weeks. [Discussion] SASP was used to treat patients with above background factors, and the results were comparable to those in patients without these background factor.

W82-2

Investigation of factors affecting renal function by MTX mono-therapy in Phase 1 treatment

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Conflict of interest: None

[Objective] It is not well known to what extent small intermittent doses of MTX affect renal function (RF). Therefore, we decided to investigate the effect of MTX therpy on RF, which is commonly given to RA patients at relatively early stage of onset. [Methods] One-year eGFR trends were observed in 221 RA patients who received MTX therapy within 2 years of onset. The background factors of the study were age, weight and BMI at the time of initiation, sex, risk of atherosclerosis, CDAI and eGFR during the study period, as well as cumulative MTX dose (cMTX), NSAID dose (ASAS NSAID intake) and GCs use to determine their effect on RF. Anal-

ysis was performed by logistic regression analysis using propensity scores for CKD progression and change in eGFR, respectively, adjusted for sex, age, eGFR category, and risk of atherosclerosis. [Results] eGFR showed a downward trend in all observation periods. We found a negative correlation between cMTX/BMI and ΔeGFR. Next, Analysis of CKD progression adjusted for risk factors showed a difference in cMTX/BMI. The analysis on ΔeGFR<-2.62 showed differences in cMTX/BMI and CDAI integral values. [Conclusion] The results suggest that MTX is a drug for which treatment plans need to be adjusted as needed to avoid future CKD transition.

W82-3

Efficacy of adding iguratimod therapy in rheumatoid arthritis patients who had inadequate response to biologic DMARDs

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Conflict of interest: Yes

Objective Iguratimod (IGU) was approved in June 2012. Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant biologic DMARDs (Bio). Therefore, we investigated efficacy of concomitant IGU therapy in RA patients who had inadequate response to Bio at the author's institution. ***Methods*** Subjects were 151 patients adding IGU who had inadequate response to Bio from Janually 2014 to Sep 2019. Previous treatment Bio was ADA. Mean concomitant MTX of 147 patients were 12.0 mg/week. And baseline characteristics were Mean age 54.9 years, mean duration of illness 67.0 months, corticosteroid use 9.9% (mean 3.3 mg/day). The course of DAS28, SDAI, CDAI and remission rates were analyzed for three years. ***Results*** Mean DAS28-ESR, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 52 weeks (3.00→2.14, 6.99→2.41, 6.01→2.12), at 152 weeks (2.15, 2.47, 2.12). Remission rates of DAS28-ESR, SDAI, CDAI were74.2%,79.5%,73.5% at 52 weeks, 74.2%,81.1%,78.8% at 152 weeks. ***Conclusion*** IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio.

W82-4

Iguratimod-induced rash in patients with rheumatoid arthritis

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Conflict of interest: None

[Objects] The risk factors for iguratimod (IGU)-induced rash are unknown and we aimed to explore them. [Methods] Of 379 patients with rheumatoid arthritis, 152 with a history of IGU use were included. Clinical characteristics, comorbid organ damage, and history of allergies and adverse reactions to other anti-rheumatic drugs were retrospectively investigated. We compared groups that did and did not develop IGU rash. [Results] There were 15 patients in the IGU rash group and 137 in the non-rash group. Univariate analysis revealed that history of allergy was significantly more common in the IGU rash group ($p < 0.001$). There were significant group differences in food allergy, sun sensitivity, and NSAID allergy, but not in hay fever, allergy to antibacterial agents, or asthma. In terms of history of adverse reactions to anti-rheumatic drugs, history of rash when on busillamine was significantly more common in the IGU rash group ($p = 0.04$). Multivariate analysis of the associations among age, gender, and history of allergy, busillamine rash and IGU rash revealed an association between IGU rash and history of allergy (odds ratio = 8.7, $p = 0.02$). [Conclusions] Patients with a history of allergy should be alert to the potential for rash development at the time of IGU initiation.

W82-5

Long-term clinical results of leflunomide over ten years

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Conflict of interest: None

[Objective] To analyze long-term clinical results over ten years of leflunomide. [Methods] 19 RA patients (pts) were analyzed for clinical data. Disease activity score 28 with erythrocyte sedimentation rate (DAS28-ESR) at entry, 6 months, 1 year, 5 years, final observation (over 10 years) were measured. Major complications and joint destruction in X-ray were also analyzed. [Results] Patient's demographic data were as follows; sex: male 6 pts, female 13 pts; disease duration at the start of medication of leflunomide: 56.9 months: follow up periods taking leflunomide: 159.4 months; dose of leflunomide: 20 mg/d (10 pts), 15 mg/d (3 pts), 10 mg/d (6 pts); MTX: 12 pts; Biologics: Infliximab 1, Tocilizumab 2, Etanercept 1; PSL: 3.3 mg/d: DAS28-ESR at baseline, 6 months, 1 year, over 10 years were respectively 4.92, 3.28, 2.82, 2.89, 2.66. Major complications were THA 6, TKA 1, breast cancer 1, femoral neck fracture 1, extensor tendon rupture 1, osteonecrosis of the jaw 2, cardiac arrythmia 1, hypertension 1. In X ray analysis, some patients show repairment of joint erosion. In 2 shoulder and 2 knee joints, joint destructions were improved. No pulmonary complications were observed. [Conclusions] Long- term results over 10 years of leflunomide were relatively satisfying.

W82-6

Clinical features and long-term comparison of serum creatinine value in patients with rheumatoid arthritis and systemic lupus erythematosus

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Conflict of interest: None

(Objective) We aimed to clarify long-term transition of serum creatinine (Cr) value in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), treated with tacrolimus (TAC). (Methods) Our study included patients with RA and SLE who have been treated with tacrolimus. Clinical information of those patients including serum Cr values over the past 3 years was collecte. (Result) Seventy six patients (RA 53, SLE 23) were taking tacrolimus regularly. Mean age and female ratio of the patients with RA and with SLE was 62.5 and 40.6, 75% and 83%, respectively. Serum Cr values in patients with RA and SLE were 0.95 mg/dl and 0.71 mg/dl at the start of TAC, and were 1.05 mg/dl and 0.73 mg/dl 36 months later. There was no significant difference between the patients with RA and with SLE in terms of serum Cr value at both points. Fifty-one percent and 35% of RA and SLE patients showed more than 10% increase of serum Cr value 36 months after starting TAC. Sixty-eight percent of the patients aged 65 or over and 33% of the patients aged below 65 showed more than 10% increase of serum Cr and this difference was significant (p=0.005). (Conclusion) The increase of serum Cr value in patients with TAC was attributed to patient's age rather than underlying diseases.

W83-1

Risk factors for vertebral fractures requiring surgery in ankylosing spondylitis

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Conflict of interest: None

[Objective] Vertebrae with advanced ankylosing spondylitis (AS) can be fractured by even minor trauma, often resulting in surgery. Early treatment, such as TNF inhibitors, is expected to delay spinal x-ray progression. However, risk factors for vertebral fractures requiring surgery in AS

are not well understood. In this study, we investigated the risk factors for vertebral fractures requiring surgery in AS in our department. [Methods] The subjects were 61 patients with AS diagnosed by the 1984 revised New York criteria and treated in our department from 2004 to 2022. Age, gender, disease duration, CRP, presence of sacroiliac joint ankylosis, the maximum number of consecutive ankylosed vertebrae, and treatment were evaluated. [Results] The mean age at the last visit was 49 years, 75% of the patients were male, the mean disease duration was 19 years, 9 patients underwent surgery, and 70% of the patients were treated with medication. The vertebral fracture surgery group did not use bDMARDs preoperatively and had significantly higher CRP. In addition, multivariate analysis showed that preoperative CRP was significantly associated with vertebral fracture surgery. [Conclusion] Early treatment, such as TNF inhibitors, to reduce disease activity leads to vertebral fracture control.

W83-2

The factor of sacroiliac joint ankylosing in ankylosing spondylitis using CT image

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Conflict of interest: None

[Objective] To investigate the factor of sacroiliac joint ankylosis in ankylosing spondylitis using CT image. [Methods] 55 patients diagnosed or treated for AS at our hospital between January 2004 and July 2022, whose sacroiliac joints could be evaluated by CT were included in the study. [Results] Of the 45 patients tested for HLA-B27, 27 were positive. Compared with the group without ankylosis (38%), the group with ankylosis (62%) had a higher proportion of males (88% vs. 57%), a higher age at CT (44 vs. 32 years), a longer disease duration (15 vs. 6 years), a longer time from onset to diagnosis (11 vs. 6 years), and higher CRP level at diagnosis (2.8 vs. 0.82 mg/dl). The proportion of patients with ankylosis was higher the longer the duration of illness, the longer the time from onset to diagnosis, and the higher the CRP level at diagnosis. [Conclusions] Factors associated with sacroiliac joint ankylosis in AS were identified as male, age, disease duration, time from onset to diagnosis, and high CRP level. The longer the disease duration, the higher frequency of sacroiliac joint ankylosis. Early diagnosis is important to prevent sacroiliac joint ankylosis, and patients with high CRP levels at diagnosis require aggressive therapeutic intervention.

W83-3

Relationship between changes in bone growth around the hip joint and forward leaning posture in patients with ankylosing spondylitis

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Conflict of interest: None

[Objective] It is known that patients with ankylosing spondylitis have kyphosis of the spine. We hypothesized that these changes might affect the hip joint. [Methods] Patients diagnosed with AS at our hospital between 2004 and 2022 who underwent bilateral hip and total spine simple x-rays (Xp) were included. Joint space narrowing was evaluated in the frontal view of hip simple Xp, and head-neck offset ratio and CE angle were evaluated as bone growth changes. Spinal alignment was evaluated on the whole spine simple Xp lateral view (standing position). [Results] Among 15 patients with AS seen at our hospital who underwent bilateral hip and total spine Xp, the mean age at Xp evaluation was 43.1 years, mean disease duration was 15.7 years, HLA-B27 positivity was 72.7%, and 15 patients (100%) met the NY criteria. Head-neck offset ratio was correlated with spinal SVA ($r=-0.606$, $P<0.05$), and head-neck offset ratio was correlated with spinal SVA ($r=-0.606$, $P<0.05$, $P<0.05$). CE angle was correlated with spinal SVA ($r=0.606$, $P<0.001$) and with LL and SS (LL: $r=0.381$, $p=0.038$ SS: $r=0.480$, $p=0.007$). CE angle was correlated with spinal SVA ($r=0.489$, $P=0.006$) and with LL and SS (LL: $r=-0.516$, $p=0.004$ SS: $r=-0.629$, $p<0.001$). [Conclusions] Hip deformity in AS patients was related to spinal alignment.

W83-4

Evaluation of mSASSS in Ankylosing Spondylitis (Comparison of Simple X-Ray and CT)

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Conflict of interest: None

Background: The Modified Strokes AS Spinal Score (mSASSS) is a method of evaluating spinal lesions in ankylosing spondylitis (AS), but there are areas that are structurally difficult to read in detail on a simple lateral X-ray image, such as the cervicothoracic and lumbosacral transition area. Objective: To compare the mSASSS evaluation of AS between simple X-ray and CT. Methods: Twenty-nine patients diagnosed or treated as AS at our hospital between January 2004 and July 2022, and who had contemporaneous simple x-rays and CT scans of the cervical and lumbar spine, were included. Two rheumatologists independently read the simple lateral X-ray and CT images and evaluated of each vertebral body based on mSASSS. Results: Twenty-two male patients, mean age 42±16 years, mean disease duration 17.8±12.5 years, and 17 HLA-B27-positive patients were included. The CT scan was evaluable at all sites in all patients. The cases that could not be evaluated by plain X-ray but were scored by CT were 3 cases of C7 upper border/6 cases of lower border, 6 cases of Th1 upper border, 1 case of L5 lower border, and 1 case of S1 upper border. Discussion: The mSASSS is a useful method of evaluation, but it may underestimate the results, and a CT scan is recommended when simple X-rays are difficult to evaluate.

W83-5

The Andersson lesion in ankylosing spondylitis using CT image

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Conflict of interest: None

[Objective] To investigate the incidence and characteristics of Andersson lesion (AL) in ankylosing spondylitis (AS) using CT. [Methods] 31 patients diagnosed or treated with AS at our hospital from January 2004 to July 2022 who were evaluated with intervertebral lesions using CT were included. Patients with irregular or eroded vertebral endplates on CT were considered to have AL. [Results] 8 of 31 patients (25.8%) had AL. 2 patients had AL between singe vertebrae and 6 patients had AL between multiple vertebrae. One case showed AL only in the cervical spine, 2 cases in the thoracic spine, 2 cases in the lumbar spine, one case in the cervical and thoracic spine, and 2 cases in the thoracic and lumbar spine. No statistically significant differences in age, gender, disease duration, or HLA-B27 positivity between patients with and without AL. BASDAI tended to be higher in cases with AL than in those without (group with AL vs. group without AL=4.11 vs. 2.11, $P=0.059$). [Conclusions] 25.8% of the AS patients showed AL on CT evaluation. AL was often found between multiple vertebrae, occurring in the cervical, thoracic, and lumbar spine regions.

W83-6

Spinal ankylosis and physical function in patients with ankylosing spondylitis

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Conflict of interest: None

[Objective] To investigate the relationship between spinal ankylosis

and physical dysfunction in ankylosing spondylitis (AS). [Methods] The Bath Ankylosing Spondylitis Functional Index (BASFI) was used to assess physical dysfunction. 20 patients diagnosed or treated with AS at our hospital from January 2004 to July 2022 who were evaluated with spinal ankylosis using CT and BASFI were included. [Results] BASFI were mean 2.3, and the average number of intervertebral ankylosis was 9.4 (0-24). The number of intervertebral ankylosis of all vertebrae and BASFI were positively correlated (r=0.48, p=0.032). No statistically significant correlation were between the number of intervertebral ankylosis in the thoracic and lumbar spine and BSAFI. On the other hand, the number of intervertebral ankylosis of cervical vertebrae and BASFI were positively correlated (r=0.6, p=0.006). [Conclusions] The progression of spinal ankylosis in AS was associated with deterioration of physical function. In particular, progressive ankylosis of the cervical spine was thought to worsen physical function and interfere with daily life.

W84-1

Disease activity and treatment after 1 year in patients who discontinued biologic agents because of stable activity of disease

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Conflict of interest: None

[Objective] To follow-up patients whose bDMARDs (IFX, ETN, TCZ, ADA, ABT, GLM, CZP, SAR, and biosimilar, if available) were discontinued by their physicians because of stable disease at 1 year. [Methods] Patients whose bDMARDs were discontinued for stable disease at the year were included in the NinJa data. Successful discontinuation was defined as meeting both of the following criteria: (1) CDAI ≦10 and (2) no bDMARD, tsDMARD, or steroid use. [Results] A total of 317 patients with bDMARD discontinuation due to stable disease were enrolled in NinJa 2015-2019 over a 5-year period. The gender of the subjects was 82% female, age at bDMARD discontinuation was 61±14 years, disease duration was 9.9 ± 8.2 years, and mHAQ was 0.17 ± 0.35. Of the subjects, 234 (73.8%) could be followed for CDAI in the following year, with a median CDAI of 2.95. The following year's data showed that (1) (CDAI≦10) was met in 84.8% of the patients, and the discontinuation success rate (meeting both (1) and (2)) was 59.4%. [Discussion] About 60% of patients whose disease was judged to be stable by their physicians and bDMARD was discontinued met the criteria for successful discontinuation after one year.

W84-2

Mortality in patients with rheumatoid arthritis from the IORRA cohort

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Conflict of interest: None

[Objective] To evaluate the prognosis of Japanese patients with RA in recent years. [Methods] The patients with RA who participated in the IORRA cohort between October 2007 and October 2021 were enrolled. Standardized mortality ratios (SMRs) were calculated based on the number of deaths ascertained. As previously reported (Kauppi M. J Rheumatol 2005), we assumed that the mortality rate of lost follow-up cases was 1.65 times higher than that of follow-up cases. [Results] A total of 10,634 patients (84% female) were included. The mean age was 57 years, and the mean disease duration was 10 years. Sixty percent of patients could be followed until the end of the follow-up period. In the total 94,994.7 person-years of follow-up, 817 deaths were confirmed. The main causes of death were malignant disease (26%) and respiratory disease (24%). The SMR using the confirmed cases of death was 0.88 [95%CI 0.82-0.94] for all patients. The SMR adjusted for lost to follow-up was estimated to be 1.60 [95%CI 1.50-1.71]. [Conclusion] The prognosis of Japanese patients with RA remains worse compared with that of the general population as previously reported from the IORRA cohort (Nakajima A. Scand J Rheumatol 2010).

W84-3

Outcomes and prognostic factors in patients with rheumatoid arthritis and lung cancer

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Conflict of interest: None

[Objective] To clarify the outcomes and prognostic factors in patients with rheumatoid arthritis (RA) and lung cancer. [Methods] In this retrospective longitudinal study, we reviewed the medical records of RA patients who were newly diagnosed with lung cancer between January 2013 and May 2022 at our hospital. The Kaplan-Meier method was used to analyze survival and the Cox proportional hazard model was applied to identify predictive factors. [Results] We included 26 RA patients with lung cancer. The median age was 69 years, and 61.5% were male. Most common lung cancers were adenocarcinoma (14 [53.8%]) and squamous cell carcinoma (8 [30.8%]). Among all patients, 2- and 5-year overall survival rates were 61% and 47%, respectively. Univariable analysis revealed prognostic factors assessed at diagnosis of lung cancer: male, smoking history, interstitial pneumonia, poorly controlled RA, and RF ≧71 IU/mL. After treatment of stage 1 and 2 lung cancer, 4 of 16 patients were recurrent during RA treatment, and their cancer histology tended to be squamous cell carcinoma. [Conclusions] Early detection for lung cancer is needed for especially male RA patients with interstitial pneumonia who have smoking history. Recurrence of squamous cell carcinoma should be noted after lung cancer treatment.

W84-4

Cluster Analysis of Clinical factors and Physical Dysfunction in Patients with Early-Stage Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We report a cluster analysis of patient demographics, disease activity, and physical disability to investigate trends in patients with early-stage rheumatoid arthritis (early RA). [Methods] We included 161 patients who first visited our department between April 2017 and November 2021 with disease duration less than 2 years. Non-hierarchical cluster analysis (k-means method) was performed for age, gender, BMI, ACPA, CRP level, TJC28, number of tender joints among 24 joints in both feet (TJCFoot), CDAI, HAQ-DI and Lower HAQ-DI calculated for lower limb function. [Results] Overall, the female rate was 70.8%, with a mean age of 61.3 (20-90) years. There was a weak correlation between TJCFoot and Lower HAQ-DI (ρ=0.30, $p<0.001$). Cluster analysis identified four clusters (CLs), with significant differences in age among all CLs. CL1 was the oldest and had the worst results in all the endpoints except ACPA, especially HAQ-DI and Lower HAQ-DI, which were higher only in CL1 than in the others. CL4 was worse than CL2 and CL3 as well as CL1 for TJC28 and CDAI, and more patients were ACPA positive than others. [Conclu-

sions] In the cluster analysis, age and ACPA were important factors in classification, allowing us to classify patients with early RA into four disease types.

W84-5

The effects of differences in living environment in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose was to investigate the effects of differences in living environment in patients with rheumatoid arthritis (RA). [Methods] RA patients participating in a prospective observational study were included. The amount of activity, family structure and means of commuting to the hospital were investigated. Comparison was made between 77 subjects in the metropolitan city group (group M) and 67 subjects in the regional city group (group R). [Results] The mean age was 68.3 years for group M and 68.2 years for group R (p=0.96). The rate of solitary residence was 27.3% in group M and 23.9% in group R (p=0.70). The means of transportation to the hospital was transportation for 97% of the patients in group R, but 20.8% in group M (p<0.001). Corrected limb skeletal muscle mass was 6.4 kg/m^2 in the group M and 6.0 kg/m^2 in group R (p=0.005). The mobility activity was significantly higher in group M (median 693 METs/min/week) than in group R (median 0 METs/min/week) (p<0.001). [Conclusions] Among RA patients, there were significant differences in means of commuting to hospitals between the regional city group and the metropolitan city group. Muscle mass was significantly lower in the regional city group, and mobile activity was also significantly lower.

W84-6

Using Physical Functioning Assessment Characteristics of Elderly Rheumatoid Arthritis Patients

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Conflict of interest: None

[Background] The aging of rheumatoid arthritis (RA) patients, combined with age-related physical dysfunction, may lead to a decline in ADL. The purpose of this study was to investigate the characteristics of elderly RA patients. [Methods] Fifty-three RA patients aged 65 years or older who underwent physical function assessment in our outpatient RA clinic were included. Patients were divided into two groups: elderly patients aged 75 years or older and quasi-elderly patients aged 74 years or younger. [Results] Thirty-seven RA patients (69.8%) were aged ≦75 years. In the group aged 75 years or older vs. 74 years or younger, the physical function assessment was gait speed (1.14 vs. 1.06 m/s), and five stances (12.3 vs. 10.9 seconds). There were significant differences between the two groups for the right lower extremity (5.29 vs. 6.23 kg, P=0.050), left lower extremity (5.35 vs. 6.34 kg, P=0.034). No significant differences were found for the right upper limb (1.53 vs. 1.68 kg), left upper limb (1.51 vs. 1.62 kg), and trunk (19.75 vs. 19.83 kg). [Conclusions] Elderly RA patients are characterized by muscle weakness mainly in the lower limbs, not in the upper limbs or trunk, despite the fact that the HAQ-DI, an evaluation of physical function, is not influenced by age.

W85-1

Bone structure analysis of the proximal femur of rheumatoid arthritis patients using 3D-SHAPER

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA), anti-CCP antibody (ACPA) and inflammatory cytokines activate osteoclasts. In this study, we investigated the structural strength and stiffness of the proximal femur of RA patients using 3D-SHAPER. [Methods] ACPA-positive RA cases (RA group: 127 cases, 61 ± 12 years) and ACPA-negative non-RA cases (Control group: 259 cases, 62 ± 12 years) was used to perform the three-dimensional bone structure analysis with 3DS using DXA data of the proximal femur. [Results] BMD in the proximal femur was significantly lower in the RA group than in the control group (-3.7%, p<0.05). Cortical BMD was significantly lower in the RA group (-2.3%, p<0.01), and cortical surface density was significantly lower in the RA group (-4.8%, p<0.01). HSA showed significantly lower cross sectional moment of inertia (-7.2%, p<0.05) and section modulus (-5.1%, p<0.05) in the RA group. [Conclusions] The bone structure of the proximal femur in the RA group showed significant changes in cortical bone. The HSA parameters, which indicate the difficulty of deforming the bone cross section and the stress on bending strength, were lower in the RA group. In this study using 3DS, it was suggested that the structural strength of the proximal femur of RA patients is reduced.

W85-2

Roles of membrane-bound and soluble forms of RANKL in inflammation-associated bone destruction

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Conflict of interest: Yes

[Objective] Excessive RANKL signal leads to bone loss in rheumatoid arthritis (RA), osteoporosis and bone metastasis. RANKL is synthesized as a membrane-bound molecule, and cleaved into its soluble form by proteases. Our studies using soluble RANKL-deficient mice have shown that soluble RANKL is dispensable for physiological bone remodeling. Notably, serum RANKL level was reported to be associated with several clinical disease activities such as RA. Thus, we aimed to clarify the roles of two forms of RANKL in bone destruction during arthritis. [Methods] By generating soluble RANKL-deficient (ΔS) and membrane-bound RANKL-deficient (ΔM) mice, we investigated the pathological significance of each type of RANKL. [Results] ΔS mice exhibited normal bone phenotype, while ΔM mice displayed osteopetrosis. In a mouse model of arthritis, ΔS mice developed erosive bone destruction to the same extent as wild-type mice. In contrast, in ΔM mice, the number of osteoclasts in the inflamed synovium was markedly reduced, and bone destruction was suppressed. [Conclusions] We revealed that membrane-bound RANKL mainly contributes to inflammation-associated bone destruction, indicating the importance of local regulation through direct interactions between RANKL+ synovial fibroblasts and osteoclast precursors.

W85-3

Secretome analysis of rheumatoid arthritis synovial fibroblast subsets

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) synovial fibroblast (SF) and its recently identified subsets are important for the development of new bio-

markers for early RA and new treatment strategies for difficult-to-treat RA. Secretome is the totality of substances secreted by cells, including proteins and extracellular vesicles (EV), and useful as a liquid biopsy biomarker and a drug. In this study, we analyzed the secretome of RASF subsets. [Methods] Three major RASF subsets were cell sorted with the surface markers, THY1 and CD34, from the synovial tissues of RA patients and expanded in culture. Gene expression, EV surface markers, and secreted proteins were evaluated with qPCR, Western blot, and protein array. EVs were purified with phosphatidylserine affinity column and analyzed with NanoSight. [Results] Among 3 major RASF subsets (THY1-CD34-, THY1+CD34-, and THY1+CD34+), THY1+CD34+ subset secreted abundant chemokines and proteins involved in angiogenesis. All subsets secreted similar amounts of EVs positive for EV surface markers, CD63, CD81, and CD9, and fibroblast marker podoplanin, with mean vesicle diameter 184 nm. MicroRNAs within EVs are now under investigation with microarray. [Conclusions] The secretome may explain mesenchymal stem cell-like potentials of THY1+CD34+ subset.

W85-4

The dysregulation of cytokine and chemokine gene expression by transcription factor SOX11 in rheumatoid arthritis synovial fibroblasts

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Conflict of interest: None

[Objective] The activation of synovial fibroblasts (SFs) plays an important role in rheumatoid arthritis (RA) pathogenesis. We examined which transcription factors (TFs) were involved in the activation of RASFs and which genes were regulated by the TFs. [Methods] We examined open chromatin, including promoters and enhancers, by FAIRE-seq in RASFs and osteoarthritis (OA)SFs. We identified RASFs-specific TFs that bound to the open chromatin. We compared the expression of the TFs in RASFs and OASFs. We repressed the expression of the TFs by siRNA in RASFs and investigated which gene expression was suppressed by trasncriptome analysis. [Results] We identified SOX11 that bound to RASFs-specific open chromatin by FARE-seq. SOX11 was highly expressed in RASFs compared with OASFs. The decrease in SOX11 expression by siRNA induced the downregulation of IL-8, IL-15, IL-33, CCL2, CXCL5, and CXCL12 in RASFs [Conclusions] SOX11 is suggested to be involved in the activation of RASFs through upregulation of particular cytokines and chemokines.

W85-5

Involvements of immune checkpoint-related molecules in RA patients

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Conflict of interest: None

<Objective> Immune checkpoint molecules are involved in the pathogenesis of autoimmune diseases. T cell immunoglobulin and mucin domain-3 (TIM-3) as a negative immune checkpoint molecule in RA patients. Carcinoembryonic antigen-related cell-adhesion molecule 1 (CEACAM1) is a TIM-3-associated molecule. To analyze TIM-3 and CEACAM1 on the surface of immune cells isolated from RA patients and determine their relevance to the pathogenesis of RA. <Methods> Thirty-seven RA patients and twenty healthy controls (HC) were included. TIM-3 and CEACAM1 on the surface of immune cells were analyzed by flow cytometry. <Results> CEACAM1 was expressed on the surface of neutrophils and was significantly expressed in RA patients compared to HCs (p<0.001). CEACAM1 was also significantly expressed within RA patients in the CRP-positive group and in the non-remission group in SDAI (p=0.001, p=0.042). TIM-3 was expressed on the surface of monocytes but did not differ between RA patients and HCs. Among rheumatoid inflammatory cytokines, TNF-α and GM-CSF stimulations induced CEACAM1 expression of neutrophils. <Discussions> We suggest that CEACAM1 on the surface of neutrophils may be involved in the inflammatory pathogenesis of RA patients through the TNF-α or GM-CSF-mediated inflammatory pathways.

W85-6

Relationship between EBV EA-IgG antibodies and disease activity and autoantibodies in rheumatoid arthritis

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Conflict of interest: None

[Objective] Several studies have demonstrated that Epstein-Barr virus (EBV) infection is an environmental factor in the pathogenesis of rheumatoid arthritis (RA). However, there is no clinical evidence that EBV infection is involved in disease activity or autoantibody production. In this study, we aimed to analyze the involvement of EBV in RA activity by evaluating the degree of disease activity and autoantibody production in positive and negative cases using anti-EBV EA IgG antibody, an indicator of EBV reactivation. [Methods] We analyzed the relationship between RA disease activity and the production of autoantibodies and EBV by examining age, gender, duration of RA disease, disease activity, laboratory findings, treatment, and complications in RA patients who currently have anti-EBV EA IgG antibodies measured at our hospital. [Results] There were 54 RA cases in which EBV EA-IgG antibodies were measured, 17 positive and 37 negative. Ten of the positive cases underwent EBV DNA PCR and 8 were positive; DAS28-CRP, -ESR, peripheral blood lymphocyte count, and anti-CCP antibodies were significantly higher in the EBV EA-IgG antibody positive cases. [Conclusions] It was suggested that EBV is partly involved in disease activity and autoantibody production in RA.

W86-1

The association between clinical arthritis of the foot and disease activity-related physical dysfunction in patients with early rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the relationship between clinical arthritis of the foot and physical dysfunction related to lower limb function in patients with early rheumatoid arthritis (ERA). [Methods] We included 121 patients with ERA whose disease duration was less than 6 months, and defined clinical arthritis as swelling of the joints. The effects of the whole foot, MTP joint and talocrural joint on physical impairment (HAQ-DI), especially on functional impairment in each domain related to lower limb function (arising, walking and activity) were analyzed using multiple logistic regression models adjusted confounders. [Results] Overall, the median age was 67.0 years, BMI was 22.1, and disease duration was 0.21 years. In a comparison of median values between 36 patients (29.8%) with at least one clinical foot arthritis and the patients without foot arthritis, there were statistically significant differences in disease duration, CDAI and HAQ-DI. In multiple logistic regression analysis, ankle arthritis was significantly associated with walking dysfunction (adjusted odds ratio (95%CI, p-value) 5.35 (1.30-22.0, p=0.02)). [Conclusions] In ERA, clinical arthritis of the foot, especially talocrural joint arthritis, was associated with gait dysfunction.

W86-2

One-year changes in bone structure in ACPA-positive patients who did not develop rheumatoid arthritis ~HR-pQCT Study~

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Conflict of interest: None

[Objective] In this study, we used HR-pCT to examine changes in bone structure in ACPA-positive non-RA patients (ACPA group) over a period of one year. [Methods] Objects were 16 women (ACPA group: 45.6 ± 12.2 years old) who were measured by HR-pQCT at one-year intervals, and compared with 16 ACPA-negative non-RA women (control group) who were age- and measurement interval-matched. [Results] Comparing the measured values of the two groups, there was no significant difference in the volumetric bone mineral density (vBMD) of the total, cortical, and trabecular. There was no significant difference in geometry. Trabecular thickness was significantly lower in the ACPA group. In 1-year changes, the control group showed a significant decrease in total vBMD, cortical vBMD, and trabecular vBMD. There was no significant vBMD change in the ACPA group. Geometry showed a significant decrease in cortical area and cortical thickness and an increase in trabecular area in both the control and ACPA groups. The trabecular number decreased significantly in the control group. [Conclusions] In the ACPA-positive non-RA cases, bone resorption, mainly in cancellous bone, which is thought to be accelerated by ACPA, is decreased, and there are more than a few cases in which bone formation occurs.

W86-3

Prospective study of association with rheumatoid arthritis-related autoantibodies and rheumatoid arthritis development in anti-CCP positive subjects at-risk for developing rheumatoid arthritis

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Conflict of interest: None

[Objective] We aimed to investigate the association between initial titers of rheumatoid arthritis (RA)-related autoantibodies and RA development in anti-CCP positive subjects at-risk for RA. [Methods] Twenty-five anti-CCP positive subjects visiting our clinic for joint stiffness/pain without clinical arthritis and three anti-CCP positive asymptomatic healthy subjects identified at health screening were followed prospectively. Anti-CCP antibodies and rheumatoid factor (RF) were evaluated at baseline and the development of clinical arthritis was monitored. [Results] RA developed in 10 subjects (36%) during follow-up (359 days in median). The anti-CCP titers were significantly higher in the progressors to RA than those in the non-progressors (in median, 123 U/mL vs. 13 U/mL; $p < 0.05$). RA developed more frequently in the anti-CCP high-titer group (>3x upper limit of normal) than in the anti-CCP low-titer group (9/18 vs. 1/10; $p < 0.05$). The RF levels were significantly higher in the progressors to RA than those in the non-progressors (in median, 55 IU/mL vs. 19 IU/mL; $p < 0.05$). [Conclusion] Our study suggests that high titers of anti-CCP antibodies or RF at initial presentation predict the future development of RA in anti-CCP positive at-risk subjects.

W86-4

Usefulness of Platelet-derived Microparticles in Inflammatory Arthritis Diagnosis

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Conflict of interest: None

BACKGROUND: Platelets are activated in rheumatoid arthritis (RA), and platelet depletion ameliorates arthritis in mice. Platelet-derived microparticles (PMPs) are extracellular vesicles that are released from platelets, present in the synovial fluid of RA, and are involved in inflammation. This study aimed to investigate the relationship between PMPs and inflammatory arthritis. METHODS: This study included patients with arthritis who visited our hospital from 2016 to 2021. The RA met the 2010 ACR/EULAR classification criteria. Undifferentiated arthritis (UA) was defined as patients with at least one joint with arthritis but not fulfilling any criteria for rheumatic diseases. PMPs are measured using a commercial enzyme-linked immunosorbent assay kit. RESULTS: This study enrolled 41 RA, 18 UA, and 19 PMR. The median age of RA was 65 (range: 50-74), with 18 males and 23 females. Serum PMPs were higher in RA compared to UA, PMR, and healthy controls. The PMP level in RA was significantly related to C reactive protein and matrix metalloproteinase 3. The PMPs in RA with interstitial pneumonia (IP) were significantly higher than those without IP. CONCLUSION: Our study revealed a higher PMP level in patients with RA among inflammatory arthritis.

W86-5

Clinical features of suspected rheumatoid arthritis

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Conflict of interest: None

Objectives: To clarify the clinical features of the cases of suspected rheumatoid arthritis (RA). **Methods:** There were 319 cases (113 males, 206 females) who visited our hospital with suspected RA from January 2021 to July 2022. The average age at the first visit was 62 years old, and the average duration from the onset of symptoms to the first visit was 28 weeks. The final diagnosis and clinical findings were investigated. **Results:** The reasons for consultation were wrist pain (74 cases), shoulder pain (58 cases), increased CRP (75 cases), RF positive (69 cases), and MP joint pain in the middle finger (33 cases) and so on. Among them, 147 cases were diagnosed with RA according to the ACR/EULAR (2010) RA classification criteria. The mean DAS28-ESR (4) was 4.4 and 83 cases were the elderly-onset RA (≧65 years old). In the differential diagnosis, psoriatic arthritis (25 cases), Heberden's nodules (22 cases), and Bouchard's nodules (18 cases) were common, and seven cases were collagen diseases other than RA. The mean CRP (mg/dL) was 2.0 in RA patients and 1.1 in non-RA patients. The mean HAQ-DI was 0.66 and 0.44, respectively. **Conclusion:** About half of the suspected RA cases were non-RA cases. Accurate early diagnosis of RA is important because it greatly affects the patient's prognosis.

W86-6

The phase angle derived from bioelectrical impedance analysis could be a screening indicator for osteopenia in female patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate whether the phase angle (PA), an index obtained by bioelectrical impedance analysis (BIA) can be a screening indicator for osteopenia (OP) in female rheumatoid arthritis (RA) patients. [Methods] Seventy-four female RA patients who were assessed by BIA method and BMD of the femoral neck by DXA were included. Patients with a T-score less than 1 were evaluated as OP group. For each indicator obtained by the BIA method, cutoff values for the OP group were calculated by ROC analysis, and the accuracy of each indicator was analyzed by sensitivity, specificity, and logistic regression analysis. [Results] Seventy-five percent subjects surveyed were in the OP group, and ROC analysis showed that 1: PA, 2: total body muscle mass, 3: lower limb muscle mass were all statistically significant items ($p<0.05$). The cutoff value of PA for OP was 4.95°. The diagnostic accuracy of the cutoff values of each indica-

tor were as follows: sensitivity (1: 82%, 2: 54%, 3: 73%), specificity (1: 74%, 2: 84%, 3: 68%). In logistic regression analysis, PA was a factor significantly associated with being in the OP group (OR = 9.63, 95%CI: 2.08 - 44.50). [Conclusions] The PA obtained by the BIA method could be an indicator for screening of OP group in female RA patients.

W87-1

The role of complement system in IgG4-related kidney disease (IgG4-RKD): multi-center study of IgG4-RKD working group in Japanese Society of Nephrology

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Conflict of interest: None

[Objective] To elucidate the role of complement system in IgG4-related kidney disease (IgG4-RKD). [Methods] We retrospectively examined the clinicopathological features of 60 patients with IgG4-RKD, with reference to the presence of hypocomplementemia. [Results] Hypocomplementemia was evident in 70%. Serum total IgG minus IgG4 were significantly higher in the hypocomplementemia group. There was no significant inter-group difference in the level of serum IgG4. Levels of C3, C4 and CH50 were inversely correlated with the total IgG minus IgG4 value. Renal pathology was evaluated in 53 of the 60 patients. In the hypocomplementemia group, light microscopy demonstrated a significantly broader extent of renal interstitial inflammation. Levels of C3 and CH50 were inversely correlated with the extent of interstitial inflammation. Immunofluorescence revealed a tendency for a high frequency of IgG or complement deposition on the renal tubular basement membrane (TBM) in the patients with hypocomplementemia. C1q deposition on the TBM was evident only in the hypocomplementemia group. [Conclusions] Types of IgG other than IgG4 may result in hypocomplementemia, and that complement activation may be related to progression of renal interstitial inflammation mainly via the classical pathway.

W87-2

Tertiary lymphoid tissue is associated with high disease activity in IgG4-related kidney disease

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Conflict of interest: None

[Objective] We aimed to clarify the clinicopathological association between IgG4-related kidney disease (IgG4RKD) and tertiary lymphoid tissue (TLT). [Methods] Nine patients with IgG4RKD diagnosed by renal biopsy between January 2014 and December 2021 at Kanazawa University Hospital and affiliated hospitals were included. Ten patients with interstitial nephritis were included as controls. TLT was defined as "dense clusters of CD20- and CD3-positive cells, including Ki-67-positive cells" and classified into three stages according to maturity, and stages 2 and 3 were defined as advanced stage TLT (adTLT). [Results] The number of TLT was not significantly different between the two groups (p = 0.65), while the number of adTLT significantly increased in the IgG4RKD group as compared to the control group [0.27/mm^2 (median; IQR 0.09-0.48) vs. 0.00/mm^2 (0.00-0.07); p = 0.028]. In the IgG4RKD group, the number of adTLT was significantly positively correlated with the formation of storiform fibrosis (SF) (p = 0.007, R^2 = 0.67). [Conclusion] The formation of adTLT in IgG4RKD was significantly frequent compared to other types of interstitial nephritis. The correlation of SF and adTLT suggests that the formation of adTLT in IgG4RKD may be associated with higher disease activity.

W87-3

Comparison and pathway analysis of T/B cells specific differentially expressed genes (DEGs) by RNA-Seq between affected salivary glands and peripheral blood in patients with IgG4-related disease (IgG4-RD)

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Conflict of interest: None

[Objective] To clarify T/B cells specific DEGs by RNA-Seq between affected tissues and peripheral blood in IgG4-RD patients. [Methods] Pathologically confirmed submandibular glands (SMGs) and PBMC were collected from treatment naïve definite IgG4-RD patients (N=3), subsequently $CD3^+$T/$CD19^+$B cells were sorted. We compared the gene expression of T/B cells between SMGs and PBMC by RNA-Seq. We performed 1) principal component analysis (PCA) and identification of DEGs, 2) Ingenuity Pathway Analysis (IPA), 3) validation by qPCR. [Results] 1) In PCA, gene expression patterns of T/B cells of SMGs differed from those of PBMC. 214 up-regulated and 50 down-regulated DEGs for T cells, 630 up-regulated and 109 down-regulated DEGs for B cells were identified in SMGs compared with PBMC. Up-regulated DEGs in SMGs included several cytokines, chemokines, and transcriptional factors. 2) In IPA, Th1, Th2, IL-17, SLE, TLR, and wound healing signaling were up-regulated in T cells of SMGs. SLE, complement, fibrosis, IL-8, and IL-15 signaling were up-regulated in B cells of SMGs. 3) The mRNA expression of IL-21 and EGR2 in T cells of SMGs was significantly increased than those of PBMC. [Conclusions] Using RNA-Seq, we identified DEGs and possible pathogenic pathways in T/B cells from affected SMGs of IgG4-RD.

W87-4

Change of serum IgG4/IgG ratio after glucocorticoid treatment in IgG4-related disease

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Conflict of interest: None

[Objective] IgG4-related disease (IgG4-RD) is a systemic chronic fibrotic inflammatory disease. Its diagnostic criteria include an elevated serum IgG4 level. Previous reports have shown that sensitivity and specificity of the serum IgG4 levels and IgG4/IgG ratio (IgG4/IgG-R) for diagnosis is above 90%. However, there is no report evaluating between serum IgG4 levels and IgG4/IgG-R before and after treatment. We aimed to clarify the changes of serum IgG4 levels and IgG4/IgG-R before and after treatment. [Methods] We retrospectively reviewed the medical records of 58 IgG4-RD cases between April 1, 2015 and August 31, 2022, who were treated at our hospital. Serum IgG4, IgG, and IgG4/IgG-R at 1 month (mo), 3 mo, and 1 year after treatment were analyzed (Wilcoxon's signed rank test) for 12 cases (41.7% male, mean age at diagnosis 64.4 years) who were started on prednisolone. [Results] Serum IgG4, IgG, and IgG4/IgG-R significantly decreased at 1 mo (256.5 mg/dL, 1118.5 mg/dL, 0.24), 3 mo (114.5 mg/dL, 858.0 mg/dL, 0.14), and 1 year (156.0 mg/dL, 1048.5 mg/dL, 0.17) after treatment compared with before treatment (median 586.5 mg/dL, 1828.5 mg/dL, 0.32) ($p < 0.05$). [Conclusion] Serum IgG4/IgG-R as well as IgG4 and IgG decreased after treatment in patients with IgG4-RD.

W87-5

Case series of IgG4-related disease mimicker in retroperitoneal fibrosis and periaortitis

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Conflict of interest: None

[Objective] In this narrative review, we will discuss the findings that influenced the diagnosis of secondary retroperitoneal fibrosis in a patient referred to our department with retroperitoneal fibrosis (RPF) /periaortitis-like imaging findings. [Methods] We investigated retrospectively the patient background, final diagnosis, laboratory tests, presence or absence of biopsy and pathological findings, imaging findings such as PET-CT, and inclusion score of 2019 ACR/EULAR classification criteria. [Results] The affected sites were the periaortic region in 7 cases, the renal ureter in 3 cases, and the pelvic retroperitoneum in 4 cases. The final diagnosis was malignancy in 7 cases. The mean value of CRP was 6.59 mg/dL, while 5 patients with malignant tumors had low CRP < 1 mg/dL. Tissue biopsy was performed in 7 cases, 2 were biopsied in the retroperitoneum and 4 were biopsied in other regions based on the PET-CT findings, and all cases were confirmed by the biopsy. The mean inclusion score of the 2019 ACR/EULAR classification criteria was 10. Although 2 patients scored more than 20, they were diagnosed as malignant tumors on pathological findings, [Conclusions] When CRP is low in secondary RPF, a tissue biopsy should be considered because of the high possibility of malignancy.

W87-6

Evaluation of periaortitis/periarteritis and retroperitoneal fibrosis in patients with IgG4-related disease

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Conflict of interest: None

(Background) Most patients with IgG4-related periaortitis/periarteritis and retroperitoneal fibrosis (PA/RF) have few subjective symptoms and are often detected incidentally on imaging studies. **(Methods)** We evaluated the vascular lesions in patients with IgG4-related disease using the diagnostic guidelines created by The Japanese Circulation Society and the IgG4-Related Disease Study Group (Ann Vasc Dis. 2019), and evaluated the vascular lesions according to the classification by Peng et al. (Arthritis Res Ther. 2020). **(Results)** 33% of patients had vascular lesions. The number to fulfill each item: 1a) 14, 1b) 0, 1c) 0, 2) 15, 3) i, ii, iii, iv all 0, 4) 10. Confirmed diagnosis 10, Semi-confirmed diagnosis0, and Suspected diagnosis 4. Splenic artery aneurysm was observed in 1 patient. The number of distribution type: Type 1) 1, Type 2a) 2, Type 2b) 10, Type 3) 1. Suspected cases were inflammatory aortic aneurysms in 2 patients and hydronephrosis in 2 patients. **(Conclusions)** The diagnostic guideline for IgG4-related PA/RF was clinically satisfactory. Most of the lesions were occured around the bifurcation from the abdominal aorta to the common iliac artery. In some cases, the lesions worsened during the course of the disease. Therefore screening for PA/RF lesions is important.

W88-1

The Impact of Early Optimization of Infliximab Blood Concentrations more than 1μg/mL on Therapeutic Effectiveness with Rheumatoid Arthritis

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Conflict of interest: Yes

[Objective] Infliximab (IFX) is the only biological agent whose blood concentration can be measured using the RemicheckQ (RemiQ) kit. In this study, we measured RemiQ 14 weeks after IFX induction to evaluate its usefulness as a predictor of treatment response. [Methods] RemiQ was measured 14 weeks after IFX induction, and DAS28, retention rate, and IFX dose escalation were evaluated in 76 patients enrolled in a multicenter clinical study. [Results] RemiQ results after 14 weeks of IFX induction were positive in 46 patients and negative in 30 patients. DAS28 was significantly lower in RemiQ-positive patients (R+) than in RemiQ-negative patients (R-). At 12 months, 38 of 46 R+ patients (82.6%) and 6 of 30 R- patients (20%) were receiving 3 mg/kg, and the 14-week R- patients received IFX dose increases after 14 weeks. The continuation rate was 93.5% for RemiQ-positive cases and 70.0% for RemiQ-negative cases. [Conclusions] Early dose escalation of TNF inhibitor in combination with clinical evaluation of disease activity at the time of remission induction is important to prevent secondary ineffectiveness, and stabilization of disease activity control improves the continuation rate. These results suggest that RemiQ results at 14 weeks may be a predictor of treatment response.

W88-2

The different clinical and functional remission rates of biologics in different disease duration groups in biologic naïve rheumatoid arthritis patients: a multicenter cohort study -the ANSWER cohort-

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Conflict of interest: None

[Objective] Although sooner initiation of biological DMARDs (Bio) are recommended, if necessary, there here been no data about the initiation timing of Bio and outcomes in real-world settings. We aimed to investigate the outcomes of Bio in rheumatoid arthritis (RA) patients with different disease duration groups. [Methods] RA patients treated with Bio were extracted from ANSWER cohort database. Patients were divided into 3 groups (Early (E), Intermediate (I), Delayed (D)) according to the tertiles of disease duration. The 1-year remission rates were compared between 3 groups. [Results] The mean disease duration of 3 groups were as follows: E 0.5 (±0.3), I 3.1 (±1.5), and D 17.5 (±10.3). The mean baseline CDAI and HAQ were significantly different between 3 groups. The 1-year CDAI remission rates were as follows: E 46.6%, I 38.2%, and D 22.9%. The 1-year HAQ remission rates were as follows: E 73.4%, I 75.5%, and D 49.0%. The adjusted odds ratio (OR) for CDAI remission were as follows: E vs. I 1.7 (95%CI 1.1-2.8) (p=0.02), E vs. D 4.1 (2.5-6.9) (p<0.001). About OR for HAQ remission, E vs. I 1.9 (95%CI 0.97-3.6) (p=0.06), E vs. D 4.3 (2.3-8.0) (p<0.001). [Conclusions] The 1-year clinical and functional remission rates were higher in the RA patients with shorter disease duration.

W88-3

Fibrosis-4 index before initiating treatment can predict SDAI remission for 26 and 52 weeks on MTX monotherapy in elder onset rheumatoid arthritis

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Conflict of interest: None

[Objective] Elder onset RA (EoRA) has an acute onset of symptoms and rapidly leads to ADL impairment, so we need to treat it early. However, treatment for EoRA involves polypharmacy. Treatment for EoRA with the goal of early remission are aggressively used high-dose MTX in our hospital. Therefore we determined what factors make MTX monotherapy feasible for EoRA for 52 weeks after treatment. [Methods] We analyzed 116 patients aged 65 years or older diagnosed with RA and introduced MTX from 2015 to 2021, using a maximum of 12 mg/week or more. The observation period was 13/26/52 weeks after treatment. Cases who maintained SDAI ≦5 on MTX alone after treatment were considered responders, and others were considered non-responders. Logistic regression analysis was performed to examine the impact of predictor in responder. [Results] The mean age of onset for all cases was 74.6±5.8 years and the proportion of cases maintained responder at 13/26/52 weeks after treatment was 56/62/64%. Results of analysis showed RF positivity at 13 weeks (odds ratio; 0.162, p=0.009) and FIB-4 at 26/52 weeks (odds ratio; 4.886, p=0.015/odds ratio; 7.655, p=0.005) as predictors for responder. [Conclusions] FIB-4 before treatment may be a useful predictor of remission for 26/52 weeks on MTX monotherapy for EoRA.

W88-4

Clinical features of patients with rheumatoid arthritis (RA) refractory to multiple molecular-targeted drugs

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Conflict of interest: None

[Objective] To clarify the clinical features of RA refractory to multiple molecular-targeted drugs. [Methods] We examined b/tsDMARDs naive RA patients who were administered infliximab (IFX), tocilizumab (TCZ) IV, or abatacept (ABT) IV between Jan 2012 and Jan 2022. Patients who had changed b/tsDMARDs two or more times due to ineffectiveness were classified as treatment-resistant (TR) group, and those who had no history of change or discontinuation due to ineffectiveness as well-controlled (WC) group. 1) Clinical background, 2) laboratory findings and disease activity, and 3) usage of drugs at baseline were compared between the two groups retrospectively. [Results] Among 90 patients (IFX: 11/TCZ: 33/ABT: 46), 7 cases in TR and 64 cases in WC group were identified. 1) Age, gender, disease duration, and concomitant CTDs were comparable between groups. Interstitial pneumonia (IP) was significantly more frequent in TR group (42.9% vs 10.9%, p=0.04). 2) RF, ACPA, and disease activity were similar between groups. 3) Usage rate of IFX was significantly higher (57.1% vs 6.3%, p<0.01) and that of ABT was significantly lower (14.3% vs 56.3%, p=0.04) in TR group. [Conclusions] TR group had significantly higher frequency of IP, higher usage rate of IFX, and lower usage rate of ABT than WC group.

W88-5

Effect of changes in serum IL-6 levels in RA patients on the continuous use of TNF inhibitors and achievement of clinical remission in one year

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Conflict of interest: None

[Objective] Although bDMARDs have significantly improved the treatment outcomes in RA, not all patients achieve long-term remission. We examined whether serum IL-6 concentrations of RA patients are useful in predicting the effectiveness of TNF inhibitors (TNFi) in one year. [Methods] Fifty-two RA patients introduced bDMARDs from 2010 to 2018 in our hospital were included in this study (tocilizumab: 16, abatacept: 15, and TNFi: 21). We quantified serum IL-6 concentration before introduction of the DMARDs, and 5 (± 1) weeks and 14 (± 2) weeks after treatment, using a bead-based immunoassay, Bio-Plex (Bio-Rad). [Results] All three bDMARDs decreased DAS28-ESR significantly at 14 weeks. Serum IL-6 levels also decreased significantly at 14 weeks in the abatacept group. Although they decreased significantly in the TNFi group at 5 weeks, the significance disappeared at 14 weeks because some patients showed a rebound. The rebound of IL-6 levels at 14 weeks (at least 20%) proved to be a risk factor of TNFi failure (discontinuation of the TNFi or DAS28-ESR > 2.6) in one year (relative risk: 2.40, 95% confidence interval: 1.14 - 2.40). [Conclusions] Patients with the rebound of serum IL-6 level after TNFi introduction are likely to fail to achieve clinical remission in one year.

W88-6

Analysis of Difficult-to-treat RA (D2TRA) in our hospital - Investigation of background factors involved in D2TRA

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Conflict of interest: None

[Objective] To analyze D2TRA and its background factors in clinical practice. [Methods] Patients with RA who visited our outpatient clinic between April 2021 and March 2022 were included in the study and their progress was investigated until September 2022. The patients who fulfilled D2TRA (defined as b/tsDMARDs ≧2 and ≧MDA) were selected (D2TRA group). [Results] There were 328 RA patients, 247 (75.3%) women, 66.3±13.4 years of age, 37 (83.7%) patients in the CDAI-MDA group, and 17 (88.2%) patients in the D2TRA group, 67.7±14.5 years of age, and 233.0±161.5 months of disease duration. D2TRA patients had longer disease duration (p=0.0017), higher Steinbrocker Stage classification, and fewer patients continued MTX (p=0.0324). There was a higher number of anti-CCP antibody-positive patients in the D2TRA group (16 patients, 94.1%), but the difference was not significant (p=0.0829). 4 (23.5%) patients in the D2TRA group had treatment difficulty due to complications, and 6 (35.3%) patients refusal. [Conclusion] Patients in the CDAI-MDA group had longer disease duration, higher Steinbrocker Stage classification, and difficulty continuing MTX. Most patients in the D2TRA group were positive for anti-CCP antibodies. Psychological and socioeconomic factors were also observed.

W89-1

Cost-benefit analysis on biologics in patients with rheumatoid arthritis stratified by joint index vector

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Conflict of interest: None

[Objective] To analyze efficacy of expensive bDMARDs in RA patients stratified by joint index vector (J Big Data 2018; 5: 37). [Methods] Of 6366 two-year continuous registered RA patients in NinJa from 2019 (BL) who did not use bDMARDs at BL, 239 each of bDMARDs user (B+) in the next year and propensity-matched non-user (B-) by EZR (Bone Marrow Transplant 2013: 48, 452) were selected. Patients with vector Z > 0.2 at BL were named as large-joint prominent (L) group. [Results] At BL, there were no significant differences of clinical features between B+ and B-. The remission rate of DAS28 and HAQ did not differ between them in the next year; however, DAS28 remission rate of B- and B+ was 31.3% and 50.6% (p=0.018) in L group, and was 64.7% and 59.6% (p=0.41) in non-L group, respectively; HAQ remission rate of B- and B+ was 47.0% and 62.7% (p=0.061) in L group and was 78.8% and 63.5% (p=0.004) in non-L group, respectively. Mean drug cost a day in L and non-L group at

BL was ¥727 and ¥468, respectively. In the next year, the cost changed ¥818 (B-) to ¥3,240 (B+) in L group, and ¥531 (B-) to ¥3,457 (B+) in non-L group, respectively. [Conclusions] Efficacy of expensive bDMARDs on large-joint prominent group was confirmed and selective use of bDMARDs to this group may improve cost efficiency.

W89-2

Healthcare Resource Utilization and Economic Burden of Patients with Adequate and Inadequate Responses to Advanced Therapies for Rheumatoid Arthritis in Japan

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Conflict of interest: Yes

Purpose: To compare HCRU and direct cost burden between patients (pts) with RA who responded (rsp) or did not respond (non-rsp) to advanced therapies (AT) in Japan. Methods: This retrospective study included data from MDV database between Apr 2018 and Sep 2020. Pts who initiated ≧1 AT (index date was the initiation date), had ≧1 RA diagnosis claim during the 6-mo pre-index period, ≧2 RA diagnosis at any time, and 12-mo follow-up, were included. Non-rsp and rsp were identified using a validated Curtis algorithm. HCRU and all-cause and RA-related direct medical, ED, lab, and pharmacy costs, were compared. Results: Of the 2446 pts, 74% (1817) vs 26% (629) were categorized as non-rsp and rsp. A greater number of days of hospitalization, ED visits, and prescription fills, were found in non-rsp. Mean all-cause inpatient (¥301,974 vs ¥168,922) and outpatient (¥228,921 vs ¥188,087) costs were higher for non-rsp, contributing to 40% higher all-cause total medical costs; RA-related costs showed a similar trend. Mean all-cause lab costs (¥166,892 vs ¥145,601) were higher in non-rsp; RA-related were similar. All-cause pharmacy costs were similar, while RA-related were higher in rsp. Conclusion: Non-rsp had greater HCRU and economic burden suggesting a need for more effective therapies for RA.

W89-3

The association between b/tsDMARDs use and the burden of treatment costs on daily life (financial toxicity) in RA patients: NinJa cohort study

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Conflict of interest: None

[Objective] In this study, we investigated whether the use of b/tsDMARDs is associated with financial toxicity in RA patients. [Methods] Cross-sectional study using data from 2 of the NinJa database participating sites in 2020. Exposure was defined as the use of bDMARDs (including biosimilar) or JAK inhibitors. The outcome was financial toxicity as measured by the 11-item COST (The COmprehensive Score for financial Toxicity) [total score 0-44]. Multiple regression analysis with adjusted variables as age, gender, DAS28-CRP, type of work, and new cancer incidence was used to analyze the association between b/tsDMARDs use and financial toxicity. Missing values were complemented by multiple imputation. [Results] Of the 3031 patients at the two sites, 1732 were included, for whom exposure and outcomes could be obtained. The median age was 70 years and 83.3% were women. 624 (36%) were using b/tsDMARDs, with median financial toxicity of 26. Multiple regression analysis showed that b/tsDMARDs use significantly worsened financial toxicity [-1.77 points (95% CI -2.39 to -1.45)]. [Conclusion] b/tsDMARDs use significantly worsened financial toxicity. Future studies adjusting for annual household income, costs for other comorbidities, and indirect medical costs are needed.

W89-4

Inhibitory Effect of Abatacept against Joint Inflammation Shown by Ultrasound Power Doppler Scoring in Japanese Bio-Naive Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Objective] The aim of this study was to investigate the early improvement effect of abatacept on joint ultrasound power Doppler (PDUS). [Methods] From December 2018 to June 2021, we enrolled bionaive RA patients with inadequate response to at least one csDMARD, and SDAI>11 CDAI>10 or DAS28>3.2. Subcutaneous abatacept was administered weekly. The rate of improvement in the PDUS score totaled for 36 joints at week 8 was evaluated. Peripheral blood at week 8 was analyzed RNA expression by next generation sequencing. [Results] 21 cases were enrolled and all ACPA positive. Baseline scores were SDAI 21.2±10.3, CDAI 19.7±9.5, and DAS28-CRP 4.1±0.9. Average PDUS score was 9.0±4.8 at week 0 and 7.2±6.4 at week 8, with no significant change. However, there were 9 cases with an improvement of 35% or more, which were classified as the effective group and those less than the ineffective group. There was no difference in disease activity, PDUS score, and ACPA titer between two groups at week 0, but at week 8, the rate of decrease in ACPA was significantly greater and RNA analysis showed significantly low expression of HLA-DQB1, HLA-DQA1, and HLA-DRB1 in the effective group. [Conclusions] In early phase, Abatacept suppressed joint inflammation due to inhibition of co-stimulatory signals.

W89-5

Accumulation of damage due to comorbidities in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Object] Multi-comorbidities are associated with decreased physical function in rheumatoid arthritis (RA). This study aims to assess the accumulation of damage due to comorbidities. [Methods] Baseline data from patients enrolled in a multicenter prospective cohort study of RA aged 50 years or older were used. Accumulation of damage from comorbidities was assessed by the number of items with or without cardiac (7 items), respiratory (5 items), infectious (6 items), osteoarticular (5 items), malignancy (6 items), autoimmune (4 items), cerebrovascular (3 items), gastrointestinal (4 items) and renal (3 items) diseases, and depression was assessed with the Patient Health Questionnaire-2 (PHQ-2). [Results] Patients with HAQ-DI >0.5 (n=137) had lower rates of SDAI remission and higher Rheumatic Disease Comorbidity Index (RDCI) and PHQ-2 than those with HAQ-DI ≦0.5 (n=194). Multiple logistic regression analysis showed that a higher number of items was associated with HAQ-DI >0.5 in osteoarticular disease and depression. The osteoarticular disease with more items had a higher number of items for all comorbidities and more RDCI. [Conclusions] Among comorbidities, osteoporosis/fracture was strongly associated with poor physical function, and was also associated with multi-comorbidities.

W89-6

Study of central sensitization in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] RA pain has been shown to involve not only nociceptive pain, but also central sensitization mechanisms. The purpose of this study was to examine central sensitization in RA patients using the Central Sensitization Inventory. [Methods] 160 patients (46 males and 114 females, mean age 69.0 years) diagnosed with RA at three centers were administered questionnaires on CSI, mHAQ, Pain Catastrophizing Scale (PCS), and HADS (anxiety, depression). The patients were divided into two groups, one with less than 30 and the other with 30 or more, and the evaluation items were BMI, history of disease, RF, DAS28-CRP, Pain VAS, presence of painful areas not included in DAS28, CSI score, mHAQ, PCS, and HADS. [Results] The overall CSI score was 18.8±13.4. Comparing CSI<30 and CSI≧30 groups, disease duration was significantly longer in the CSI≧30 group and the DAS 28-CRP, VAS, mHAQ, PCS, and HADS (anxiety) were significantly worse in the CSI≧30 group. VAS, PCS, and mHAQ were positively correlated with CSI. mHAQ and HADS (anxiety) were found to be significant items, with odds ratios of 5.1 and 1.3, respectively. [Conclusions] Our results suggest that central sensitization in RA patients may be related to mHAQ and HADS (anxiety) rather than disease activity.

W90-1

Factors associated with improvement in locomotion syndrome after total knee arthroplasty

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Conflict of interest: None

[Objective] Osteoarthritis of the knee is considered one of the factors of locomotive syndrome. The purpose of this study was to prospectively investigate the improvement in locomotion with total knee arthroplasty (TKA) and to examine factors associated with such improvement. [Methods] Patients who underwent TKA from July 2020 to April 2021 were included. The LS was evaluated preoperatively and one year postoperatively. In addition, the Knee Society Score (KSS), quadriceps muscle strength, range of motion, gait speed, and skeletal muscle mass were measured and statistically analyzed in relation to LS improvement. [Results] 70 patients were included (57 women, mean age 74.9 years, mean BMI 25.6). Preoperatively, 84.2% were in LS stage 3, 11.4% in stage 2, and 4.4% in stage 1. One year after surgery, 54% of the patients were in stage 3, 37% in stage 2, and 9% in stage 1, which was a significant improvement. Locomo 25 was most correlated with improvement in the stage of LS. In the multivariate analysis, only KSS had an effect on the improvement of the stage of LS. [Conclusions] Improvement in the stage of LS could be expected with TKA, especially the improvement in locomo 25 was significant. The factor associated with improvement in LS was the KSS.

W90-2

Current status of hemophilic arthropathy in Ehime Prefecture

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Conflict of interest: None

[Objective] At Ehime University, we have been inolved in a multidisciplinary hemophilia comprehensive care program since 2016. In this study, we investigated the current status of hemophilic arthropathy (HA) in Ehime Prefecture. [Methods] Forty-two patients (mean age 26 years) who received comprehensive medical care in Ehime Prefecture in 2021 were included in this study. Thirty-six had hemophilia A and six had hemophilia B. Thirty-three had the severe type. X-rays of the knee, ankle, and elbow joints were evaluated according to Arnold-Hilgartner stage classification (A-H classification), and the incidence of HA, the preferred site of the affected joint, and the relationship between HA and age were examined. [Results] In this series, bleeding control was good during the period of this study. The prevalence of HA was 42.9%, and ankle joint disorders were the most frequent. The number of joints affected increased with age, showing a moderate correlation (correlation coefficient: 0.61); the number of joints affected increased after the late 20s, and after the age of 40, most patients had 3 or more joints affected, all of which were A-H classification stage 4 or higher. [Conclusions] It is important to link regular joint evaluation with prevention of progression of joint disorders.

W90-3

Construction of an AI System to Detect Osteoarthritis (OA) of the Hand from Multimodal Images

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Conflict of interest: None

[Objective] To construct an image analysis AI to detect osteoarthritis (OA) of the hand. [Methods] Image data acquisition was performed on hand, using three modalities: RGB, motion capture (video images with hand joint motion recognition), and thermographic images. In motion capture, each joint angle was calculated by hand pose estimation and converted into feature vectors. For thermographic and RGB images, features of regions of interest were extracted by key point annotation for images of the dorsal and palm side of the left and right hands, and inputted to a multistream convolutional neural network to obtain binary classification results for each joint. Data augmentation for skin color was also performed. [Results] 173 patients were included, 135 as training data and 38 as test data. The prevalence of OA on echo findings was 38/24/6% for DIP/PIP/MP joints, respectively. In the prediction system that analyzed the information of the joint and whole hand, analysis for PIP and DIP joints showed accuracy: 70% and 80% and F1 score: 45% and 76%, respectively. The MP joint had a low prevalence rate and was difficult to validate adequately. [Conclusions] Although there is scope for further improvement in this system, it demonstrated relatively robust and promising prediction results.

W90-4

Association of ferroptosis signaling in the pathogenesis of Japanese patients with hip dysplasia

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Conflict of interest: Yes

[Objective] The purpose of this study was to investigate the association between developmental dysplasia of the hip (DDH) and disease-related loci in a Japanese cohort. [Methods] A genome-wide association study (GWAS) was conducted on 238 Japanese DDH patients and 2,044 healthy subjects. GWAS results for 3,315 patients from the UK Biobank data were also analyzed. The reproducibility of variants in Japanese DDH could not be replicated in the UK Biobank results. This result may be due to the wide range of genes associated with DDH. To address this issue, functional analysis of the genes was performed. We also performed transcriptome analysis of cartilage specimens from osteoarthritis (OA) and femoral neck fractures associated with DDH. [Results] Ontology analysis using FUMA and ingenuity pathway analysis (IPA) identified important pathways in the gene set of Japanese patients, culminating in the ferroptosis signaling pathway. Transcriptome analysis showed that genes involved in the ferroptosis pathway are expressed in chondrocytes, and their expression is decreased in the DDH-related OA group. [Conclusions] The ferroptosis signaling pathway may be relevant to the pathogenesis of DDH.

W90-5

Comparative study of pathological feature of secondary osteoarthritis of the knee in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] TKA associated with secondary knee osteoarthritis (SKOA) in patients with rheumatoid arthritis (RA) is reported to be increasing. The purpose of this study is to examine whether the pathological findings were associated with SKOA on x-ray. [Methods] Forty-seven RA patients who were able to obtain synovial samples at TKA were included in this study. The patients were divided into low-grade synovitis group (LG) and high-grade synovitis group (HG) according to Krenn synovitis score, and compared the patients background, joint space width and the osteophyte grade score (OGS). [Results] There were no significant differences in age, disease duration, BIO use (LG: 50% vs HG: 31.6%), FTA (LG: 178.4 vs HG: 182.8), joint space and OGS (LG: 7.3 vs HG: 7.1, p=0.76). CRP (LG: 0.34 vs HG: 1.12, p<0.001) and ESR (LG: 17.6 vs HG: 36.4, p<0.01) were significant higher in HG than in LG. [Conclusions] 60% of RA patients requiring TKA had controlled synovitis with low activity. Regardless of the presence or absence of pathologic synovitis, osteophyte formation, which is considered a characteristic of OA, was observed on x-ray. Patients with residual inflammatory findings may also have residual synovitis, and we may be very conscious of RA even if we determine that the patient has SKOA on x-ray.

W90-6

The mechanism of angiogenesis in OA synovium

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Conflict of interest: None

[Objective] To clarify the mechanism of angiogenesis in OA synovium. [Methods] Synovial tissue, joint fluid, and cartilage tissue from degenerated areas were collected from 32 OA knee joints. mRNA was extracted from the synovial tissue, and the expression of 9 genes related to angiogenesis (ANGPT2, TEK, KDR, END1, EDNRA, PLAT, F2R, ACTA2, CD34), IL1B, and TNF were examined by qPCR. Concentrations of angiopietin-1 and 2 (ANG-1 and 2) were measured in joint fluid, and degenerated cartilage was subjected to a load equivalent to that applied to cartilage during walking to release the protein. The proteins were then added to HUVECs and primary cultured OA synoviocytes and changes in gene expression were examined. [Results] The expression levels of the above 9 genes showed a strong positive correlation with each other, but there was no significant correlation between the expression levels of these 9 genes and IL1B or TNF. The average concentration of ANG-2 in joint fluid was 3.3 ng/ml, more than twice the reported plasma concentration. Proteins from degenerated OA cartilage induced ANGPT2 expression in both HUVECs and OA synoviocytes. [Conclusions] These results suggest that ANG-2 production may be induced in the OA synovium by some factor released from degenerated cartilage.

W91-2

Comparing the effectiveness and safety of biological DMARDs in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We aimed to compare the effectiveness and safety of abatacept (ABT) and tocilizumab (TCZ) in elderly patients with rheumatoid arthritis (RA). [Methods] Total 125 elderly patients with RA (>65 years) who began therapy with either ABT (n = 47) or TCZ (n = 78) between 2014 and 2021 at our institute were enrolled. We compared the drug retention rate and clinical response at 24 weeks between two groups. Adverse events (AEs) and the reasons for drug discontinuation were assessed. [Results] There was no significant difference in demographic characteristics except for the use of glucocorticoid and the drug retention rate between the two groups. The proportion of the patients archiving low disease activity or remission at 24 weeks did not differ significantly between the two groups. However, in the TCZ-treated group, the concomitant use of methotrexate (MTX) significantly increased the incidence of AEs leading to the discontinuation of TCZ. Whereas these was no significant impact of concomitant use of MTX on the incidence of AEs leading to discontinuation in ABT-treated group. [Conclusions] Our data indicated that the rates of discontinuation due to AEs were significantly higher in elderly patients with RA receiving TCZ plus MTX than those receiving TCZ monotherapy.

W91-3

Comparison of joint ultrasound improvement findings in large and small joints of elderly-onset rheumatoid arthritis treated with biologic DMARDs

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Conflict of interest: None

[Objective] EORA often causes acute major arthritis, and physical dysfunction is likely to occur. Therefore, early treatment is desired, but selection of Bio have not been determined. Therefore, the effect of Bio was evaluated by US. [Methods] EORA patients who were able to be evaluated by US for 24 weeks were included in our study. The evaluation method is GS and PD for large joints, small joints, and all joints. [Results]: Mean age 76.5 years, 46 females (73%), duration 3.4 years. RF 73%, average 237.0 IU/ml, ACPA 68.3%, average 547.3 U/ml, MTX rate 35.0%, average 6.7 mg, PSL rate 46.0%, average 5.7 mg, Bio There were 19 TNF, 18 IL-6, 16 CTLA-4, and 10 JAK. CDAI averaged 11.2. There was no significant difference in the improvement rate between formulations in the amount of change in CDAI before the introduction of Bio and at 24 weeks. However, in US findings, IL-6 (37.6) showed significant improvement compared with JAK (16.0) and TNF (15.7) in all joints (IL-6 vs JAK, p=0.028, IL-6 vs TNF, p<0.01)., IL-6 (16.7) showed significant improvement compared to ABT (6.4) and TNF (3.9) in large joints (IL-6 vs ABT, p=0.03, IL-6 vs TNF, p<0.01). [Conclusions] IL-6 may be a more effective therapeutic option than TNF in EORA, which is frequently associated with large joints.

W91-4

Comparison of the efficacy and safety of abatacept on elderly and young patients with rheumatoid arthritis: 52 weeks results from ABT-ATS study

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Conflict of interest: Yes

[Objectives] To clarify the efficacy of abatacept (ABT) in elderly and young patients with RA. [Method] Refractory to csDMARDs and bionaïve patients were enrolled in a multicenter observational registry (ABT-ATS study). Either ABT or csDMARDs was administered at the discretion of physicians to elderly (65 years and older) and young (20-64 years) patients (ABT-elderly (AO), ABT-young (AY), csDMARDs-elderly (CO), and csDMARDs-young (CY)). Efficacy of the treatment for 52 weeks was compared between 4 groups. [Result] 202 patients (AO, 67; AY, 47; CO,

48; CY, 40 patients) were analyzed. DAS28-ESR was significantly decreased in AO than CO group (-2.110±1.232 vs -0.63±1.124, p<0.001). DAS28-ESR was significantly improved in AY than CY group (-2.017±1.365 vs -0.929±0.893, p<0.001). In contrast, no significant differences were found between AY and AO (p=0.732). After IPTW using propensity score matching, similar results were obtained for the comparison of each group. ABT continuation rates after 52 weeks were comparable (AO 80% vs AY 76.9%, p=0.825). Serious adverse events were observed in 4 patients in AO, 2 in AY, 3 in CO and 0 in CY. [Conclusion] The efficacy of ABT on elderly RA is comparable to that of young patients.

W91-5

Incident ratio of opportunistic infections in RA patients with biological DMARDs and JAK inhibitor from NDB data

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Conflict of interest: None

[Objective] We compared the incidences of four opportunistic infections (OI) in patients with rheumatoid arthritis (RA) treated with molecular-targeted drugs from big claims data. [Methods] We identified 205 906 patients with RA who were prescribed molecular-targeted drugs 2010-2017 from the National Database of Japan, and calculated the incidence of four OIs (Pneumocystis pneumonia [PCP], tuberculosis [TB], nontuberculous mycobacterial infection [NTM], and herpes zoster [HZ]). [Results] The total number of PCP, TB, NTM, and HZ patients with biological disease-modifying antirheumatic drugs (bDMARDs) or tofacitinib treatment history in RA were 765, 1158, 834, and 18 336, respectively. The incidence rates (IRs) of each OI for all bDMARDs were 0.14, 0.14, 0.09, and 2.40 per 100 person-years, respectively; while for tofacitinib they were 0.22, 0.22, 0.07, and 7.00 per 100 person-years. No big difference was observed among bDMARDs. All OIs showed higher incidence in those older than 65 years; but PCP, NTM and HZ showed no difference between those 65-74 years old and those over 75 years old. The median of occurrence was the third, seventh, ninth, and thirteenth month after treatment, respectively. [Conclusion] We counted real IRs of OIs for the whole nation from big claims data.

W91-6

Biologic Agents Survival Analysis in Patients with Rheumatoid Arthritis Concomitant with End-Stage Kidney Disease

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Conflict of interest: None

[Objective] The survival rate of initially introduced biologic agents (BA) were compared between hemodialysis (HD) and non-dialysis (non-HD) groups in rheumatoid arthritis (RA) patients with CKD stages 4 or 5. [Methods] RA patients with CKD stage 4/5 who were newly introduced to BA from 2004 to 2019 were included. The primary endpoint was 36-month BA survival. [Results] A total of 38 patients (18 in the HD group and 20 in the non-HD group) received TNFα inhibitors (32), IL-6 inhibitors (4), and abatacept (ABC) (2), with survival rates of TNF 30%, IL-6 75%, and ABC 0%, respectively. 36-month survival rate of BA overall was 36% in the HD group and 32% in the non-HD group, with no significant difference. Cox proportional hazards analysis by gender, age, HD status, and type of BA showed no significant difference in survival rate among BA (IL-6: HR = 0.25, p = 0.18, 95%CI 0.03-1.91, ABC: HR = 0.97, p = 0.97, 95%CI 0.19-5.02), and there was no significant difference in BA survival between patients with and without HD (HR = 0.84, p = 0.69, 95%CI 0.36-1.98). [Conclusions] In RA patients with CKD stage 4/5, HD was not a significant risk factor for BA survival. IL-6 inhibitor showed higher survival rate among BA, but with no significant difference.

W92-1

Effectiveness and Safety of Abatacept in Biologics-naïve rheumatoid arthritis Patients with Moderate Disease Activity for Three Years in Japanese Multicenter Investigational Study (ORIGAMI Study)

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Conflict of interest: Yes

[Objective] The ORIGAMI study is an ongoing 5-year observational study to evaluate effectiveness and safety of subcutaneous abatacept (ABTsc) in rheumatoid arthritis (RA) patients. Here, we report the interim results at 3-year. [Methods] Biologic-naïve RA patients with moderate disease activity (SDAI: >11 and ≦26) and inadequate response to at least one conventional synthetic DMARDs (csDMARDs) were enrolled from May 2016 to October 2018 at 64 sites. The retention rates were calculated using the Kaplan-Meier method. For effectiveness, changes in SDAI, DAS28-CRP and J-HAQ were evaluated. For safety, adverse events (AE) by system organ class were summarized. Data extracted from IORRA registry, were used as control. [Results] Of 298 patients for a safety group, 116 patients had been treated with ABTsc for 3 years. The retention rate was 45%. The change from baseline in SDAI, DAS28-CRP and J-HAQ was SDAI -13.7±7.9, DAS28-CRP -1.98±1.05 and J-HAQ -0.41±0.50, respectively. The frequency of AEs showed stable or decreasing trend over time in almost all classes. The most frequent serious AEs were infections and parasitic (14 events, 4.7%) and neoplasms benign, malignant and unspecified (11 events, 3.7%). [Conclusion] The effectiveness and safety of ABTsc for up to 3 years were confirmed.

W92-2

Outcome of Abatacept Treatment over Five Years in Rheumatoid Arthritis Patients in Clinical Practice

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Conflict of interest: None

[Objective] Long-term treatment outcomes of ABT in RA patients were retrospectively investigated using the Toyohashi RA Database. [Methods] A total of 62 patients with RA treated with ABT from October 2010 to August 2017 were included. Baseline patient characteristics, disease activity time-course, MTX and PSL concomitant rates, continuation rates of ABT, and reasons for ABT discontinuation were investigated. [Results] Mean age was 69.3 years old, females were 77.4%, RA duration was 16.7 years, and concomitant rate of lung disease was 67.7%. Mean SDAI was significantly decreased as follows: 21.5 at baseline, 8.0 at 1 year, and 7.8 at 5 years. Mean MMP-3 (ng/ml) was also significantly decreased as follows: 248.8 at baseline, 95.9 at 1 year, and 98.7 at 5 years. Concomitant rates of PSL were decreased from 60.0% at baseline to 12.9% at 5 years, and MTX were decreased from 47.3% at baseline to 12.9% at 5 years. Continuation rates of ABT were 80.7% at 1 year and 52.0% at 5 years. ABT was discontinued in 15 cases due to adverse events, 8 cases due to the lack of efficacy and 5 cases due to other reasons. [Conclusions] Outcome of long-term ABT treatment in RA patients which included older patients and patients complicated with lung disease was acceptable. Concomitant drugs were tapered.

W92-3

Retention ratio and efficacy of abatacept with or without MTX in patients with RA

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Conflict of interest: None

[Objective] We investigated real-world data with and without methotolexate (MTX) in patients with rheumatoid arthritis (RA) started abatacept (ABT). [Methods] 149 RA patients who started ABT and followed more than one year were included. They were divided into a group of 68 patients without MTX (non-MTX group) and a group of 81 patients with MTX (MTX-used group). [Results] The non-MTX group was longer disease duration, older, decreased renal function and higher rete and dose of steroid than MTX-used group. No significant difference was observed between the two groups in the retention rate at 52 weeks (63.2% vs 63.0%, p=0.778). DAS28-CRP was changed 4.7/3.9/3.5/3.1/2.8/2.4 in non-MTX group and 4.4/3.4/2.9/2.4/2.3/2.2 in MTX-used group, CDAI was changed 23.6/18.2/14.6/12.2/10.8/7.8 in non-MTX group and 22.3/14.5/11.2/8.1/7.3/6.7 in MTX-used group at 0/4/12/24/36/52 weeks. Moreover, the level of MMP-3 was changed 314.2/228.1/199.0/167.6/159.5/136.8 in non-MTX group and 215.1/152.0/90.9/73.6/75.3/75.9 in MTX-used group. [Conclusions] The retention ratio of ABT with and without MTX was almost same. However, it is possible that the suppression of synovitis might be insufficient without MTX.

W92-4

Efficacy of Abatacept (ABT) in rheumatoid factor (RF)/anti-cyclic citrullinated peptide antibody (ACPA)-positive rheumatoid arthritis (RA) patients using the NinJa database

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Conflict of interest: None

[Objective] ABT has been reported to have a high efficacy and retention rate in patients with RF/ACPA-positive RA. In this study, we examine the relationship between the efficacy of ABT and RF/ACPA, as well as other factors using the NinJa database. [Methods] Among RA patients registered in the NinJa database, 230 patients newly injected with ABT between 2013 and 2019 were included. From these database, serologic factors such as RF and ACPA, disease duration, and whether Bio was used or not were extracted. DAS28 response, ACR improvement rate and the retention rate were evaluated. [Results] The ACR70 improvement rate was significantly higher in RF-positive patients than in RF-negative patients (14.7% vs. 0%, P=0.0055), and it was also significantly higher in RF/ACPA-positive patients than in RF/ACPA-negative patients (15.1% vs. 0%, P=0.0283). Retention rates tended to be higher in RF/ACPA-positive patients than in RF/ACPA-negative patients (median 5 years vs. 2 years, P=0.235). Patients with disease duration of less than 2 years had a significantly higher ACR70 improvement rate than those with disease duration of more than 2 years (42.9% vs. 10.6%, P=0.0358). [Conclusions] ABT was suggested more effective in patients with RF/ACPA-positive early RA.

W92-5

Therapeutic Effects of Abatacept on PRO in Rheumatoid Arthritis - Evaluation at 1 Year Using RAPID3 -

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Conflict of interest: Yes

[Objective] To evaluate the effect of abatacept (ABT) on patient-reported outcomes (PROs) in patients with rheumatoid arthritis treated with ABT at our hospital. [Methods] Ninety-one patients (males: 13, females: 78) who started ABT treatment at our hospital and continued for at least 1 month were included. PRO was evaluated using RAPID3 at baseline, 2 weeks, 1, 2, 3, 6 months, and 1 year. [Results] RAPID3 decreased significantly ($p<0.01$ at 2 weeks, $p<0.001$ at 1, 2, 3, 6 month and 1 year, respectively) from 2 weeks onward, averaging 13.66 at baseline, 12.18 at 2 week, 11.08 at 1 month, 10.15 at 3 months, 9.45 at 6 months, and 9.20 at 1 year. RAPID3 remission rates were 7% at baseline, 19% at 3 months, 21% at 6 months, and 23% at 1 year. Low disease activity was 21% at baseline, 27% at 3 months, 38% at 6 months, and 46% at 1 year. Meaningful improvement ($\geqq 3.8$) in RAPID3 was 19% at 2 weeks, 31% at 1 month, 33% at 3 months, 43% at 6 months, and 43% at 1 year. [Conclusions] ABT is expected to improve and sustain improvement in PRO from the early stage of treatment.

W92-6

Predictors of achievement of PD remission on ultrasonography in patients with rheumatoid arthritis treated with Abatacept therapy

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Conflict of interest: Yes

[Objectives] To evaluate the clinical efficacy of Abatacept (ABT) therapy patients with rheumatoid arthritis (RA) using ultrasonography (US). [Methods] We used ABT treated 53 RA patients. We evaluated the improvement of gray scale (GS) and power doppler (PD) score from baseline to week 52. [Results] The mean age and disease duration were 70.5±12.5 and 13.7±13.4 years, and RA disease activity was DAS28-ESR, 5.14±0.97. Comparison of baseline factors for patients who achieved PD remission or not at 52 weeks showed that the DAS28-ESR (4.64 vs 5.38, p=0.017), CDAI (16.5 vs 23.5, p=0.003), MMP3 (139 vs 317, p=0.003), total GS (13.4 vs 26.9, $p<0.001$), PD score (8.1 vs 17.7, $p<0.001$), and PD remission (8.1 vs 17.7, $p<0.001$) were significant in the remission cases, total GS (13.4 vs 26.9, $p<0.001$), and PD score (8.1 vs 17.7, $p<0.001$) were significantly lower, and the improvement rate of US findings from start to 12 weeks was higher in the remission group (ΔGS: -41.7% vs -12.1%, p=0.003, ΔPD: -54.5% vs -14.4%, p=0.007). [Conclusion] Patients with high baseline disease activity and multiple inflammatory findings on US were less likely to achieve PD remission, suggesting that the improvement in echo findings up to 12 weeks after the start of ABT may predict the achievement of PD remission.

W93-1

Fragility Fracture Incidence in RA Patients undergoing Total Knee Arthroplasty: Challenges of Total Knee Arthroplasty in Elderly Care

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Conflict of interest: None

[Objective] We investigated the incidence of fragility fracture after total knee arthroplasty (TKA). [Methods] From 2009 to 2022, 1973 knees in 1485 patients who underwent primary TKA were included. The survival rate of joint prosthesis with revision surgery, the infection rate, and the incidence of limb/pelvic fractures requiring surgery (fracture) were compared between RA and non-RA patients by the Kaplan-Meier method and the COX proportional hazards model (adjusted for age, gender and BMI). [Results] Mean age 73 y.o., 80% female, total follow-up 6300 person-years (PY), 367 RA knees, 1606 non-RA knees. In RA patients, TKA decreased (2009-12: 26%, 20-22: 11%) and the age at surgery increased (2009-12: 66 y.o., 20-22: 71 y.o.) over time. Fracture occurred in 70 cases (3.6%), and the mean age with fracture was 80 y.o.. The incidence rate of fracture was 12.8% at 10 years, and 3% at 5 years and 11% at 10 years in group: under 70 y.o. (6.8/1000 PY), 14% at 5 years and 40% at 10 years in group: over 80 y.o. (23.9/1000 PY). RA was a significant risk factor for infection (HR: 2.4) but not for revision surgery and fracture. [Conclusions] We speculated that falls due to bone fragility and gait impairment were risk factors for the increased incidence of fracture in RA patients over 80 y.o..

W93-2

Are the incident rate and the healing process of surgical site infection and delayed wound healing after orthopaedic surgery for rheumatoid arthritis affected by the use of b/tsDMARD?

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Conflict of interest: None

[Objective] To investigate the clinical course of surgical site infection (SSI) and delayed wound healing (DWH) after orthopaedic surgery in patients with rheumatoid arthritis (RA) and to assess the impact of b/tsDMARD use for the outcome of SSI/DWH. [Methods] We retrospectively reviewed the medical records of 1,003 cases who underwent orthopaedic surgeries in our hospital between 2013 and 2021. The mean postoperative observation period was 40.1 months. We investigated the outcome of the treatment of SSI/DWH and discontinuation period and timing of resume of b/tsDMARDs. [Results] SSI and DWH were observed in 20 cases (2.0%) and 29 cases (2.9%), respectively. The mean duration required for the treatment of SSI and DWH was 56.3 days and 77.2 days respectively. The b/tsDMARD was used in 3 patients (15.0%) in the SSI group and in 13 patients (44.8%) in the DWH group. The b/tsDMARD had been resumed before wound healing in 27 cases (93.1%) of the DWH group, without the flare of RA. All cases achieved the cure of SSI/DWH, and there was no significant difference in the duration required for SSI/DWH treatment between patients with and without b/tsDAMRD. [Conclusions] The use of b/tsDMARD did not affect the outcome of SSI and DWH, with proper discontinuation and appropriate timing of resume.

W93-3

Blood management following total hip arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To identify demographic and clinical risk factors associated with receiving a blood transfusion following total hip arthroplasty (THA) among patients with RA. [Methods] A retrospective study included 13 patients with 15 hips who underwent THA via a direct anterior approach in our institute. The study analyzed the blood transfusion after THA, patients demographic data and surgical factors. [Results] average bleeding volume was 311 g and operative time was 85 minutes. One patient received a blood transfusion (7%) who had past history of hepatomma. No serious complication occured includins DVT and infection. [Conclusions] Specific risk factor for the receipt of blood transfusions among RA patients who have undergone THA was not identified.

W93-4

Thoracolumbar spinal fusion surgeries in patients with rheumatoid arthritis; Trends in the last two decades

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Conflict of interest: None

[Objective] The purpose of the current study was to clarify the changes in demographic and surgical characteristics of patients with rheumatoid arthritis (RA) who undergo thoracolumbar spinal fusion surgery. [Methods] We included 156 patients with RA who underwent thoracolumbar spinal fusion surgery from 2001 to 2020. We compared the clinical characteristics of the early group (2001-2010, 50 patients) and the late group (2011-2020, 106 patients). We collected clinical data including medication type, blood test results, and surgical characteristics. [Results] In the late group, preoperative Hb and Alb levels and the number of patients treated with biological DMARDs were significantly higher than in the early group. The gender distribution and preoperative C-reactive protein levels of the two groups were similar. In the late group, the number of fixed vertebral bodies was higher; estimated blood loss and operative time per fixed vertebral body were significantly lower. The number of transforaminal lumbar interbody fusion procedures was higher in the late group. [Conclusions] Along with the improvement in the general condition of patients and surgical procedures, over time thoracolumbar spinal fusion surgery has become safer and has offered better quality of life for patients with RA.

W93-5

21 cases of rheumatoid arthritis patients undergoing orthopedic surgery while receiving JAK inhibitors

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Conflict of interest: None

[Objective] To report the results of orthopedic surgery performed on patients with rheumatoid arthritis (RA) during treatment with JAK inhibitors. [Methods] 21 patients (20 female) underwent orthopedic surgery while receiving JAK inhibitors. Patient background (mean disease duration, methotrexate (MTX) and prednisolone (PSL) dosage and administration rate, preoperative DAS28-CRP, delayed wound healing, surgical site infection (SSI), and flare ups) was investigated. [Results] The mean age of the patients was 69 years, the mean disease duration was 20 years, the MTX administration rate was 43%, the mean MTX dose was 6.4 mg/week, the PSL administration rate was 33%, and the mean dose was 4.2 mg/day. The mean preoperative DAS28-CRP was 2.69. The major surgeries performed were total knee arthroplasty in 6 patients, toe arthroplasty in 5 patients, hand arthroplasty in 3 patients, wrist arthroplasty in 2 patients. 3 patients had delayed wound healing, all of them after foot arthroplasty. One patient had postoperative infection, and one patient had flare-up. [Conclusions] Surgery was performed while JAK inhibitors were discontinued, and wound healing was delayed and SSI was observed.

W93-6

Identification of risk factor for postoperative delirium in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] We tried to identify the risk factor for postoperative delirium in all patients and rheumatoid arthritis (RA) patients. [Methods] We evaluated 239 patients' data who was performed orthopaedic surgery in 2019 (Rheumatoid arthritis (RA: 72). We evaluated weight, height, sex, duration of operation, duration of anesthesia, type of anesthesia, type of surgery, blood albumin, diabetes mellitus, hyper tension, heart disease, brain disease, psychiatric disorder, dementia, history of delirium, post operative nausea, drain, use of hypnotic, duration and of recumbency. [Results] Twenty five patients affect postoperative delirium, 5 patients was RA and 20 patients were others. There were no statistical differences of rate of postoperative delirium between RA patients and others. Higher age, higher height, history of brain disease, history of delirium, use of hypnotic, and lower blood albumin increased postoperative delirium in all patients. Use of drain, longer duration of recumbency, and use of hypnotic increased postoperative delirium in RA patients. [Conclusions] Our findings showed that there are several risk factors for postoperative delirium. Especially, there are RA patients specific risk factors for postoperative delirium.

W94-1

The incidence and risk factors for newly developing interstitial lung diseases in RA

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Conflict of interest: None

Purpose: To determine the incidence and risk factors of newly developing interstitial lung disease (ILD) in patients with rheumatoid arthritis based on a cohort observational study. Methods: Cohort observational study. Participants were 499 consecutive RA patients who visited our hospital in Apr 2010. We analyzed patients without ILD at the entry of the study. Clinical information, including the presence and development of ILD, was obtained through referring medical records. Kaplan-Meier method and the log-rank test were used to determine the cumulative incidence rate and risk factors. Results: We analyzed 422 RA patients with102 men/320 women, mean age 58.5 years, and 127 (38%) smoking history. Biologics, MTX, and PSL were used in 155 (37%), 251 (62%), and 229 (54%) patients. The cumulative incidence rate at 10 years was 9%. Females and the elevation of CRP level (>1.0 mg/dl) were identified as risk factors for newly developing ILD, but not smoking history. Moreover, MTX suppressed the development of ILD, whereas biologics and PSL failed. Conclusions: The cumulative incidence rate for newly developing ILD at 10 years was approximately 10%. CRP elevation was a risk factor, and MTX usage was a protective factor for new ILD. To prevent the development of ILD, RA control is critical.

W94-2

Analysis of sequential blood corpuscle change on IP acute exacerbation and MTX pneumonia in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Identifying factors reflecting the pathologic difference and the factor which can become useful for differentiation. [Methods] We intended for 44 cases that IP-AE (31) and MTX-IP (13) were diagnosed by among RA patients who presented acute pulmonary disorder from 2009~2022, and became this course hospitalization in total. We analyzed it about at the time of the patient backgrounds and hospitalization of both at admission or prehospital blood test views. [Results] IP-AE was older than MTX-IP, but other difference was not seen in the backgrounds including sex and treatment regimens. Hospitalization WBC count had no difference in both groups, but hospitalization had many lymphopenia examples in IP-AE group (IP-AE: 81% vs MTX-IP: 38%; $p<0.01$). And the number of the lymphocytes was low value in IP-AE group (average value; IP-AE: 1079±616 vs MTX-IP: 2156±1562 /μL; $p<0.01$). In addition, the number of the lymphocytes decreased in IP-AE group at hospitalization in comparison with just before the hospitalization when we compared the number of just before hospitalization and the lymphocytes at admission each in both groups. [Conclusions] There was lymphopenia at the time of hospitalization in IP-AE. It may suggest the pathologic difference of some kind of both, and may become useful for differentiation.

W94-3

Factors affecting worsening of pre-existing interstitial lung disease in RA: biologics suppressed the worsening of ILD

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Conflict of interest: None

[Objective] To determine the incidence and risk/ protective factors for worsening interstitial lung disease (ILD) in rheumatoid arthritis (RA) based on a cohort observational study. [Methods] Participants were 499 consecutive RA patients who visited our hospital in Apr 2010. We analyzed patients with ILD at the entry of the study. Clinical information was obtained through referring medical records, including the presence and worsening of ILD. Kaplan-Meier method and the log-rank test were used to determine the cumulative incidence rate and risk/protective factors. [Results] We analyzed 77 RA patients, 32 men and 45 women, mean age of 66.9 years, 36 MTX use, and 57 glucocorticoids (GC) use. Biologics were administered in 28 at the entry of the study and 43 in the total observation period. The cumulative incidence rate of worsening ILD at 10 years was 48%. The elevation of CRP level (>1.0 mg/dl) was identified as a risk factor for the worsening ILD but not age and sex. Moreover, biologics suppressed the worsening of ILD and the development of acute exacerbation of ILD. MTX and GC failed to suppress the deterioration of ILD but did not promote it [Conclusions] RA activity may contribute to the worsening of ILD. Biologics could suppress the deterioration of ILD.

W94-4

Comparison of changes of the levels interstitial pneumonia markers and of CT scores between under the treatment of bDMARDs and JAK inhibitors in the patients with RA-ILD

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Conflict of interest: None

Object: To clarify the effects of JAK inhibitors (JAKi) to the pulmonary lesions of RA, we compared the changes of the levels of ILD markers and CT scores at the time under the treatment of bDMARDs (Bio group) to that of JAKi (JAKi group) in the same patients group. Methods: 79 patients used Bio before JAKi. 29 patients (36.7%) had the interstitial lung disease (ILD) with RA. The changes of the levels of ILD markers were compared Bio group to JAKi group. While 32 patients underwent CT scans before and during the treatment of Bio and that of JAKi. We compare the changes of amount of CT scores Bio group and JAKi group. Result: Comparing the changes of the levels of ILD markers, they were no difference between Bio group and JAKi group. 32 cases were performed CT before and during the treatment of Bio and JAKi, 22 cases (68.8%) had ILD. Compared the changes of the amount of CT scores, the reticular pattern was 0.91 in Bio group and 0.15 in JAKi group. The honeycomb was 0.90, 0.56, respectively. The changes of amount of CT scores were smaller in JAKi group than in Bio group. Conclusion: Jaki might have little effect to the ILD of RA.

W94-5

Investigation of changes in pulmonary lesions and disease activity after administration of JAK inhibitors in rheumatoid arthritis

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Conflict of interest: None

[Objective] In the treatment of rheumatoid arthritis (RA), pulmonary complications often interfere with treatment. We investigated changes in pulmonary lesions and disease activity in RA patients treated by JAK inhibitors (JAKi). [Methods] A total of 49 RA patients who received JAKi from August 2015 to July 2022 were followed up at the first visit, JAKi initiation, 0.5, 1, 1.5, 2, 2.5, 3 years, evaluated pulmonary lesions on CT scan and compared them with disease activity. [Results] At JAKi initiation, mean age 62.3, female 75.5%, 7 past smokers, 12 current smokers. CT showed a total of 20 pulmonary lesions at the first visit. Among them, 7 were IP, 3 each were emphysema, NTM and bronchiectasis, and 1 each was GGO, rheumatoid nodule, pleural effusion and infiltrate. DAS28CRP at the first visit was 4.59. 1 year after the start of JAKi, DAS28CRP significant improved to 2.58. Pulmonary lesions improved in 3 cases of IP, but

new onset of NTM was noted in 5 cases, all of which subsequently deteriorated. There was also 1 each of lung cancer, LPD and PCP. All new onset of pulmonary lesions occurred with in 1 year of JAKi administration. [Conclusions] We should pay close attenuation to new onset and exacerbation of NTM for at least 1 year after administration of JAKi.

W94-6

Efficacy and Safety of Nintedanib in Interstitial Lung Disease Associated with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Although the efficacy and safety of nintedanib have been demonstrated for SSc-ILD, information of the efficacy and safety for RA-ILD is limited. In this study, we compared the efficacy and safety of nintedanib in RA-ILD with those in CTD-ILD, including SSc-ILD. [Methods] Ten patients who visited our department and received nintedanib were divided into two groups: RA group and non-RA group. Pulmonary function tests at the time of nintedanib administration, those at 6 months after nintedanib administration, and adverse events were compared between the two groups. [Results] Among the RA and non-RA group, at the time of nintedanib administration, FVC (ml) was 1977±867 and 1748±534, %FVC (%) was 66.9±20.7 and 55.6±11.0, and %DLco (%) was 54.8±8.9 and 46.2±15.9 (P=0.67, 0,52, and 0.51 respectively). After 6 months of nintedanib treatment, ΔFVC was -18.3±113.4 and -42.5±78.0, Δ%FVC was 0.75±5.03 and -2.8%±1.89, and Δ%DLco was 0.375±4.02 and -7.27±6.54 (P=0.83, 0.20, and 0.28 respectively). In the both groups, the incidence of adverse events was 50% and the continuation rate was 100%, respectively. [Conclusions] In the RA group, nintedanib tended to reduce the decline in pulmonary function tests. Treatment with nintedanib could be safely continued in both groups.

W95-1

Clinical courses of cases using inhaled corticosteroid therapy for the management of bronchiectasis with rheumatoid arthritis

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Conflict of interest: None

[Objective] We investigated the effectiveness of inhaled corticosteroid (ICS) therapy for the management of bronchiectasis (BE) with rheumatoid arthritis (RA). [Methods] From April 2013 to October 2022, patients with RA and BE was extracted from medical records in our hospital. Then we divided the group into ICS group and non-ICS group. Each clinical course was analyzed retrospectively. [Results] Twenty patients were enrolled. Median duration of RA was 12 years and BE was 4 years. Median titer of anti-CCP antibody was 106 U/mL. ICS was introduced in 11 patients (55%), and there was no statistically significant difference in backgrounds between the two groups. After 55 weeks from the introduction of ICS, the median increase ratio of the forced expiratory volume in 1 second % (FEV1.0%) to the previous value was 1.04 in the ICS group, which tended to improve compared to the non-ICS group (0.99), but there was no significant difference ($P = 0.12$). The median cumulative number of re-admissions for exacerbations of BE was significantly higher in the ICS group (ICS: 3, non-ICS: 0, $P < 0.05$). However, mortality was no significant difference between the two groups. [Conclusion] In RA-BE treatment, ICS may tend to improve FEV1.0% in the long-term clinical course.

W95-2

Mechanism of plaque formation by pericoronary fat in rheumatoid arthritis

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Conflict of interest: None

[Objective] Ischemic heart disease is a prognostic factor in rheumatoid arthritis. In recent years, the mechanism of plaque formation by cytokines derived from pericoronary adipose tissue (PCAT) has been clarified, and the perivascular fat attenuation index (FAI) in coronary artery CT has attracted attention as a marker for predicting cardiac events. The purpose of this study was to clarify the mechanism of plaque formation by PCAT in rheumatoid arthritis. [Methods] PCAT analysis was performed on rheumatoid arthritis patients who underwent coronary CT from April 2016 to April 2022 at Showa University Hospital. Additionally, in SKG mice on days 7, 14, and 28 after induction of arthritis, histological evaluation of joint synovium, thoracic aorta, and periaortic fat, bulkRNA-seq, and μCT bone analysis were serially evaluated. [Results and Conclusions] FAI was associated with the degree of plaque stenosis, and a positive correlation was observed with the calcification score. In arthritis model mice, temporal changes in synovial inflammation, bone destruction, perivascular fat, and thoracic aorta during the exacerbation of arthritis were revealed. Furthermore, we identified a perivascular fat plaque-forming factor in arthritis.

W95-3

Diagnosis and treatment of musculoskeletal tumor and tumor-like lesion in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA), rheumatoid nodules, ganglion, and synovitis are similar to neoplastic lesions, and it is often difficult to differentiate them from tumors. We investigated the diagnosis and treatment of RA and neoplastic lesions in our hospital. [Methods] Patients with RA having musculoskeletal tumor-like lesion who visited our department between January 2013 and April 2021 were included. Basic information (sex, age), RA-related information (duration, disease activity, treatment) of 30 patients with RA-related lesions (13 with a history of RA, 17 with newly diagnosed RA) and 18 patients with RA with bone and soft tissue tumors were collected. contents), and neoplastic lesions. [Results] The RA-related lesions were 2 rheumatoid nodules, 3 ganglions, and 25 synovitis, and the tumors were 8 benign, 2 intermediate malignant, and 8 malignant. Twenty-three patients (48%) required pathologic diagnosis by biopsy. Multivariate analysis for diagnosing bone and soft tissue tumors was more likely in patients with extra-articular disease. [Conclusions] In our department, 36% were diagnosed as bone and soft tissue tumors, and 38% were diagnosed as new RA. Extra-articular lesions were likely tumors, and a definitive diagnosis required pathologic diagnosis.

W95-4

Impact of ACPA on bone mineral density change in rheumatoid arthritis patients with osteoporosis treated with denosumab

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Conflict of interest: None

[Objectives] We examined that the impact of ACPA on BMD change in 131 RA patients with osteoporosis treated with denosumab (DENO). [Methods] One hundred one patients were ACPA positive (ACPA+ group) and 30 patients were ACPA negative (ACPA- group). We evaluated BMD at 0, 12 months after DENO treatment. DXA were performed at the lumbar spine (LS), at proximal femoral (PF) and at femoral neck (FN). [Results] There were no differences in baseline BMD at LS (0.77 vs 0.77 g/cm^2, p=0.7), at PF (0.58 vs 0.61 g/cm^2, p=0.13) and at FN (0.48 vs 0.47 g/cm^2, p=0.68) between groups. Improvement ratio of BMD in ACPA+ group and ACPA- group were 6.1% (0 vs 12 months; p<0.01), 5.8% (p<0.01) at LS, 3.6% (p<0.01), 2.3% (p=0.01) at PF and, -0.18% (p<0.49), 3.7% (p<0.01) at FN. Though, there were no differences in improvement ratio of BMD at LS (p=0.86) and PF (p=0.72) between groups, improvement ratio of BMD at FN was significantly lower in ACPA+ group than ACPA- group (p=0.03). Multivariate linear regression analysis revealed that ACPA positive (β=-0.2, p=0.04) and low BMD at FN in baseline (β=-0.35, p<0.01) inhibited the improvement of BMD at FN. [Conclusions] Though, DENO improved BMD at LS and PF independently regardless of ACPA in RA patients, RA patients with ACPA positive were difficult to improve BMD at FN.

W95-5

Characteristics of patients with carpal tunnel syndrome at the onset of rheumatoid arthritis

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Conflict of interest: None

[Objective] This study aims to determine the clinical characteristics of patients with carpal tunnel syndrome (CTS) at the onset of rheumatoid arthritis (RA). [Methods] We retrospectively analyzed 236 patients with newly diagnosed RA at a single institution between 2012 and 2021. Patient demographic and laboratory data, 2010 ACR/EULAR classification criteria, and days to RA diagnosis were compared for RA patients with CTS at initial diagnosis (RA with CTS) and those without CTS. [Results] 12 patients (5.1%) had CTS, and 4 (1.7%) were referred as CTS. RA with CTS cohort were older (75 [66-78 years]/64 [54-73], p=.019), predominantly female (100%/65.2%, p=.010), and having lower ACR/EULAR scores (5 [4-6]/7 [6-8], p<.001), shown as median [IQR], p-value, respectively. The level of Anti-CCP antibody and C-reactive protein was low, and it took a long time to be diagnosed with RA. In all CTS patients, ultrasonography (US) showed power doppler positive tendon sheath synovitis in the carpal tunnel, which is not usually seen in idiopathic CTS. [Conclusions] RA with CTS is relatively rare, however is more common in elderly women, and there are many seronegative cases or cases which do not fulfill the RA classification criteria, it is difficult to diagnose of RA. US is useful for diagnosis.

W95-6

A case of methotrexate-associated lymphoproliferative disorders arising in the thoracic spine resulting in paralysis of both lower limbs, and remission after treatment with tocilizumab

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Conflict of interest: None

The patient is a 40-year-old woman who developed rheumatoid arthritis (RA) 23 years ago and had been taking methotrexate (MTX) for 13 years, her MTX dosage was 14 mg/week and her RA was well controlled. MRI showed tumor lesions in the thoracic spine, and he was referred to our hospital. Sensation was lost except in the perianal area, and muscular contractions of both lower limbs, including the anal sphincter, were not observed. An emergency Th11-12 laminectomy was performed to resect and decompress the tumor as much as possible. Pathology revealed CD20-positive diffuse large B-cell lymphoma (DLBCL). Based on the course of the disease, a diagnosis of MTX-associated lymphoproliferative disease (MTX-LPD) was made. MTX was discontinued postoperatively, but tumor growth was observed one month after surgery, and chemotherapy (R-CHOP) was added. After completion of chemotherapy, RA flare-up was observed and tocilizumab was started. Three years have passed since surgery, and the lymphoma has not relapsed and RA is in remission. MTX-LPD can rarely occur near the spinal cord, and tocilizumab is an effective treatment option for RA flare-up after MTX withdrawal in MTX-LPD.

W96-1

Ncx-deficient intestinal neuronal dysplasia attenuates arthritis severity in mice

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Conflict of interest: None

[Objective] To clarify the relationship between the intestinal nervous system and autoimmune arthritis. [Methods] We used Ncx-deficient (KO) mice, which have alterations in the composition of the microbial flora caused by overproduction of nitric oxide due to intestinal neuronal dysplasia, and SKG mice, which is Th17-dependent arthritis model mice. All mice were bred under super-pathogen-free conditions and arthritis was induced with mannan. Arthritis was evaluated by joint swelling scores and histopathologic analysis. [Results] At first, SKG mouse-derived CD4 T cells were adoptively transferred into wild-type (WT) and Ncx-KO mice, respectively, followed by inductions of arthritis. Ncx-KO mice transferred with SKG-CD4 T cells had lower joint swelling scores than Ncx-WT ones. Next, Ncx-KO mice and SKG mice were mated to generate SKG/Ncx-KO mice. Severity of mannan-induced arthritis in SKG/Ncx-KO mice, compared with SKG/Ncx-WT, was attenuated in joint swelling scores and histopathologic analysis. [Conclusions] Ncx-deficient intestinal neuronal dysplasia decreased arthritis severity. It was suggested that the enteric nervous system may influence the pathogenesis of inflammatory arthritis via altered microbial flora in intestine.

W96-2

Anti-inflammatory effects of novel NF-kB inhibitory compounds identified by high-throughput screening in two inflammatory animal models

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Conflict of interest: None

[Objective] We investigated the physiological effect of a novel NF-kB inhibitory compound, 1*H*-pyrazolo. [3,4 *d*] pyrimidin-4-amine derivative (INH #1), which we identified by cell-based high-throughput screening, on two inflammatory animal models. [Methods] LPS-induced TNFα was measured after pre-treatment of INH #1 in C57BL/6J mice. Collagen-induced arthritis (CIA) was induced in DBA/1J mice by immunizing with type II collagen (CII) emulsified in Freund's adjuvant. Arthritis scores assessment and INH #1 administration were conducted daily. Histopathology of ankle joints, anti-CII antibodies in serum, CII-induced IFN-γ production and proliferation by splenocytes were analyzed at the end of the experiments. [Results] INH #1 showed inhibition of LPS- induced TNFα production. In CIA, INH #1 significantly reduced arthritis scores and joint inflammation. Additionally, IFN-γ production and cell proliferation were

attenuated in the treated mice. The titers of anti-CII IgG antibodies were comparable regardless of the treatment. [Conclusions] Here, we revealed that 1*H*-pyrazolo [3,4 *d*] pyrimidin-4-amine exerted anti-inflammatory effects in vivo via suppressing TNFαproduction and adaptive cellular immune responses. Our novel compound would be a candidate for novel NF-κB inhibitory compounds.

W96-3

Dantrolene improves arthritic score and production of pathologic autoantibodies in collagen-induced arthritis mice

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Conflict of interest: None

[Object] We investigated the effect of dantrolene, a stabilizer of the ryanodine receptor, on collagen-induced arthritis (CIA) in mice. [Methods] CIA mice were treated with oral administration of dantrolene (100 mg/kg/day). Arthritic scores, serum levels of anti-type II collagen (CII) IgG, and histopathological findings were assessed on day 63. [Results] Dantrolene resulted in significantly lower arthritic scores than those in the control mice. Serum levels of anti-CII IgG were positively correlated with the arthritic scores ($r = 0.704$, $p < 0.01$). In addition, the serum levels of anti-CII IgG were significantly lower in the dantrolene group than those in the control group ($p < 0.05$). [Conclusions] These results suggest that oral administration of dantrolene to CIA mice inhibits the production of serum anti-CII IgG and consequently prevents arthritis.

W96-4

N-glycan in the monoclonal ACPA, CCP-Ab1 variable region promotes the exacerbation of experimental arthritis

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Conflict of interest: None

[Objective] The variable region of most ACPA IgG molecules in the serum of RA patients carries *N*-glycan (N-glycan^{V}). To analyze the pathogenicity of N-glycan^{V} of ACPA, we analyzed the pathogenicity of a monoclonal ACPA, CCP-Ab1, with or without N-glycan^{V} (CCP-Ab1 N-rev). [Methods] CCP-Ab1 N-rev was generated and antigen binding, the effect on *in vitro* differentiation of osteoclasts from bone marrow mononuclear cells of autoimmune arthritis-prone SKG mice, and the *in vivo* effect in SKG mice were evaluated in comparison to glycosylated CCP-Ab1. [Results] Amino acid residues in citrullinated peptide (cfc-1), which are essential for binding to CCP-Ab1 N-rev and CCP-Ab1, were almost identical. The size of TRAP+ cells was larger and osteoclast bone resorption capacity was enhanced in the presence of CCP-Ab1, but not CCP-Ab1 N-rev. This enhancing activity required the sialic acid of the *N*-glycan and Fc region of CCP-Ab1. CCP-Ab1, but not CCP-Ab1 N-rev, induced the exacerbation of arthritis in the SKG mise. [Conclusions] These data showed that *N*-glycan^{V} was required for promoting osteoclast differentiation and bone resorption activity in both *in vitro* and *in vivo* assays. The present study demonstrated the important role of *N*-glycan^{V} in the exacerbation of experimental arthritis by ACPAs.

W96-5

Possible involvement of GM-CSF producing Bhlhe40+ CD4+ T cell in inflammatory pathologies in IL-1 Receptor antagonist knockout mice

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Conflict of interest: None

[Objective] Interleukin-1 receptor antagonist knockout mice (IL-1Ra KO) spontaneously develop aortitis, arthritis and skin rashes in which T cells are involved. In this study, we aimed to identify pathogenic T cell subsets in IL-1Ra KO mice. [Methods] The proportion of T cell subsets in splenocytes from IL-1Ra KO and BALB/c mice (WT), and the production of GM-CSF by splenic CD4+ T cells stimulated with PMA/ionomycin were analyzed by FACS. The comprehensive gene expression of splenic CD4+ T cells and identification of the cells infiltrated into the inflammatory sites were carried out by RNA-seq and Immunohistochemical analysis, respectively. [Results] The proportion of effector memory CD4+ T cells in splenic lymphocytes was significantly increased in IL-1Ra KO compared to WT. As a result of RNA-seq, the expression levels of *Csf2* and *Bhlhe40* in splenic effector memory CD4+ T cells from IL-1Ra KO were higher than WT. Moreover, GM-CSF production by splenic Bhlhe40+ CD4+ T cells was elevated in IL-1Ra KO as compared to WT. In addition, Bhlhe40+ CD4+ T cells were infiltrated into inflammatory sites of IL-1Ra KO. [Conclusions] Our data suggest that GM-CSF producing Bhlhe40+ CD4+ T cells are involved in the pathogenesis of inflammatory diseases induced by activation of IL-1 signaling pathways.

W96-6

Inflammatory arthritis, an immune-related adverse event caused by anti-PD-L1 antibodies, exacerbates joint pain via synovial fibroblast proliferation and accelerated neuronal apoptosis

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Conflict of interest: None

[Objective] Immune checkpoint inhibitors (ICI) have become an innovative treatment in cancer treatment, but there is a problem of decreased QOL due to inflammatory arthritis (ICI-IA), an immune-related adverse event. The effects of anti-PD-L1 antibodies on arthritis are largely unknown. Therefore, we will clarify the effect of anti-PD-L1 antibody on arthritis mainly on synovial fibroblasts. [Methods] Anti-PD-L1 antibody was administered to arthritis-induced SKG mice, and the arthritis score, μCT analysis, and von Frey test were evaluated. We also examined PD-L1 expression in rheumatoid arthritis synovial fibroblasts (RA-FLS) and mature neurons derived from human neuroblastoma SH-SY5Y, and the effects of anti-PD-L1 antibodies. [Results] Anti-PD-L1 antibody treatment reduced the pain threshold without aggravating arthritis and bone destruction in SKG mice. RA-FLS and PD-L1 expression in mature neurons were elevated by TNFα stimulation. Anti-PD-L1 antibody administration promoted RA-FLS cell proliferation and increased the percentage of Annexin V-positive apoptotic cells in mature neurons treated with RA-FLS culture supernatant. [Conclusions] Anti-PD-L1 antibody may exacerbate pain in arthritis through proliferation of synovial fibroblasts and promotion of neuronal apoptosis.

W97-1

Clinical features of patients with rheumatoid arthritis positive for human T-cell leukemia virus with increased human T-cell leukemia virus type 1 proviral loads: A retrospective cohort study

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Conflict of interest: None

[Objective] This study aimed to clarify the clinical characteristics of patients positive for HTLV-1 with RA and increased HTLV-1 PVLs. [Methods] This study included 56 participants in the Miyazaki HTLV-1-positive RA Registry. These patients were divided into two groups according to the HTLV-1PVL (copies/100 PBMCs) that increased more than twice from 2019 to 2021. The clinical characteristics were compared between groups. Furthermore, the population of HTLV-1 infected cells analyzed by flow cytometry (HAS-Flow) was compared between the two groups. [Results] The median PVL of all participants increased to 1.27, 2.21, and 2.62 during the 3-year observational periods. In 2019, the median age of the increased (n=30) and non-increased (n=20) groups was 69 and 72.5 years, respectively. The ratio of PSL users was higher in the non-increased group (36.7% and 72%, p=0.02). Conversely, the ratio of MTX users was higher in the increased group (56.7% and 26.9%, p = 0.03). The HAS-Flow analysis revealed the ratio of HTLV-1-infected cells in the increased and non-increased groups as 13% and 15.1% and the ratio of ATL-like cells as 3.35% and 3.5%, respectively. [Conclusion] The ratio of MTX usage was higher in the PVL-increased group than in the non-increased group during the short observational period.

W97-2

A Case-control study on risk factors of pneumocystis pneumonia in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] Pneumocystis pneumonia (PCP) is an opportunistic infection with a high mortality rate. However, there are no consensus criteria for prophylaxis in rheumatoid arthritis (RA) patients. Therefore, we aimed to investigate the risk factors for PCP in RA patients. [Methods] A case-control study was conducted in our center. From April 2018 to October 2022, 14 PCP cases with RA were included. As controls 743 RA patients treated with methotrexate, biologics, and JAK inhibitors seen in the last 3 months were included. Information on age, gender, PCP prophylaxis, WBC, lymphocyte, RF, ACPA, KL-6, and use of corticosteroids were taken from clinical records and risk factors for PCP were investigated. [Results] The clinical characteristics of PCP cases were: median age 72, male 28.5%, median lymphocyte 745/μl, RF/ACPA positivity 100/92.3%, KL-6 positivity 69.2%, and no patients had PCP prophylaxis. Controls were: median age 68, male 27.2%, median lymphocyte 1444/μl, RF/ACPA positivity 65.8/59.4%, KL-6 positivity 25.3%, and PCP prophylaxis administration 8.8%. PCP cases had significantly higher RF/ACPA positivity, lower lymphocyte count, and higher KL-6 positivity. [Conclusions] RF/ACPA positivity, lymphocytopenia, and KL-6 positivity were considered risk factors for PCP in our RA patients.

W97-3

A case of pyogenic hand arthritis caused by MSSA which shows symptoms resembling rheumatoid diseases in a dialysis patient with extensive bone destruction in a short term without systemic symptoms

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Conflict of interest: None

A 79-year-old man on hemodialysis due to diabetic nephropathy having history of tuberculosis developed swelling and arthralgia in his left wrist joint 2 months ago. Autoantibodies were negative and MRI showed normal. Because his symptoms were little improved with administration of both NSAIDs and steroids, he was referred to our outpatient clinic. Inflammatory reaction was mild, X-rays showed extensive bone destruction of the carpal bones rapidly. Blood culture and tuberculosis-specific T-SPOT were negative, and CT and echocardiography showed normal. Considering tuberculosis, a tissue biopsy was performed for diagnosis. Operative findings showed granulation tissue with pus filling around the metacarpal joint, and bone destruction, therefore scraping and external fixation were performed. Tissue culture test showed MSSA, but tuberculosis PCR was negative. Histopathology showed granulomatous tissue with neutrophilic infiltration. After diagnosis of pyogenic arthritis, he was treated with both antibiotics and debridement, thereafter symptoms were improved. Clinical Implications: We report a case of atypical pyogenic arthritis of the hand resembling rheumatoid diseases in a hemodialysis patient with localized extensive joint destruction in a short term without systemic symptoms.

W97-4

Fungal septic knee arthritis caused by Aspergillus fumigatus during tocilizumab therapy for rheumatoid arthritis: a case report

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Conflict of interest: None

Case presentation: A 62-year-old female with a history of RA for 19 years. Tocilizumab (TCZ) therapy was started in 2015, and disease activity was controlled with self-injection of 162 mg TCZ every 2 weeks. In July 2022, she developed pulmonary aspergillosis. During the hospitalization in the department of thoracic surgery, she developed right knee pain and was referred to our department. On examination, swelling in the right knee joint was observed. Laboratory findings were as follows: WBC 14000, CRP 7.8, RF 123, and MMP-3 131. Radiographs showed narrowing of medial femorotibial joint space without bone destruction. Aspergillus fumigatus (Af) was detected by the joint fluid culture. Arthroscopic synovectomy was performed under spinal anesthesia. Voriconazole was administered in the perioperative period, and the postoperative course was uneventful. Clinical significance: In recent years, fungal arthritis has been increasing in patients with weakened immune ability, such as patients with diabetes mellitus or oral steroids. However, it is a relatively rare disease with few reports in Japan. Most of the causative bacteria are Candida, and Af knee arthritis is extremely rare. As in this case, it may occur in rheumatoid patients due to immunosuppression of TCZ, so caution is required.

W97-5

Analysis of clinical markers useful for distinguishing between ANCA-positive infective endocarditis and ANCA-associated vasculitis

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Conflict of interest: None

[Objective] We analyzed clinical markers for distinguishing between infective endocarditis (IE) and ANCA-associated vasculitis (AAV) in ANCA-positive patients. [Methods] We assessed 8 patients with ANCA-positive IE and 65 patients with AAV (34 MPA, 31 GPA) in our hospital. Age, sex, clinical symptoms (fever, cutaneous involvements, musculoskeletal pain, peripheral neuropathy), laboratory findings (CBC, eGFR, CRP, complement levels, IgG, MPO/PR3-ANCA, antinuclear antibody, rheumatoid factor, urine examination) and imaging findings (pulmonary involvements, splenomegaly) were compared between the two groups. [Results] The positive rate of PR3-ANCA, hypocomplementemia and splenomegaly, and serum levels of IgG were significantly higher in the IE group, and the positive rate of pulmonary involvements and platelet count were significantly higher in the AAV group. Presence of ≧ 3 out of 6 items (PR3-ANCA, hypocomplementemia, splenomegaly, IgG ≧ 1571 mg/dL, no pulmonary involvements, platelet count ≦ 26.6×10^4/μL) was a useful clinical index for distinguishing between IE and AAV with a sensitivity of 100% and a specificity of 92%. [Conclusions] The use of clinical markers for distinguishing between IE and AAV allows efficient differential diagnosis.

W97-6

Vaccination rate, adverse reactions and reasons for non-vaccination of COVID-19 vaccine in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To know the vaccination rate, adverse reactions (ARs), and reasons for non-vaccination of COVID-19 vaccine (CV) in RA patients. [Methods] We investigated the vaccination rate, ARs, and reasons for non-vaccination of CV in RA patients. This study investigated up to 3rd vaccines. [Results] Patient background (n=462): Mean age 67.8 years, female 76.6%, RA duration 14.5 years, The vaccination rate was 7.6% for non-vaccination, 92.4% for the 1st dose, 92.0% for the 2nd dose, and 87.2% for the 3rd dose. A significant decrease over time was observed (p=0.02). Non-vaccination was observed in 13.9%, 7.5%, and 1.3% of those aged 0-64, 65-74, and 75 and over. Higher rate of non-vaccination was observed in younger group (p=0.01). 86.1/92.5/98.7% for the 1st dose, 86.1/91.8/98.1% for the 2nd dose, 76.6/88.4/96.8% for the 3rd dose among 0-64 yo/65-74 yo/75 yo and over. There was a statistically significant decrease in vaccination rate over time only at age 0-64 (p=0.03). ARs occurred in 9.8% in the 1st dose, 16.0% in the 2nd dose, and 16.9% in the 3rd dose. Among the reasons for non-vaccination, 23 cases were concerned about ARs to the vaccine. [Conclusions] COVID-19 vaccination rate has been steadily declining in RA patients, with a stronger trend in younger age groups.

W98-1

Characteristics of 48 patients with rheumatic diseases admitted to our hospital with COVID-19

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Conflict of interest: None

[Objective] To investigate the characteristics of patients with rheumatic and musculoskeletal diseases (RMDs) who were admitted to our hospital with COVID-19. [Methods] We extracted the patients with RMDs from the database of 3,312 patients with COVID-19 admitted to our hospital between February 1, 2020 and September 30, 2022. We obtained information on demographic characteristics, drugs (disease modifying anti-rheumatic drugs, immunosuppressive agents and biologics), COVID-19 treatment and outcome retrospectively. [Results] Forty-eight patients were identified (median age, 71 years [range 18-94], 77.1% female, BMI 21.6±4.4). The underlying diseases of the patients were rheumatoid arthritis (35.4%), systemic lupus erythematosus (18.8%), vasculitides (12.5%) and systemic sclerosis (8.3%). Twelve patients (25%) received prednisolone (PSL) and the mean PSL dosage was 5.8±4.4 mg/day. Fourteen patients (29.2%) received immunosuppressive agent, 7 (14.6%) biologics (rituximab 4, abatacept 2, infliximab 1). The patients with moderate or higher severity of COVID-19 accounted for 37.5%. Five patients (10.4%) died. [Conclusion] Our results were similar to previous reports in Japan.

W98-2

Three cases of prolonged COVID-19 pneumonia in patients with rheumatic diseases receiving rituximab

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Conflict of interest: None

[Case 1] A 66-year-old female with a history of GPA developed fever and was diagnosed with COVID-19. She was on RTX maintenance therapy. Two weeks later, she developed a fever and dyspnea. CT showed ground-grass and infiltrative opacities in both lungs. Dexamethasone (DEX) and TCZ were administered. Her pneumonia worsened until she required HFNC, but gradually improved. She was discharged on the day 46. [Case 2] A 70-year-old female with a history of MPA developed flu-like symptoms and was diagnosed with COVID-19. She was on RTX maintenance therapy for flare of MPA. Her fever resolved within a few days, but she developed a dyspnea on the day 11. DEX was started because she required oxygen and CT showed pneumonia in both lungs. Her pneumonia gradually improved and she was discharged on the day 23. [Case 3] A 75-year-old female with a history of TAFRO syndrome developed fever and diagnosed with COVID-19. She was on RTX maintenance therapy. On the 2nd day of onset, her fever subsided, but on the day 9, she developed high fever. A chest X-ray showed bilateral ground glass opacities. DEX was started. She gradually improved and was discharged on the day 24. [Clinical Significance] It should be noted that COVID-19 in patients on RTX can have a bimodal and prolonged course.

W98-3

Inpatient mortality and severity of COVID-19 in patients with or without rheumatic diseases: a monocentric observational study

Naoto Yokogawa[1], Yoshiki Nagai[1], Kei Karakida[1], Keisuke Hirobe[1], Yuki Terashima[1], Issei Takahashi[1], Tomohiro Kato[1], Eisuke Kanematsu[1], Tomoko Sano[1], Daisuke Asatori[1], Naoki Tanomogi[1], Masahiro Iida[1], Yoshitaka Ueda[1], Nanase Honda[1], Eisuke Takamasu[1], Kae Onishi[1], Yuji Miyoshi[1], Masako Utsunomiya[1], Takahiro Nunokawa[2], Kota Shimada[1]
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Conflict of interest: None

[Objective] To compare the mortality and severity of COVID-19 in patients with or without rheumatic diseases at a tertiary care hospital with the largest number of COVID-19 hospitalized patients in Japan. [Methods] From all COVID-19 patients admitted between 2/1/2020 and 9/30/2022, we matched patients with rheumatic diseases and controls using age, sex, and admission date in a 1:3 ratio. Mortality during hospitalization and the worst oxygenation status were evaluated. [Results] The total number of COVID-19 patients was 3312, with 5.4% mortality, 49.8% receiving oxygen, 5.7% receiving HFNC/NPPV, 4.9% receiving ventilator, and 1.7% receiving ECMO. After matching, 40 patients with rheumatic diseases (RMD group) and 120 patients without rheumatic diseases (non-RMD group) were extracted. Females were 75.0% in both groups. Mean age (SD) in RMD and non-RMD groups was 68.0 (18.4) and 68.0 (18.7), respectively. Mortality in RMD and non-RMD groups was 10.3% (4/39) and 0.88% (1/113), respectively (p=0.015). Oxygen administration was 40.0% and 36.7%, respectively (p=0.710). HFNC/NPPV use was 5.0% and 3.3% (p=0.640), respectively. Ventilator use and ECMO use were absent in both groups. [Conclusion] Inpatient mortality of COVID-19 was higher in patients with rheumatic diseases.

W98-4

COVID-19 pneumonia in an aged rheumatoid arthritis: A case report

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Conflict of interest: None

[Background] Rheumatoid arthritis (RA) patients are susceptible to infections because of the immune suppressive reagents and the risk of severity should also be high. Here we present a case of covid-19 pneumonia in an aged RA who couldn't be rescued because of the recurrence of ARDS. [Case] 85 years old Japanese female who has been treated RA for 30 years presented with sudden cough and fever. The current treatment was prednisolone and upadacitinib. Covid-19 test was positive and dexamethasone was initiated. Tocilizumab was also administered on day 1 and 2. In spite of the above treatment, respiratory condition got worse, and mPSL pulse therapy was performed on day 5. The high requirement of oxygen seemed to be relieved temporally, repeated exacerbation of pneumonia caused her to death on day 27. [Discussion] A Meta-Analysis re-

ports that risk of covid-19 infection in RA patients is estimated as OR 1.53, and risk of death is estimated as OR 1.74. Another report indicates that anti-covid-19 antibody titer is lower than healthy group and the close association is indicated between those reduction of antibody and the use of JAK inhibitors. A screening assessment of post-vaccine covid-19 antibody titer would be a choice for the management of infection in the future RA treatment.

W98-5

A case of rheumatoid arthritis who developed COVID-19 pneumonia while receiving tocilizumab, but was successfully treated with baricitinib

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Conflict of interest: None

A 74-year-old woman who had rheumatoid arthritis (RA) at age 36 and had been treated with MTX and TNF inhibitors, recently with tocilizumab (TCZ) and prednisolone (PSL). Interstitial pneumonia was noted, but there was no history of treatment for it. Some family member living with her had COVID-19. Subsequently, she herself developed malaise. She was admitted to our hospital with hypoxemia, SARS CoV-2 positive. Chest CT showed diffuse frosted shadows in both lungs. She was diagnosed as COVID-19 pneumonia and started on remdesivir and baricitinib (BAR) with steroid pulse therapy. Respiratory condition gradually improved, and she was discharged after BAR was completed in 14 days. TCZ was restarted after discharge, but the arthritis worsened. The arthritis became mild when she was reintroduced to BAR. She had also been vaccinated against COVID-19 and had received a third booster dose one month prior to contracting COVID-19. It has been reported that immune response to COVID-19 vaccine is weak in RA and other autoimmune diseases. The response to the vaccine in patients receiving immunosuppressive drugs such as glucocorticoids and MTX has also been reported to be weak, suggesting the need to be careful about severe illness caused by COVID-19 disease even after the booster vaccination.

W98-6

Outcome of COVID-19 infections in a single outpatient rheumatology

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Kanazawa University Hospital

Conflict of interest: None

[Objective] The use of glucocorticoids and immunosuppressive drugs has been cited as a risk factor for severe cases of COVID-19. Therefore, we investigate the characteristics of patients with rheumatic diseases who contracted COVID-19. [Methods] We conducted a retrospective survey of COVID-19-infected patients in our collagen disease outpatient clinic from January to October 2022 using electronic medical records. [Results] We identified 39 COVID-19-infected patients, with a mean age of 57.3 years, and 26% males. The number of vaccination was 3 cases with 4 times, 9 cases with 3 times, 5 cases with 2 times, 2 cases with 1 time, and 7 cases with no vaccination. The background diseases were SLE in 13 cases, RA in 9 cases, IgG4-related diseases in 6 cases, SS in 3 cases, and other diseases in 7 cases. The median dose of glucocorticoids was 5 mg (PSL equivalent), 13 patients used immunosuppressive drugs, 6 patients used biological agents, and 2 patients used JAK inhibitors. Three patients were asymptomatic, 32 had mild disease, 3 had moderate disease, and 1 had severe disease. Three patients had sequelae. [Conclusion] Few patients developed severe disease or sequelae, even with the use of glucocorticoids and immunosuppressive drugs.

W99-1

SARS-CoV-derived ORF3a and ASC splice variant lacking exon2 cooperatively enhance the activation of NLRP3 inflammasome

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Conflict of interest: None

[Objective] It has been reported that SARS-CoV-derived ORF3a activates NLRP3 inflammasome by ubiquitination of inflammasome adaptor ASC (Siu KL et al., FASEB J, 2019). We have previously found the ASC splice variant lacking exon2 (Δexon2 ASC) that increases IL-1β production compared to the wild-type (Suganuma Y et al., Asian Pac J Allergy & Immunol, 2022). In this study, we investigated the effects of ORF3a, wild-type and Δexon2 ASC on NLRP3 inflammasome function. [Methods] THP-1 cells were transfected by using wild-type or Δexon2 ASC and ORF3a expression vectors independently or concurrently. The cells were stimulated with PMA 0.5 μM and MSU 100 μg/mL. Secreted IL-1β and IL-18 in the culture supernatant were quantified by using ELISA. [Results] As compared to the case with ORF3a solely expressed cells, ORF3a and Δexon2 ASC coexpressed cells promoted significantly elevated IL-1β ($P<0.01$) and showed a higher tendency to produce IL-18 ($P=0.099$) than in the case with ORF3a and wild-type ASC coexpressed cells. [Conclusions] SARS-CoV-derived ORF3a and ASC splice variant lacking exon2 cooperatively enhance the activation of NLRP3 inflammasome and produce IL-1β and IL-18.

W99-2

Inhibition of FAS-mediated alveolar epithelial cell death suppresses lung injury in murine COVID-19 model

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Conflict of interest: None

[Objective] COVID-19, caused by SARS-CoV-2, induces irreversible or sometimes fatal lung injury, which is refractory to anti-viral therapy and anti-inflammatory treatments such as glucocorticoids or IL-6 signaling blockade. We assumed that alveolar epithelial cells undergoing cell death could exacerbate tissue inflammation and further injury in COVID-19. The aims of this study are to examine the effect of the inhibition of FAS-mediated cell death in alveolar epithelial cells on the murine COVID-19 model. [Methods] To examine the involvement of FAS-mediated cell death, FAS-deficient MRL/MpJ-*lpr/lpr* (MRL *lpr/lpr*) mice or Fas-sufficient MRL/MpJ-+/+ (MRL +/+) were infected with a mouse-adapted SARS-CoV-2. [Results] COVID-19-induced body weight loss was milder in MRL *lpr/lpr* compared with that in MRL +/+. Histologically, in MRL *lpr/lpr*, TUNEL-positive dead alveolar epithelial cells were less frequent, and ALI-score and DAD-score were milder compared with those in MRL +/+. Type I interferon-inducible genes including *Oas2, Iflit2,* and *Iflit3* were upregulated in the lungs in MRL +/+ compared with those in MRL *lpr/lpr.* [Conclusions] FAS-mediated cell death of alveolar epithelial cells could promote lung injury in COVID-19, and its inhibition is expected to be a new therapeutic target.

W99-3

PD-1highCXCR5-CD4+ Peripheral Helper T (Tph) cells Promote CXCR3+ Plasmablasts in the early phase of COVID-19

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Conflict of interest: None

[Objective] T cell-B cell interaction is the key immune response to protect host from severe viral infection. However, how T cells support B cells to exert protective humoral immunity in human is not well understood. [Methods] Here, we used COVID-19 as a model of acute viral infections and analyzed $CD4^+$ T cell subsets associated with plasmablasts expansion and clinical outcome. [Results] Peripheral helper T cells (Tph,

denoted as PD-1^{high}CXCR5^{-}CD4^{+} T cells) were significantly increased, as were plasmablasts. Tph cells exhibited "B-cell help" signatures and induced plasmablasts differentiation *in vitro*. Interestingly, expanded plasmablasts showed increased *CXCR3* expression, which is positively correlated with higher frequency of activated Tph cells and better clinical outcome. Mechanistically, Tph cells helped B cell differentiation and produced more IFNg, which induced CXCR3 expression on plasmablasts. [Conclusions] These results elucidate a critical role for Tph cells in regulating protective B cell response during acute viral infection.

W99-4

Functional immunophenotyping by using immune response to SARS-CoV-2 vaccine in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To analyze the factors that predict the individual differences in antigen-specific immune responses requires antigen immunization under the same conditions, and vaccination is a valuable opportunity. In this study, we will investigate the antigen-specific immune responses to SARS-CoV-2 vaccines among the patients with rheumatoid arthritis. [Methods] We performed PBMC isolation from about 500 patients with rheumatoid arthritis after vaccination. (1) Anti-SARS-CoV-2 spike protein antibody by ELISA, (2) T cell subset classification, (3) Antigen-specific T cells and their cytokine-producing ability after SARS-CoV-2 peptide stimulation by using Flow Cytometry, were measured and statistically analyzed with the clinical information. [Results] "Antigen-specific antibody production" decreased with aging and MTX/PSL. "Antigen-specific T cell resoponse" showed the positive correlation only with RF. IL-2 and IFNγ-producing cells were positively associated with "Th1", while no correlation was found between IL-4-producing cells and "Th2", or IL-17-producing cells and "Th17". We divided the patients into three clusters according to the cytokine production patterns. [Conclusions] We identified the factors affecting antigen-specific immune responses in the patients with rheumatoid arthritis.

W99-5

SARS-CoV-2 spike proteins directly activate macrophages differently according to the variant, reflecting the clinical severity of COVID-19

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Conflict of interest: None

[Objective] Excessive activation of macrophages (MΦ) is associated with the severity of COVID-19. The SARS-CoV-2 S-protein mRNA vaccines cause adverse inflammatory reactions frequently. To elucidate the mechanisms, we examined whether S-proteins can activate MΦ directly. [Methods] CD14^{+} cells isolated from healthy adults were cultured in the presence of M-CSF and stimulated with the trimeric recombinant S-protein of the wild-type, Delta, and Omicron strains. IL-6, TNF-α, and IP-10 were measured by ELISA. NF-κB-related molecules were analyzed by Western blot. IKKβ, TLR2, or TLR4 inhibitors were used to explore the mechanisms. [Results] Regarding IL-6 and TNF-α, but not IP-10, Delta or Omicron S-protein stimulations draw higher or lower area under the curves, respectively, compared with the wild-type. The productions of IL-6 and TNF-α were suppressed by the addition of either IKKβ, TLR2, or TLR4 inhibitors. The NF-κB phosphorylation and IκBα downregulation were induced by S-protein, while these were suppressed in the presence of the IKKβ inhibitor. [Conclusions] The S-protein stimulation was NF-κB dependent. The cytokine-producing capacities of variant S-proteins were consistent with the clinical pathogenicity in COVID-19.

W99-6

Characteristics of COVID19 in Patients with Rheumatoid Arthritis and Collagen Disease in Our Hospital

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Conflict of interest: None

Objective: To clarify the prognosis of patients with rheumatoid arthritis (RA) affected by the SARS-CoV-2 Omicron variant. Methods: This study included 391 patients with COVID-19 (mean age, 67.5 years) admitted to our hospital between 1st January 2022 and 31st August 2022. Patient background, severity of illness, and length of hospital stay were compared between 38 patients with RA and collagen disease and 353 other patients. Results: There was no difference in age, length of hospital stay, severity of illness, treatment, or prognosis between groups. Furthermore, there was no difference in severity or length of hospital stay between patients with and without the use of prednisolone, conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs), biological DMARDs, or Janus kinase inhibitors. However, the severity of illness was higher in patients using ≥10 mg of prednisolone. Discussion: We compared COVID-19 patients with rheumatic and non-rheumatic disease during the period when SARS-CoV-2 infection was predominantly from the Omicron variant. There was no difference in severity of illness except in patients using ≥10 mg of prednisolone, and there was no difference in length of hospital stay or prognosis between patients with rheumatic and non-rheumatic disease.

W100-1

Safety and Efficacy of Upadacitinib in Patients with Rheumatoid Arthritis and Inadequate Response or Intolerance to Biologic DMARDs: Results Through 5 Years From the SELECT-BEYOND Study

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Conflict of interest: Yes

Purpose: To evaluate the long-term efficacy and safety of upadacitinib (UPA) over 5 yrs in long-term extension (LTE) of SELECT-BEYOND study. Methods: Patients (pts) with an inadequate response or intolerance to ≧1 bDMARD (s) received UPA 15, 30 mg or PBO, each with csDMARD. From wk12, PBO switched to UPA 15 or 30 mg. All pts who completed wk24 visit could enter LTE of up to 5 yrs. Data up to wk260 are reported. Results: Of the 498 pts, 418 completed wk24 and entered LTE. During LTE, 197 pts (40%) discontinued study drug due to the following: TEAEs 13%, withdrawal of consent 7%, lack of efficacy 6%, lost to follow-up 4%, or other reasons 11%. At wk260, 36/36% and 81/77% of pts receiving UPA 15/30 mg achieved CDAI remission or LDA (AO). Boolean remission was achieved by 28/23% (AO). The mean change from baseline was -0.6/-0.6 for HAQ-DI and -39/-37 mm for pts' assessment of pain (AO). No apparent loss of benefit was observed with UPA 15 mg pts who switched from 30 mg. Dose-dependent increases in herpes zoster and CPK elevation were observed. Deaths were comparable between both UPA doses. Conclusion: UPA is effective in improving clinical and functional outcomes in rheumatoid arthritis. Overall, 5 yrs safety profile was consistent with earlier assessments of UPA treatment in this population.

W100-2

Is switching to JAK inhibitors effective in patients with rheumatoid arthritis in TNF inhibitor or IL6 inhibitor ineffective cases?

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Conflict of interest: None

[Objective] We investigated whether the mechanism of action of the first drug, BIO, would affect the efficacy when switching from the first drug, BIO, to the second drug, JAKi. [Methods] Subjects were 54 patients who switched from the first drug BIO to JAKi by December 2021 at related facilities. JAKi was categorized by mechanism of action, switching from TNF inhibitors (TNFSW group, 38 cases) and switching from IL6 inhibitors (IL6SW, 16 cases), and a 52-week follow-up study was conducted on the persistence rate and efficacy of JAKi. [Results] The continuation rates up to 52 weeks after the JAKi switch were 57.8% and 50.0%, respectively, in the TNFSW group and the IL6SW group, respectively. Changes in DAS28ESR in 52-week continuous patients were 0 w (4.9, 3.6), 4 w (4.1, 3.6), 12 w (3.7, 3.8), 24 w (3.6, 4.1), 52 w (3.6, 4.4), and changes in CDAI were 0 w (18.6, 18.2), 4 w (10.6, 11.4), 12 w (9.0, 10.9), 24 w (9.4, 12.0), 52 w (8.7, 18.7), MMP3 changes 0 w (165.4, 108.2), 4 w (133.6, 92.3), 12 w (86.9, 100.0), 24 w (80.0, 76.3), 52 w (90.1, 102.2), significantly improved 52 weeks after the switch in the TNFSW group ($p<0.05$), but significantly improved in the IL6SW group no improvement was seen. [Conclusions] Switching to JAK inhibitors was more effective in TNF inhibitor ineffective cases.

W100-3

Comparing the efficacy of the bDMARD switcher group and JAK cycler group in patients with rheumatoid arthritis with failure to the JAK inhibitors

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Conflict of interest: Yes

[Objective] We analyzed the efficacy of the bDMARD switcher group and the JAK cycler group as the next treatment for JAKi-refractory cases. [Methods] 347 patients met the ACR/EULAR RA classification criteria and started receiving JAKi. Efficacy analysis was evaluated by continuation rate and CDAI improvement rate. [Results] JAKi were administered to 347 patientsfor an average of 64.5 weeks. There were 75 cases (21.6%) who discontinued the JAKi due to insufficient effect. Of the cases in which JAKi were discontinued, 45 (60.0%) were in the bDMARD switcher group, 22 (29.3%) were in the JAK cycler group, and 8 (10.7%) were switched to csDMARD alone. The continuation rate of the next treatment in the bDMARD switcher group and the JAK cycler group was 77.8% and 89.0% at week 12, respectively, with no significant difference (Log-rank $p=0.2806$). The CDAI improvement rates in switcher group and the JAK cycler group were 43.5% and 46.2%, respectively, at week 12, with no significant difference (Wilcoxon $p=0.6397$). There was no significant difference in the CDAI improvement rate according to the treatment class and the number of b/tsDMARDs between the two groups ($p>0.05$). [Conclusions] JAK cycler, as well as bDMARD switcher, may be useful as the next treatment for patients who discontinue JAKi.

W100-4

The clinical efficacy of switching between biological agents and JAK inhibitors in the patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the clinical efficacy of switching among biological agents and JAK inhibitors (JAK) in patients with rheumatoid arthritis (RA). [Methods] We evaluated the disease activities for 12 weeks (W) in RA patients who received the switching from TNF inhibitors (TNF) to JAK (TNF-JAK group, N=61), from IL-6 inhibitors (IL-6) to JAK (IL-6-JAK group, N=33), and from JAK to IL-6 (JAK-IL-6 group, N=8). [Results] The mean DAS28-CRP of TNF-JAK, IL-6-JAK, and JAK-IL-6 groups were 4.22, 4.13, and 4.87 at baseline (BL), and 3.28 ($p<0.001$), 3.41 ($p=0.805$), and 3.24 ($p=0.065$) after 4 W (vs BL), and 2.99 ($p<0.001$), 3.56 ($p=0.115$), and 2.60 ($p=0.005$) after 12 W (vs BL), respectively. The mean values of MMP-3 (ng/ml) of TNF-JAK, IL-6-JAK, and JAK-IL-6 groups were 213.5, 237.5, and 268.5 at BL, 118.9 ($p=0.148$), 183.6 ($p=0.279$), and 196.2 ($p=0.254$) after 4 W (vs BL), and 104.0 ($p=0.089$), 176.6 ($p=0.123$), and 137.4 ($p=0.077$) after 12 W (vs BL), respectively. The disease activites significantly decreased after 4 W in TNF-JAK group, and after 12 W in JAK-IL-6 group, however, did not significantly decreased for 12 W in IL-6-JAK group. [Conclusions] In this study, it is considered that the switching from TNF to JAK and from JAK to IL-6 could be effective when RA patients need switching therapy.

W100-5

Comparative study of the efficacy of JAK inhibitors and anti-IL-6 receptor inhibitors in patients with D2TRA

Kazuya Kishimoto[1], Hirotaka Yamazawa[1], Kaori Ishimura[1], Hiroki Akazawa[1], Chisato Ashida[1], Akinori Okada[1], Daisuke Tomita[1], Tetsu Itami[1], Toshihiko Shiga[1], Shoichi Hino[2], Yuji Nozaki[1], Koji Kinoshita[1], Itaru Matsumura[1]
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Conflict of interest: None

[Objective] There are a certain number of RA cases in which disease activity is difficult to control with two or more b/tsDMARDs with different mechanisms of action. JAK inhibitors have been reported to be effective against D2TRA, but a certain view of their efficacy with aIL-6R inhibitors has not been reached. [Methods] Thirteen patients (aIL-6R group: TCZ 7 cases, SAR 6 cases) who received aIL-6R inhibitors and 26 patients (JAK group: TOF 4 cases, BAR 9 cases, PEF 5 cases, UPA 4 cases, FIL 4 cases) who received JAK inhibitors by April 2022 for D2TRA patients at our hospital and affiliated facilities were compared for retention rate, clinical evaluation, and side effects. [Results] Duration of disease was significantly longer in the JAK group (aIL-6R vs JAK: 9.6 years vs 16.7 years). 52-week retention rate was 100% in the aIL-6R group and 69.2% in the JAK group ($p=0.03$). There was no significant difference in CDAI change from baseline between the aIL-6R and JAK groups, but the achievement rate of CDAI low disease activity tended to be higher in the aIL-6R group than in the JAK group (aIL-6R vs JAK, 12 w: 15.4% vs 23.1%, 24 w: 38.5% vs 34.6%, 52 w: 61.5% vs 42.3%). [Conclusions] In addition to JAK inhibitors, anti-IL-6 receptor inhibitors may be a potential option for D2TRA.

W100-6

Analysis of clinical responsiveness by second JAK inhibitors against RA patients with inadequate response to pre-JAK inhibitors

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Conflict of interest: None

[Objective] To analyze clinical responsiveness by second JAK inhibitors against RA patients with inadequate response (iR) to pre-JAK inhibitor in clinical practice. [Methods] 37 patients in tofacitinib (TOF), 52 patients in baricitinib (BARI), 33 patients in peficitinib (PEF), 37 patients in upadacitinib (UPA), and 26 patients in filgotinib (FIL), totally 185 patients were prescribed in my clinic. From them, 21 RA patients iR to pre- JAK inhibitor were investigated for clinical effectiveness by second JAK inhibitor. [Results] Biologics were used in 14 patients and all satisfied difficult-to-treat RA. For pre-JAK inhibitors, 12 TOF, 6 BARI, 4 PEF have

been used. For second JAK inhibitor, 13 UPA, 3 BARI, 3 PEF and 3 FIL were used. Six months later, 8/12 patients in UPA, 2/3 in FIL, 2/3 in PEF, 0/3 in BARI, totally 12/21 satisfied good or moderate response in Eular clinical response criteria. UPA had little response to RF negative patients (2/5). BARI had little response to TOF iR patients (0/3). Limitations of this study are small samples and no randomization of timing of second JAK inhibitors because of clinical practice. [Conclusions] JAK inhibitors may be useful for pre-JAK inhibitor iR RA patients. However, Double-blind clinical trial may be required to get more precise information.

W101-1

Switching treatment is effective in difficult-to-treat rheumatoid arthritis patients with and without inflammation

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Conflict of interest: None

[Objective] Although the treatment of rheumatoid arthritis (RA) has improved dramatically with biologic agents (BIOs) and JAK inhibitors (JAKi), there are some difficult-to-treat rheumatoid arthritis (D2TRA) patients. D2TRA can be divided into persistent inflammatory refractory RA (PIRRA) and non-inflammatory refractory RA (NIRRA). In this study, we investigated the clinical course of PIRRA and NIRRA. [Methods] We included 147 D2TRA patients who were switched to BIO/JAKi in our hospital and related hospitals. The number of tender joints > number of swollen joints and negative CRP were defined as NIRRA and the rest as PIRRA, and their disease characteristics, retention rate and efficacy after BIO/JAKi switching were followed for 52 weeks. [Results] Comparing 33 NIRRA cases with 114 PIRRA cases, DAS28ESR (4.43, 5.25, p=0.003). The retention rates were 51.5% and 45.6%; changes in DAS28ESR were, in order, 0 w (4.4, 5.3), 4 w (4.4, 4.5), 12 w (4.5, 3.3), 24 w (4.2, 3.0), 52 w (3.9, 3.6), CDAI changes were 0 w (21.7, 22.7), 4 w (18.0,17.6), 12 w (16.7,14.9), 24 w (10.9,11.5), 52 w (12,5,11,2), and CDAI decreased in both NIRRA and PIRRA after the switch. There was no significant difference in retention rate in both NIRRA and PIRRA. [Conclusion] BIO/JAKi switch is effective in D2TRA patients with and without inflammation.

W101-2

JAKi Switch Efficacy and Safety in JAKi-IR

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Conflict of interest: None

[Objective] To clarify JAKi switch efficacy and safety in JAKi-IR in real clinical practice. [Methods] Rheumatoid arthritis (RA) patients who received another JAKi from June 2014 to October 2022 were included. Efficacy after JAKi switch was evaluated after 4 and 12 weeks for changes in overall disease activity and respective components. Serum cytokine changes after the JAKi switch were measured by ELISA. The safety of the switch was evaluated by the occurrence of adverse events within 12 weeks after the switch. [Results] JAKi was switched in 49 patients. The reasons for switching were inadequate efficacy in 78%, adverse events in 18%, and others in 4%. The SDAI LDA achievement rates for patients switched due to inadequate response were 49% at 4 weeks, and 52%at 12 weeks, respectively. Both overall disease activity and each component showed significant improvement in the early post-switch period. The group that achieved LDA showed an even greater improvement at 12 weeks compared to 4 weeks. Adverse events occurred in 8%. No adverse events were observed during the observation period in the group switched to JAKi for adverse events. Serum inflammatory cytokines IL-6 and TNF-α were significantly altered by the JAKi switch. [Conclusions] JAKi switch is an effective therapeutic strategy.

W101-3

Short-term results of Janus kinase inhibitors switching in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To evaluate the efficacy of Janus Kinase inhibitors (JAKi) Switching in patients with rheumatoid arthritis (RA) [Methods] 35 RA patients using JAKi more than 3 months and whose disease activity could be followed as of October 1, 2022, were included. Patients were classified into 3 groups, the JAKi-switch, the Bio-switch, and the JAKi-naïve group, according to their history of JAKi or Biologics (Bio) use. Disease activity (DAS28-CRP, DAS28-ESR, CDAI) before and 3 months after the start of JAKi and remission rates were evaluated. [Results] The mean values of DAS28-CRP, DAS28-ESR, and CDAI in the JAKi-switch group were 3.33, 4.35, and 10.89 before administration and 1.91, 3.34, and 5.01 after 3 months. Those in the Bio-switch group were 3.53,4.36,15.04 before administration and 2.13,3.10, and 6.24 after 3 months. Those in the JAKi-naïve group were 3.31,4.25, and 10.31 before administration and 1.63,2.69, and 2.53 after 3 months. All groups showed significant improvement in disease activity. The remission rates in DAS28-CRP in each group were 66.7% in the JAKi-switch group, 63.6% in the Bio-switch group, and 100% in the JAKi-naïve group, respectively. [Conclusions] The JAKi-switch group showed significant improvement in RA disease activity after 3 months of the administration.

W101-4

Medical economics of antirheumatic drugs

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Conflict of interest: None

[Objective] In phase 2 of the Rheumatoid Arthritis Clinical Practice Guidelines 2020 Drug Treatment Algorithm, the use of bDMARDs should be considered over JAK inhibitors from the perspective of long-term safety and medical economy. We investigated the cost-effectiveness of antirheumatic drugs in medical economics in patients with rheumatoid arthritis. [Methods] Improved CDAI per 10,000 yen drug cost per week was compared between JAK inhibitors and bDMARDs. [Results] JAK inhibitors are less expensive than anti-TNF antibodies and are not less cost-effective. [Conclusions] Medical economics is no reason not to choose a JAK inhibitor.

W101-5

The influence of multi drug resistance factor (MDR1) on the therapeutic efficacy of JAK inhibitors

Yuma Onoi[1], Kenichi Kikuchi[1], Toshihisa Maeda[1], Shinya Hayashi[1], Kensuke Anjiki[1], Kemmei Ikuta[1], Shotaro Tachibana[1], Marowa Hashimoto[3], Ken Tsumiyama[2], Keiko Funahashi[2,3], Koji Fukuda[2], Ryosuke Kuroda[1], Tsukasa Matsubara[2,3]
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Conflict of interest: None

[Object] We hypothesized that the multi drug resistance factor (MDR1) might affect the therapeutic efficacy of Janus kinase inhibitor (JAK-i) for rheumatoid arthritis (RA). To the best of our knowledge, no report has examined the relationship between MDR1 and JAK-i. Thus, we investigated the effect of MDR1 expression on the therapeutic effect of JAK-i. [Methods] Synovial fibroblast-like cells (RA-FLS) were isolated from synovial tissue collected from RA patients and used as a primary culture system. MDR1 expression was evaluated by RT-PCR and compared in two groups: high and low expression groups. RA-FLS were seeded in plates and exposed to single doses of Tofacitinib, Baricitinib, Peficitinib, Upadacitinib and Filgotinib at low, medium and high dose concentrations, respectively. Two hours later, RA-FLS were stimulated with 100 ng/ml IL-6 and sIL-6R each, and 24 hours later, cell proliferation was evaluated by

WST assay and MMP-1 expression by RT-PCR. [Results] A dose-dependent decrease in cell proliferation was observed with all five JAK-i. However, there were no significant differences in cell proliferation and MMP-1 expression between the high and low MDR1 expression groups. [Conclusions] It was suggested that JAK-i may be beneficial even in cases with high MDR1 expression.

W101-6

Influence of dosing-time of Peficitinib on antirheumatic effects in CIA rats

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Conflict of interest: None

[Objective] We investigated influence of dosing-time on antirheumatic effects after Peficitinib was given in CIA rats. [Methods] Peficitinib was perorally given once a day at 5:00 or 17:00 in CIA rats, and the efficacy and safety of Peficitinib was evaluated. [Results] When Peficitinib (30 mg/kg) was administered from day 14 after initial sensitisation, the 5:00 dosing group showed significantly less exacerbation of arthritis compared to the control group on the last measurement day. The exacerbation of arthritis in the 5:00-treated group was approximately 23% lower than in the 17:00-treated group. During Peficitinib (20 mg/kg) was administered from the next day after the first sensitization, the 5:00 dosing group significantly suppressed the exacerbation of arthritis compared with the control and 17:00 dosing groups. The peficitinib-treated groups did not show a significant reduction in white blood cell counts compared to the unsensitised group. Alanine aminotransferase (ALT) did not differ in all groups. Aspartate aminotransferase (AST) was significantly higher in the peficitinib-treated groups compared with the nonsensitised group. [Conclusions] These findings show that to treat peficitinib once a day considering suitable dosing-time may improve RA symptoms.

W102-1

Early reduction of glucocorticoid dose by combining rituximab with belimumab in two patients with systemic lupus erythematosus with immune thrombocytopenia

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Conflict of interest: None

[Patient 1] A 67-year-old woman was referred to the hematological department due to thrombocytopenia (platelet count, 5,000/μL), and diagnosed with immune thrombocytopenia (ITP) and autoimmune hemolytic anemia (AIHA). However, oral prednisolone (PSL) 50 mg/day had no effect, she was referred to our department for further assessment of systemic lupus erythematosus (SLE). Infusion therapy of rituximab (RTX) combining belimumab (BEL) for SLE with ITP and AIHA immediately improved her thrombocytopenia and anemia. PSL was tapered off over 2 months, and the patient experienced no recurrence. [Patient 2] A 16-year-old woman was referred to the hematological department due to severe anemia (Hb 2.9 g/dL) with convulsion. She was diagnosed with ITP and AIHA associated with SLE. Although oral PSL 50 mg/day had no effect, RTX combining BEL immediately improved the hematological disorder and allowed early discharge. PSL was tapered off over 18 months, and the patient experienced no recurrence. [Conclusions] Combining RTX with BEL therapy may be a promising option for refractory and severe organ involvements, including hematological manifestations such as ITP and AIHA in SLE. Moreover, combination therapy may allow the reduction of organ damage with early glucocorticoid withdrawal.

W102-2

Three cases of anifrolumab treatment in patients with systemic lupus erythematosus refractory to conventional therapy

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Conflict of interest: None

[Objective] To report 3 consecutive use of anifrolumab (ANI) for refractory SLE. [Cases] Case 1: A 33-year-old woman, diagnosed with SLE in X-1 with polyarthralgia, positive antinuclear antibody (ANA), positive anti-dsDNA antibody (αdsDNA-ab), and LN IV-G (A). SLEDAI-2K score was 15. She was treated with PSL 40 mg/day, TAC, and MMF. When PSL was reduced to 17.5 mg/day, arthralgia flared and αdsDNA-ab elevated. Belimumab (BLM) was ineffective and ANI was introduced. After 3 months, SLEDAI decreased to 4, and PSL dose was reduced. Case 2: A 42-year-old man, diagnosed with SLE due to positive ANA, positive αdsDNA-ab, and LN III. He was treated with PSL 20 mg/day, HCQ, and MMF, followed by ANI due to inadequate response. After 6 months, SLEDAI decreased to 4, and PSL dose was reduced. Case 3: A 29-year-old woman developed NPSLE in X-9. She was treated with pulsed steroids, plasma exchange, and MMF. At the first visit to our hospital in X-3, she was treated with PSL 15 mg/day and MMF. After PSL was reduced, psychiatric symptoms worsened. BLM was ineffective, so ANI was introduced. After 3 months, the SLEDAI decreased to 0, and PSL was reduced. [Clinical Significance] This report demonstrated that ANI can be a treatment option for SLE refractory to conventional therapy.

W102-3

Hypoglycemia induced by low-dose hydroxychloroquine in a non-diabetic patient with systemic lupus erythematosus

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Conflict of interest: None

[Case] 56 years old, female. [Chief complaint] dizziness. [Clinical Course] The patient had been taking hydroxychloroquine (HCQ) for 2 years in addition to PSL for SLE. The patient complained of recurrent severe dizziness and hypotension since she moved to a new house. We suspected relative adrenal insufficiency, so stopped the antihypertensive medication, and increased the PSL dose of 5 mg to 8 mg/day, but the symptoms did not improve. Several episodes of hypoglycemia were observed several times a day. Symptoms were dysarthria and severe dizziness, which quickly improved with glucose administration. Self-monitoring of blood glucose showed that the lowest level was 20 mg/dL. After HCQ discontinuation, her daytime hypoglycemia promptly disappeared. Laboratory tests revealed no abnormalities in adrenal function, negative anti-insulin and anti-insulin receptor antibodies, and normal insulin level and C-peptide value. [Discussion] HCQ is widely used in SLE patients. It is known to have antidiabetic effects, and its hypoglycemic side effect is rare. The adverse events of hypoglycemia have been reported at high-doses of HCQ, however there is only one report at low-doses of HCQ in non-diabetic SLE patients. Hypoglycemia should be considered even when using HCQ in non-diabetic patients.

W102-4

A case of refractory antiphospholipid antibody syndrome treated with immunosuppressive therapy

Tomoya Nishida[1], Masahiro Ayano[1], Goro Doi[1], Yasutaka Kimoto[2], Hiroki Mitoma[1], Nobuyuki Ono[1], Yojiro Arinobu[1], Takahiko Horiuchi[2], Hiroaki Niiro[3]
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Conflict of interest: None

An 67-year-old man was diagnosed with cerebral infarction at 58 years old (X-9). He had repeated cerebral infarctions, and diagnosed pri-

mary antiphospholipid antibody syndrome (APS). He was treated with warfarin and glucocorticoid (GC). However, after X-4, he repeated hospitalization due to recurrent deep vein thrombosis and pulmonary embolism. In X-2, hydroxychloroquine (HCQ) was started, and the recurrence of thrombosis was no longer observed along with a decrease in anticardiolipin antibody titer. After tapering of GC and discontinuation of HCQ, In June X, the patient was admitted to the previous hospital due to swelling of the left lower leg and elevated D-dimer. Since anticoagulant therapy alone did not improve his condition, he was admitted to our department. Heparin was increased and Cilostazol was started as antithrombotic therapy. Considering the past validity of HCQ, it was decided to reinforce immunosuppressive therapy by administering Rituximab and resuming HCQ. After one month, the thrombus showed a tendency to shrink. Immunosuppressive therapy is not usually used for APS, but a few effective cases of B-cell depletion therapy for APS have been reported, and it may be a treatment option for refractory APS.

W102-5

A successful bridging therapy of plasma exchange (PE) for a high school girl with severe central nerve systemic (CNS) lupus and lupus nephritis (LN) without immediately administering rituximab (RTX) due to viral infection

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Conflict of interest: None

[Present History] The patient had chronic lower limbs purpura and positivity antinuclear antibody since last year. Three weeks after the HPV vaccination, she was diagnosed SLE due to the following; febrile, butterfly shadow, lower limbs purpura, leukocytopenia, urine occult bleeding, proteinuria and alveolar hemorrhage. Even after taking oral steroids, she had to be transferred to another hospital for acute respiratory distress syndrome. She was given methyl prednisolone and cyclophosphamide. Hydroxychloroquine and mycophenolate mofetil were added for LN type IV. Nevertheless, she was diagnosed with CNS lupus twelve days later. Then, PE was performed. Although the symptoms were disappeared, they got worse again soon. In order to receive RTX, she was transferred to our hospital. She had bacterial pneumonia and was CMV positive. Therefore, PE was ordered instead of RTX. By confirming CMV was negative after third session of PE, RTX was given. The schedule of PE depended on the pharmacokinetics of RTX. Consequently, she was discharged on the 56th day of hospitalization. [Discussion and Summary] The two Japanese guidelines of SLE treatment state the effect of PE. In our case, PE played as a bridge to the next treatment. Its plan based on the pharmacokinetics worked effectively.

W102-6

Glucocorticoid withdrawal is an achievable objective in SLE early in treatment

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Conflict of interest: None

Objective We aimed to validate whether it is possible to completely withdraw glucocorticoids (GC) in SLE patients keeping then in stable disease status. ***Methods*** Patients diagnosed with SLE according to the 1997 revised ACR classification criteria between Apr. 2016 and Mar. 2021 in our hospital and treated with GC were included. We retrospectively reviewed the electric medical records and collected data about the treatment and activity of the patients. ***Results*** Twenty-four patients were included. Median age was 29 (15-77) and 20 (83%) patients were females. The initial dose ofPSL was 50 (7.5-60) mg, and baseline SLEDAI was 12 (5-34). HCQ, immunosuppressants (IS), and belimumab were used in 23, 22, and 4 patients, respectively. GC was withdrawn in 23 (96%) patients keeping them in a stable disease status during the follow-up period, which was median 41 (24-71) months. After cessation of GC, 9 (39%) patients experienced flares. Baseline SLEDAI and dose of PSL were not significantly different between patients experienced flare after the withdrawal of GC and did not. Only the use of IS was significantly different in the two groups (13 vs 75%, p=0.008). ***Conclusion*** Withdrawal of GC in less than 2 years is an achievable goal in SLE patients concomitantly treated with HCQ, IS and biologics.

W103-1

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 IFNg producing CD4+ T cell increasing in IMQ-induced SLE model mice. [Methods] After administration of IMQ in C57BL/6 Wild-type (WT) mice and IFNg knockout (KO) mice, 1) lupus phenotype was evaluated by measuring serum anti-dsDNA IgG and urinary protein/creatinine ratio, and staining of C3 and IgG in kidney. We also evaluated 2) expression of superficial antigens on splenic CD4+ T cells, 3) cytokine production from in vitro stimulated splenic CD4+ T cells, and 4) B cell subsets in spleen by Flow cytometry (FCM). [Results] 1) Anti-dsDNA IgG was significantly decreased in KO mice compared with WT mice, whereas there was no difference in urinary protein/creatinine ratio and deposition of C3 and IgG in kidney. 2) Expression of CXCR3 tended to be decreased and CXCR5 was significantly decreased in CD4+ T cells of KO mice. 3) Production of IL-10 was significantly decreased, but IL-17 was significantly increased in CD4+ T cells of KO mice. 4) Plasma cells in spleen tended to be decreased in KO mice. [Conclusion] Our results suggested the possibility that IFNg producing CD4+ T cells might have a pivotal role in autoantibody formation through the induction of plasma cell differentiation in IMQ induced lupus model.

W103-2

Therapeutic effects of vorinostat in a mouse model of lupus

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Conflict of interest: None

[Objective] We evaluated the mechanisms by which vorinostat suppresses IFN-I production and its therapeutic effects in model mice. [Methods] We administered vorinostat intraperitoneally to NZB/NZW-F1 mice and to SAVI model mice to examine survival, autoantibody titer, pathological evaluation, and gene expression. We also evaluated if vorinostat suppresses the phosphorylation of TBK1 and IRF3 in THP-1 cells and human mononuclear cells. [Results] Vorinostat improved survival, proteinuria, glomerulonephritis, and decreased autoantibody titer in NZB/NZW-F1 mice. In SAVI mice, vorinostat treatment also suppressed pulmonary inflammation and fibrosis and inhibited IFN-I-related gene expression in the kidneys and lungs. We also found that vorinostat inhibited LPS- and cGAMP-stimulated phosphorylation of TBK1, cGAMP-stimulated nuclear migration of IRF3, and LPS- and cGAMP-stimulated expression of IFN-β and ISG in THP-1 cells and human mononuclear cells. Furthermore, we found that vorinostat suppressed B cell differentiation and maturation. [Conclusion] We found that vorinostat inhibits IFN-I production by suppressing the phosphorylation of TBK1 and B cell differentiation, leading to the suppression of SLE onset.

W103-3

Cell death inhibition by Janus kinase inhibitors in vitro

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Conflict of interest: None

[Objective] To clarify the effects of Janus kinase inhibitors (JAKis) on hydroxychloroquine (HCQ) retinal and renal toxicity using cultured human retinal pigmental epithelial cell line and cultured mouse and human podocyte cell lines. [Methods] Luminescent-based cell viability plate assay was employed to quantify HCQ-induced cell death. Human retinal pigment epithelial cell line (ARPE-19), mouse podocyte cell line (AI), and human podocyte cell line (BLAK) were used to test HCQ toxicity. ARPE-19 was pretreated with a series concentrations of upadacitinib (UPA), and AI and BLAK were pretreated with a series concentrations of baricitinib (BAR) and UPA for 48 hours, and HCQ was added to these cell lines to induce cell death, until cells were subject to viability assay. The effects of JAKi on long culture cell death were also tested. One-way ANOVA was done using Prism 9 for macOS for statistical analysis. [Results] In ARPE-19, 16 nM-10 μM of UPA, 0.08 μM-50 μM of BAR and UPA in AI, and 0.08 μM-50 μM of BAR and 10 μM of UPA in BLAK significantly inhibited HCQ-induced cell death. Long culture cell death in AI was also significantly inhibited by 2.5 μM BAR or 2.5 μM UPA. [Conclusions] JAKis have protective effects on cell death in human pigment retinal epithelial cells and podocytes.

W103-4

Role of anti-dsDNA IgE antibodies and basophils in systemic lupus erythematosus

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Conflict of interest: None

[Objective] The role of basophils and anti-double-stranded DNA IgE in SLE was examined using human samples. [Methods] The correlation between disease activity and serum levels of anti-dsDNA IgE was evaluated using ELISA. Cytokines produced by IgE-stimulated basophils were assessed using RNA sequences. The interaction of basophils and B cells to promote B cell differentiation was investigated using a co-culture system. [Results] Anti-dsDNA IgE titer in SLE correlated with disease activity. Basophils produced IL-4 after anti-IgE stimulation. Co-culture of B cells with basophils increased plasmablasts. By adding dsDNA to basophils isolated from patients with anti-dsDNA IgE, IL-4 expression was increased. [Conclusions] These findings imply that basophils contribute to the pathogenesis of SLEvia dsDNA-specific IgE.

W103-5

CX3CR1+ CD14++CD16+ peripheral monocytes and Fraktalkine contribute to disease activity of systemic lupus erythematosus

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Conflict of interest: Yes

[Objective] Fractalkine (FKN) and its receptor, CX3CR1, play an important role in chemotaxis of immune cells. In this study, we investigated the possible involvement of FKN-CX3CR1^{+} axis in monocytes in the clinical features of SLE. [Methods] The CX3CR1^{+}/CD14^{++}CD16^{+} ratio in patients with active SLE (onset or relapse, n=82), inactive SLE (n=40), and healthy controls (HC, n=42) was analyzed by FACS. The serum level of FKN was measured by ELISA. The serological data of patients was collected by clinical records. [Results] The CX3CR1^{+}/CD14^{++}CD16^{+} ratio of peripheral monocytes was significantly lower in active SLE than that of inactive SLE ($p<0.001$) and HC ($p<0.001$). Moreover, CX3CR1^{+}/CD14^{++} CD16^{+} ratio of active SLE was negatively correlated with the SLEDAI score ($p=0.018$) and serum level of anti-dsDNA antibody ($p=0.011$). The serum FKN level was significantly elevated in active SLE as compared to inactive SLE ($p<0.001$) and HC ($p<0.001$) and was positively correlated with the SLEDAI score ($p=0.003$) and serum level of anti-dsDNA antibody ($p=0.05$). Notably, serum FKN level was negatively and significantly correlated with CX3CR1^{+}/CD14^{++}CD16^{+} ratio in active SLE ($p<0.001$). [Conclusions] Our results raise the possibility that FKN-CX3CR1 axis in CD14^{++}CD16^{+} monocytes reflect the disease activity.

W103-6

Analysis of microbiota in patients with systemic lupus erythematosus

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Conflict of interest: Yes

[Objective] We explored gut microbiota in patients with SLE to investigate its relation with disease activity and clinical findings. [Methods] Stool samples were collected from 25 patients with new-onset SLE (no SLE), 30 patients with SLE in remission (remSLE) and 30 healthy controls (HC). Microbial composition was determined by bacterial 16S rRNA analysis to examine α- and β- diversities and abundances of phylum, family, genus and species. [Results] Patients with noSLE displayed altered β -diversity, decreases in butyrate-producing bacteria including *Eubacterium rectale, Lachnospira pectinoshiza, Anaerostipes hadrus, Fusicatenibacter saccharivorans*, and *Anaerobutyricum halli*, and increases in *Hungatella efuluvii, Intestinibacter barrtlett*i, and *Eisenbergiella tayi*. Some had correlation with SLEDAI, while the others did not. Furthermore, the abundance of specific bacterial species was correlated with involved organs and the positivity of autoantibodies. [Conclusions] Butyrate plays a role in the homeostasis of gut and regulation of immune cells, and therefore a decrease in butyrate-producing bacteria may be involved in the pathogenesis of the disease. Our study suggests that the gut microbiota possibly contributes to the activity and clinical findings of SLE.

W104-1

Analysis of risk factors for severe infection in ANCA-associated vasculitis: a single-center retrospective cohort study

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Gunma University Graduate School of Medicine

Conflict of interest: None

[Objective] We aimed to identify risk factors for severe infection in ANCA-associated vasculitis (AAV). [Methods] We conducted a retrospective cohort study of 200 adult Japanese patients with newly diagnosed AAV at our department who were classified as microscopic polyangiitis (MPA), polyangiitis granulomatosis polyangiitis (GPA), eosinophilic granulomatosis polyangiitis (EGPA) or unclassified according to the classification algorithm proposed by Watts et al. The factors associated with severe infection were analyzed by Cox proportional hazard model. [Results] Ninety-two males and 108 females were enrolled. The mean age was 66.7 years. Prednisolone and immunosuppressants were administrated to 196 and 116 patients, respectively. In a median follow-up period of 42

months (IQR, 17-94.5), 63 patients had at least one severe infection requiring hospitalization or prolonged hospitalization. Multivariate analysis revealed that creatinine level (HR 1.18, 95%CI 1.03-1.35, P=0.017) and age (HR 1.03, 95%CI 1.01-1.06, P=0.019) at diagnosis were each independently associated with severe infection. [Conclusions] In AAV patients, high creatinine level and old age at diagnosis were risk factors for severe infection.

W104-2

Investigation of factors related to diffuse alveolar hemorrhage in ANCA-associated vasculitis

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Conflict of interest: None

[Objective] Diffuse alveolar haemorrhage (DAH) is a serious organ damage in ANCA-associated vasculitis. The purpose of this study is to compare the group with diffuse alveolar hemorrhage (DAH group) and the group without (non-DAH group), and to extract factors that are associated with DAH. [Methods] We retrospectively reviewed the medical records of 53 patients with ANCA-associated vasculitis (microscopic polyangiitis and granulomatous polyangiitis) who visited our department. A comparative analysis was carried out. [Results] The DAH group had more microscopic polyangiitis than the non-DAH group. There was no difference in organ damage of kidney and peripheral neuron. The ANCA antibody titer was higher in the DAH group, and the BVAS at the most severe stage was higher in the DAH group. Logistic regression analysis identified high CRP levels, microscopic polyangiitis, and concomitant use of antiplatelet agents as risk factors for DAH. [Conclusions] In ANCA-associated vasculitis, the presence of microscopic polyangiitis, high activity, and concomitant use of antiplatelet agents may increase the risk of DAH. It was thought that understanding these risk factors may lead to early and appropriate intervention.

W104-3

Association of serum complement 3 and serum creatinine levels with end-stage renal disease in microscopic polyangiitis

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Conflict of interest: None

[Objective] To investigate whether serum C3 level is a risk factor for end-stage renal disease (ESRD) in microscopic polyangiitis (MPA). [Methods] 74 patients, who were diagnosed with MPA at our hospital between December 2010 and June 2021, were enrolled. Patient's background, disease severity, and treatment were extracted retrospectively. Patients who met the criteria for ESRD were followed up and risk factors for ESRD progression were examined. [Results] During follow-up, 12 patients (16.2%) progressed to ESRD. Comparing the pre-treatment clinical backgrounds, in ESRD group WBC and Serum C3 levels was significantly lower than those of the non-ESRD group (P=0.02 and 0.03, respectively), and serum Cr level was significantly higher in ESRD group than that of the non-ESRD group (P<0.001). The cutoff value of serum C3 level in the ROC curve was 83.0 mg/dl. In the Kaplan-Meier curve, the rate of progression to ESRD at 5 years was significantly higher in the group with serum C3 level below 83.0 mg/dl compared with the group with serum C3 level higher than 83.0 mg/dl. (Log-rank test P=0.0008). [Conclusions] In MPA, low serum C3 level was associated with renal function and renal prognosis. Serum C3 level is a useful biomarker for predicting disease course and prognosis in MPA nephritis.

W104-4

Characteristics of patients with elderly-onset eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] Elderly-onset eosinophilic granulomatosis with polyangiitis (EOEGPA) patients were not uncommon in an aging society in Japan. However, elderly-onset is the risk factor of poor prognosis in EGPA. The aim of this study is to clarify the characteristics of the patients with EOEGPA. [Methods] We investigated 16 EGPA patients visited our department until 2014 to 2022. According to their age at onset (elderly-onset, 65 years old or above; young-onset, under 65 years old), we retrospectively analyzed the differences of clinical characteristics. [Results] The mean age of the patients with EOEGPA (n=5) and young-onset EGPA (n=11) were 72.0±7.5 years old and 55.0±8.2 years old, respectively. In EOEGPA patients, the complication rate of bronchial asthma and the positivity of rheumatoid factor were significantly lower (40% vs 100%, p=0.01; 20% vs 92%, p=0.02, respectively). The positive rate of MPO-ANCA was low without significant difference (20% vs 45%, p=0.58). There were no differences in gender, organ involvements, the number of eosinophils, IgE titer, dose of steroids, or immunosuppressants use. [Conclusions] Since EOEGPA patients have fewer bronchial asthma complications and serological findings, we need to be careful at diagnosis and to investigate the further case series.

W104-5

Evaluation of the usefulness of FDG-PET/CT in identifying disease activity and affected areas in polyarteritis nodosa

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National Center for Global Health and Medicine

Conflict of interest: None

[Objective] To compare the usefulness of FDG-PET/CT in assessing disease activity and localized vasculitis in polyarteritis nodosa. [Methods] We compared the blood test finding and FDG-PET/CT evaluation in 12 patients diagnosed with PAN or relapse between April 2003 and December 2021 at our department. [Results] Of the 12 cases, 9 were positive for FDG-PET/CT and 3 were negative. Of the 12 cases, systemic vasculitis was identified 7 cases of systemic PAN and in 2 of 5 cases of cutaneous PAN. In some sypmtoms were compared between the positives and negatives, but there were no differences. In 12 patients, CRP was 10.4 ± 7.65 mg/dL and 5.44 ± 3.56 mg/dL (Mean ± SD, p=0.73) in the positive and negative groups. Only LDH showed significant differences, 165 ± 38.5 U/L and 250 ± 59.3 U/L (Mean ± SD, P=0.036). [Conclusion] Even when the diagnostic criteria indicate a cutaneous from of PAN, there are cases in which FDG accumulation is found in medium-sized vessels of the extremities on FDG-PET/CT findings. In addition, FDG-PET/CT findings in PAN without cutaneous symptoms may allow identification of the biopsy site based on FDG accumulation. In conclusion, FDG-PET/CT can be used to identify subclinical vasculitis in PANs and to identify biopsy sites based on this identification.

W104-6

A nationwide epidemiological study of polyarteritis nodosa in Japan

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pan

Conflict of interest: None

[Objective] To clarify the clinical features of polyarteritis nodosa (PAN) in Japan. [Methods] According to the manuals of national wide epidemiological study for understanding patient number of intractable diseases and clinical epidemiology conditions, stratified random sampling was conducted from the national list of medical institutions for rheumatology, neurology, pediatrics, and dermatology. Primary survey forms regarding the number and gender of patients with PAN during the one-year period from April 2020 to March 2021, and secondary survey forms were mailed to the institutions to collect information of each patient. [Results] Primary survey forms were collected from 2235 facilities (response rate; 53.9%) out of 4148 selected from 15652 facilities (selection rate; 26.5%). The total number of patients reported was 868, for a male to female ratio of 1:1.2. The number of PAN patients nationwide was estimated to be 2200 (95% confidence interval: 1800-2600). [Conclusions] The estimated number of patients with PAN obtained from the primary survey was similar to the number of applications for intractable diseases in 2019 (2,273), and the sex ratio was similar to the result of our previous analysis based on a nationwide database.

W105-1

Case report: Hypertrophic Pachymeningitis was resisted to immuno suppressive agent, after clinical remission got with MPO-ANCA associated vasculitis (AAV) and IgG4 related disease (IgG4RD)

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Conflict of interest: None

[Objective] Therapy to Hypertrophic Pachymeningitis [Methods] 53 years old, Female. She visited to near doctor for headache and fever. Head MRI was performed, then Hypertrohic Pachymeningitis was revealed with Anti Nuclear Antibody was positive on March X-5. She was introducd our hospital on May X-5. Furthermore we found MPO-ANCA and IgG4 positive. We diagnosed ANCA associated Vasculitis (AAV), and steroid (PSL) therapy was done. AAV achieved clinical remission. According to reduce PSL dosage, Hypertrophic Pachymeningitis gradually worsened. It is difficult to reduce PSL less than 12.5 mg/day. Combined therapy was done with azathioprine on december X-4. Another Hypertrophic Pachymenintitis was revealed on april X-1. We done the Cyclophosphamide (IVCY) therapy for 12 course, and decrease PSL dosage. But it is not effective Another Hypertrophic Pachymeningitis. We treated Rituximab therapy, but not so effective. [Results] It is difficult to Hypertrophic Pachymeningitis achieve remission with combined therapy. [Conclusions] MPO-ANCA and IgG4 titer were mainteined negative level. It is significant to identify whether AAV or IgG4RD Hypertrophic Pachymeningitis. Conventional Immuno suppressive therapy showed effectiveness but sometimes not. It is important to follow the clinical course.

W105-2

Diffuse alveolar hemorrhage as a consequence of major relapse of eosinophilic granulomatosis with polyantiitis (EGPA) on mepolizumab after COVID-19 infection

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Conflict of interest: None

A 75-year-old woman with past medical history of asthma presented with rapidly progressive glomerulonephritis 16 months ago. She was diagnosed with EGPA on the basis of eosinophilia, positive MPO-ANCA, and biopsy proven crescentic glomerulonephritis with necrotizing polyangiitis. She was treated with glucocorticoid pulse and subsequent intravenous cyclophosphamide therapy for remission induction therapy. Although she was hemodialysis dependent, she had maintained complete remission with negative MPO-ANCA on oral prednisolone 7 mg/day and Mepolizumab until 3 months prior to admission. Then she was infected with COVID-19 and was treated with Sotrovimab. After 1 month from the COVID-19 onset, she developed bronchopneumonia with hemoptysis. CRP and MPO-ANCA were slightly elevated. Antibiotic treatment did not improve her symptoms, laboratory and CT findings. She was hospitalized for dyspnea. A chest CT scan showed bilateral ground glass opacities. Bronchoalveolar lavage fluid indicated diffuse alveolar hemorrhage. She was diagnosed with a major relapse of EGPA. Reinduction therapy with glucocorticoid pulse, plasmapheresis, and intravenous cyclophosphamide, was done. Here we report a rare case of EGPA major relapse under Mepolizumab treatment possibly triggered by COVID-19 infection.

W105-3

A case of ANCA-associated vasculitis with incidentally noted asymptomatic multiple cerebral infarcts

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Conflict of interest: None

A 73-year-old man was admitted to our department with suspected ANCA-associated vasculitis because of numbness in both lower limbs, CRP: 5.2 mg/dl, MPO-ANCA: 79.9 U/ml, Cre: 1.42 mg/dl. Nerve conduction studies revealed axonal damage, which was thought to be due to vasculitis. Head MRI showed multiple cerebral infarcts in the acute to subacute stage, which were thought to be caused by vasculitis. We diagnosed ANCA-associated vasculitis. He was treated with a half-pulse steroid therapy, followed by PSL 1.0 mg/kg, and two courses of rituximab, which resulted in improvement of the organ involvement. Cerebral infarction due to ANCA-associated vasculitis is a very rare organ lesion. Cerebral infarction is often noted with the onset of central nervous system symptoms. It is rare for asymptomatic cerebral infarction to be noted incidentally as in this case. Of the 220 patients diagnosed with ANCA-associated vasculitis between September 2002 and September 2022 at our hospital, head MRI was performed in 103 cases, of which two cases, including the present case, were associated with asymptomatic cerebral infarction. Early detection of cerebral infarction due to ANCA-associated vasculitis is important, but the possibility of asymptomatic cerebral infarction should be kept in mind.

W105-4

Systemic small vessel vasculitis accompanied by Epstein-Barr virus associated lymphoproliferative disorder

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Conflict of interest: None

A 77-year-old man presented with a fever and generalized erythema. He didn't respond to antibiotics. His renal dysfunction, glomerular hematuria, urinary cast, and proteinuria developed. Small vessel vasculitis was suspected, but MPO-ANCA and PR3-ANCA were negative. Biopsied specimen from his right inguinal lymph node showed EBER ISH positive, CD15 negative, CD20 positive large B lymphocytes. He was diagnosed with Epstein-Barr virus associated lymphoproliferative disorder (EBV-LPD). Despite rituximab (RTX) therapy, his fever and renal dysfunction worsened, and diffuse alveolar hemorrhage (DAH) appeared. Renal biopsy specimen showed focal segmental mesangial melting, lumen narrowing, endothelial enlargement in the arterioles and lymphocytic infiltration of the interstitium and tubulitis. He was diagnosed with systemic small vessel vasculitis accompanied by EBV-LPD. We added intravenous methylprednisolone pulse and high-dose oral prednisolone (PSL), and his fever, respiratory failure and renal dysfunction were improved. Whole blood EBV-DNA got negative. Vasculitis remained in remission with RTX and low-dose PSL. No similar reports to date. We should consider small vessel vasculitis accompanied by EBV-LPD when a single cause cannot explain the clinical course.

W105-5

A case of paraneoplastic vasculitis associated with solid tumor, complaint of abnormal skin sensation

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Conflict of interest: None

A 72-year-old woman came to the hospital with a chief complaint of abnormal skin sensations on bilateral axillary that had persisted for a month. Mild lower leg edema and decreased vibration sense was seen, but purpura was not seen. Laboratory test showed slightly elevated CRP, and CT scan showed panniculitis on both upper limbs to trunk, intrahepatic cholangiocarcinoma, multiple liver metastases, and multiple lymph node metastases. A skin biopsy revealed leukocytoclastic vasculitis associated with intrahepatic cholangiocarcinoma. Nerve conduction studies indicated multiple mononeuropathy. The intrahepatic cholangiocarcinoma and lymph node metastases as well as liver metastases were reduced by chemotherapy, and the patient's abnormal skin sensation improved after the start of chemotherapy. Paraneoplastic vasculitis represents 2-5% of all types of vasculitis, being more frequently associated with hematological tumors than with solid tumors. We report on vasculitis associated with solid tumors with a review of the literature.

W105-6

Polyarteritis nodosa in a patient receiving combination therapy with ipilimumab and nivolumab

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Conflict of interest: None

[Case] A 41-years-old man who was diagnosed with metastatic lung adenocarcinoma (stage IVA) was undergoing radiotherapy and chemotherapy with ipilimumab, nivolumab, pemetrexed and carboplatin. He was continued combination therapy with ipilimumab and nivolumab, and achieved the complete remission. One year after the start of treatment, he presented peripheral circulatory disturbance with necrosis of the fingers and toes, multiple ulcer and livedo reticularis. He was diagnosed with polyarteritis nodosa by skin biopsy, and cerebral infarction from right basal ganglia to corona radiata was detected by MRI of the head. He was treated with oral prednisolone 45 mg/day, and since necrosis of the finger expanded, alprostadil, warfarin and sarpogrelate were added sequentially. Subsequently, the skin lesion improved, and we tapered oral prednisolone from the 30th hospital day. He was discharged on the 48th hospital day without relapse. Although ipilimumab and nivolumab was discontinued from the onset of polyarteritis nodosa, lung cancer has not recurred. [Discussion] Upregulation of the immune system with immune checkpoint inhibitors (ICIs) has been recognized as a risk for developing autoimmune diseases; however, cases of developing polyarteritis nodosa during administration of ICIs are rare.

W106-1

Detection of inflammation in deltoid ligament in medial ankle by power Doppler ultrasound in inflammatory rheumatic diseases

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Conflict of interest: Yes

[Objective] To evaluate the significance of inflammation in deltoid ligament (DL) in medial ankle by power Doppler (PD) ultrasound (US) in inflammatory rheumatic diseases. [Methods] We reviewed the record of musculoskeletal US examined in Japanese Red Cross Medical Center between Jan. 2019 and Oct. 2022. In patients with PD signals in DL, US images and medical records were evaluated. Patients only with traumatic or degenerative disorders were excluded. [Results] PD signals in DL were detected in 18 patients including 8 SpA (2 PsA and 6 uSpA), 5 RA, 4 crystal-induced arthritis (CIA) (3 gout and 1 CPPD) and 1 Sjögren's syndrome. PD signals tended to locate close to outer surface of DL in RA while those tended to locate over the layers of DL in SpA. In all CIA patients, hyperechoic materials were detected in DL. By analysis of other pathologies near medial ankle, inflammation in tibialis posterior or talonavicular joint were revealed to coexist frequently in SpA while talocrural synovitis were revealed to coexist frequently in CIA. [Conclusions] Inflammation in DL can be detected by PDUS in patients with SpA, RA and CIA. Although the prevalence in each groups were not determined, it may be speculated that the frequency of inflammation in DL may be relatively high in SpA patients.

W106-2

The relationship between active ultrasound synovitis of metacarpophalangeal joints and neuropathic condition of the palmer digital nerves

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Conflict of interest: None

[Objective] The objectives of this study were to analyze the presence of dimensional alterations of the palmar digital nerves, particularly in terms of increased cross-sectional area (CSA), and to determine the variables associated with increased CSA, in RA patients. [Methods] We included 86 RA patients who underwent ultrasound examination of the 2nd to 5th metacarpophalangeal joints and digital nerves of the clinically more involved hand by an operator blinded to the clinical assessment. The assessment of synovial activity (Grade 0-3) and measurement of the CSA of each pair of palmar digital nerves were performed. CDAI, QuickDASH, and the presence of neuropathic pain features using the PainDetect Questionnaire (PDQ) were also assessed and analyzed the relationship with CSA. [Results] The CSA of the palmar digital nerves taken individually was 1.9±1.1 mm2 and 3.5±1.9 mm as a pair for finger. There was a statistically significant association with the presence of synovitis and its grade, disease activity and erosive status. Moreover, the association between PDQ and CSA was observed. [Conclusions] The presence of active synovitis correlates with an increased CSA of the palmar digital nerves. The relationship between neuropathic condition and CSA was suggested.

W106-3

Topology learning using unsupervised AI and AI-based automatic storage of the same ultrasound image site

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Conflict of interest: Yes

[Objective] Ultrasonography is helpful in the treatment of rheumatoid arthritis, but its examination time is extended. However, we have come to question whether accurate three-dimensional ultrasound is essential. When humans see ultrasound images, they can compare them in their minds without accurate three-dimensionalization. We are learning in a topological space where distances are not exact, but connections are precise. Therefore, the relationship of ultrasound images could be transformed into a topological space using AI to search images by image. We report on our study of whether we can use this method to detect the same cross-section in healthy subjects automatically. [Methods] We used 80,000 images obtained from 8 healthy subjects as the teacher images and trained an unsu-

pervised topological space transformation AI using CNN and UMAP (a dimensionality reduction AI). We verified whether it is possible to detect the same cross-section by using the distance in the topological space. MATLAB (Mathworks) was used as the programming environment. [Results] The training time was relatively fast, 25±11 minutes, and the detection time was 22±10 seconds. The advantage of this system is that it can detect the same cross-section without recording the area where the image was taken.

W106-4

Usefulness of contrast-enhanced joint MRI serial imaging in polymyalgia rheumatica

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Conflict of interest: None

Objective: To identify factors contributing to the diagnosis and differentiation of polymyalgia rheumatica (PMR) by contrast-enhanced joint Magnetic Resonance Imaging (MRI) serial imaging. METHODS: 97 patients diagnosed with PMR and underwent ultrasound (US) were included. 21 of the 97 patients underwent serial contrast-enhanced joint MRI imaging (both hands and fingers, both shoulders, and both hips). We compared the PMR alone group to the group (EORA/PMR) diagnosed with EORA within 1 year of PMR diagnosis. RESULTS: 1. Grayscale (GS) ≧2, power Doppler (PD) ≧1, and RF positive were all significantly more prevalent in EORA/PMR; 2. Contrast-enhanced MRI of both shoulder showed significant enhancement effects on the long head biceps tendon, subacromial bursa, glenohumeral joint, supraspinatus, infraspinatus, and subscapularis muscles in PMR and EORA/PMR, compared to the control group; 3. Both shoulder contrast MRI showed significantly more fluid accumulation around the left bicipital long head tendon in PMR. No significant differences were found in both hip contrast MRI. CONCLUSION: Serial contrast-enhanced joint MRI serial imaging may be useful in conjunction with US for diagnosing and differentiating PMR and differentiating EORA.

W106-5

A prospective study of cervical lesion and global spine alignment in rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study is to reveal the occurrence of development of cervical disorders in our rheumatoid arthritis (RA) patients and longitudinal changes in patient-based evaluation. [Methods] A total of 125 RA patients were prospectively reviewed and followed for 2 years. Patients who showed either AAS, VS, or SAS at the enrollment were classified as group C and the others as group N. We investigated medications, disease activity, various cervical and global spine parameters, neck pain, and HAQ-DI at the enrollment and 2 years. [Results] Cervical disorders were noted in 31 patients at the enrollment (group C) and in 29 patients at 2 years. In the group C, the prevalence of neck pain increased from 39% to 52%. The mean HAQ-DI increased from 1.1 to 2.5, and was significantly higher in group C than in group N ($p<0.001$). The mean Ranawat progressed significantly in group C. Cervical and global spine alignment did not differ significantly between the two groups. [Conclusions] There was no development of cervical disorders in our RA patients during 2-year period. The results suggest that our treatments has prevented the development of cervical disorders. However, cervical disorders progressed neck pain and QOL due to deteriorate disease activity.

W106-6

Effects of morphological features on high-resolution CT (HRCT) on lung ultrasound B-line in connective tissue disease-associated interstitial lung disease (CTD-ILD)

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Conflict of interest: None

[Objective] There were differences in morphological features of interstitial lung disease (ILD) on chest HRCT between systemic sclerosis (SSc) and idiopathic inflammatory myopathy (IIM). We investigated effects of morphological features of HRCT on total B-lines (TB) by lung ultrasound (LUS) individually in SSc and IIM. [Methods] 29 patients with SSc-ILD and 34 with IIM-ILD were selected from a single-center prospective LUS registry. The HRCT score consisted of ground-glass opacity (GGO), fibrosis, and honeycombing (HC) in SSc-ILD, while consolidation (CS) was substituted for HC in the modified score in IIM-ILD. Correlations of TB with morphological features on HRCT were assessed using a single regression model, and multiple regression analysis. [Results] TB was significantly correlated with the HRCT score, fibrosis and HC in SSc-ILD, and with the modified score, GGO and CS in IIM-ILD. The independent morphological features associated with TB were fibrosis and HC in SSc-ILD, and fibrosis and CS in IIM-ILD. [Conclusion] The ILD morphological features on HRCT associated with the LUS TB were different among the underlying CTDs.

W107-1

A case of C7 deficiency

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Conflict of interest: None

[Case] A 46-year-old woman had arthralgia two weeks before the visit to our hospital, and prednisolone had started. She was suspected of vasculitis syndrome because of the appearance of purpura, and was admitted. Blood culture revealed that 2 aerobic bottles were positive for Neisseria gonorrhoeae, and the pharyngeal gargle fluid was PCR-positive, and we diagnosed her with disseminated gonococcal infection (DGI). We stopped prednisolone and started antimicrobials, so fever and skin rash improved. Screening tests showed low CH50, normal C3 and C4 values, and cold activation was ruled out. We considered her to complement deficiency of C5 to C9. Genetic analysis revealed a large deletion of heterozygous for C7, and we diagnosed her with C7 deficiency. [Consideration] C5-C9 deficiency may be related to infection with Neisseria spp, such as Neisseria meningitidis and Neisseria gonorrhoeae. DGI occurs in 0.5%-3% of infected patients and is related to complement deficiency, SLE, and eculizumab use, and this case is most likely C7 deficiency. Reccurent infections such as pneumococcus, Neisseria meningitidis, and Haemophilus influenza type b and DGI are sometimes based on complement deficiency. Complement screening tests should be considered especially in patients with no risk of infection.

W107-2

Adult onset phalangeal microgeodic disease successfully treated with diltiazem

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Conflict of interest: None

A man in his 30s had swelling, pain, and redness in his fingers which appeared only in winter from year X-5. He was treated symptomatically, however, those symptoms didn't improve. He visited our hospital in December X because of its exacerbation. Physical examination revealed tenderness, dark reddish change and coldness near the DIP and PIP joints, whereas echography showed no evidence of synovitis. X-rays didn't show bone erosions and immunoserological tests were negative. MRI showed diffuse T2 and FLAIR signal enhancement in the bone marrow of distal and middle phalanges without evidence of osteomyelitis or bone tumor, which led to the diagnosis of phalangeal microgeodic disease (PMD). PMD mainly develops in the middle phalanges of children. Although the etiology is assumed to be intraosseous microcirculatory dysfunction due to cold exposure, the detail is unknown. Treatment is symptomatic such as warming and analgesics. We started diltiazem in December X+1 expecting a vasodilator might be effective. The symptoms improved markedly and the MRI signal enhancement disappeared. Thereafter he takes diltiazem only during winter. PMD rarely develops in adults, thus we discuss the pathophysiology, epidemiology, and treatment with the literature.

W107-3

A case of Intravascular Large B cell Lymphoma with POEMS syndrome like symptoms diagnosed by multiple bone marrow biopsies

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Conflict of interest: None

A 68-year-old man visited family doctor with complaints of numbness in both lower limbs for the past 3 months. Tehre were no findings suggestive of vasculitis or infection. Splenomegaly, high sIL-2R level were pointed out, but no malignant findings on biopsy of bone marrow aspiration. He was transferred to our hospital for further examination due to high plasma VEGF level. Neither serum immunoelectrophoresis showed M protein nor pleural effusion, ascites, or lymphadenopathy. Bone marrow biopsy, splenic biopsy, and random skin biopsy were performed, but no malignant findings were observed. The patient was treated with PSL. Fever and pancytopenia improved, but during tapering of PSL, worsening of pancytopenia was observed, so a bone marrow biopsy was performed again. The bone marrow showed CD20+ large nuclei of lymphocytes and a similar intravascular infiltrate, so the patient was diagnosed as intravascular large B cell lymphoma (IVLBCL) and started chemotherapy. IVLBCL is difficult to detect by imaging studies, and the symptoms are diverse, ranging from nonspecific symptoms to neurological and cutaneous symptoms. It is important to recognize that a suspected case cannot be ruled out until another definitive diagnosis is made, and multiple biopsies should not be hesitated.

W107-4

A case of acquired thrombocytopenic purpura (TTP) whose ADAMTS13 inhibitor was negative at onset and became positive at the time of relapse

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Conflict of interest: None

[Case] A 63-year-old woman was admitted to our hospital with upper abdominal pain for 4 days. She received transfusion of red blood cells and fresh frozen plasma for severe anemia and thrombocytopenia, but cardiac arrest occurred and cardiopulmonary assist was required. Two days later, she was diagnosed as thrombotic microangiopathy (TMA), when ADAMTS13 activity was 16% and ADAMTS13 inhibitor was negative. Antinuclear antibodies and anti-SS-A antibody were positive, but she had no connective tissue disease. TMA improved after treatment of plasma exchange and steroids. 4 months later, ADAMTS13 activity declined from 59% to 4%, but inhibitor remained negative. 10 months later, TMA relapsed and inhibitor was detected for the first time, which led to the diagnosis of acquired TTP. With continued low-dose steroids and rituximab, there has been no relapse. [Conclusion] Previous report showed that in some acquired TTP patients autoantibodies binding to ADAMTS13 does not neutralize protease activity. In such cases, ADAMTS13 activity is reduced, while inhibitor test with Bethesda assay is normal. Also, the sensitivity of ADAMTS13 inhibitor test in acquired TTP patients with neutralizing antibody is not high. Acquired TTP cannot be ruled out with the negative result of ADAMTS13 inhibitor.

W107-5

Three cases of Rheumatic meningitis cured by early diagnosis and treatment on MRI findings and CSF analysis

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Conflict of interest: None

[Background] Rheumatoid meningitis (RM) is a rare Central Nervous System manifestation that can occur in rheumatoid arthritis (RA). We report three cases of RM that cured by early diagnosis and treatment on MRI findings and cerebrospinal fluid (CSF) analysis. [Case 1] A 66-year-old man with RA for 13 years, remitted with methotrexate (MTX) and tofacitinib. He had headache, abnormal behavior, and seizures since 1 month before. [Case 2] A 49-year-old woman with RA for 6 months, remitted with MTX. She had intermittent headache, transient right hemiplegia and speech disorder since 1 month before. [Case 3] 76-year-old woman with RA for 4 years, remitted with MTX and baricitinib. She had feeling of left leg weakness since 1 month before. [Case 1-3] In all cases, CSF analysis revealed mononuclear cell dominant and elevated anti-CCP antibody index. MRI showed hyperintense signal in cerebral lobes on DWI images and leptomeningeal enhancement to gadolinium. They were diagnosed with RM and started on high-dose methylprednisolone, which was subsequently switched to oral prednisolone. [Conclusion] All three cases cured by early intervention. It is important to promptly recall RM when RA patients present with neurological symptoms.

W107-6

A case of anti-RNP antibody-positive idiopathic pulmonary arterial hypertension that responded to immunosuppressive therapy

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Conflict of interest: None

A 34-year-old woman admitted our hospital for registration for a lung transplantation. She was diagnosed with pulmonary hypertension three years earlier on the basis of dyspnea on exertion and elevated mean pulmonary artery pressure (mPAP) of 62 mmHg by right heart catheterization. She was treated with macitentan, epoprostenol and riociguat, but the mPAP was as high as 50 mmHg. Because of her positivity for anti-RNP and anti-ssDNA antibodies, she was referred to our department. Although she met no classification criteria of collagen diseases, immunosuppressive therapy was performed assuming background immunologic process. One week after the start of prednisolone administration, her dyspnea was improved. Three weeks later, the mPAP decreased to 38 mmHg. Intravenous cyclophosphamide was administered based on the efficacy of prednisolone. We continued the therapy but discontinued it due to repeated catheter-related bloodstream infections. Discussion: There are no reports on the efficacy of immunosuppressive therapy for patients with pulmonary hypertension that are autoantibody positive but do not meet the criteria for collagen disease. Immunosuppressive therapy can be a treatment option for such cases but should be carefully considered because infection can exacerbate the prognosis.

W108-1

Antimicrobial peptide dermcidin binds to NLRP3 inflammasome and inhibits IL-1b secretion

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Conflict of interest: None

[Objective] Inflammasome is a protein complex mainly composed of signal recognition molecules such as NLRP3, adaptor protein ASC, and effector protein caspase-1 and receives danger signals such as PAMPs and DAMPs to induce inflammatory responses. Although regulatory proteins that bind to inflammasomes, such as NEK7 have been discovered, other factors are still unclear. we previously searched for proteins that bind to NLRP3 inflammasome in THP-1 cells by immunoprecipitation experiments and found that dermcidin, an antimicrobial peptide, binds to ASC and caspase-1 (Kobayashi, Kataoka, et al. JCR2022). In this study, we investigated the effects of dermcidin on NLRP3 inflammasome function. [Methods] THP-1 cells, whose dermcidin expression was suppressed by RNA interference, were treated with 0.5 μM PMA for 3 hours followed by 100 μg/mL MSU, an NLRP3 inflammasome activator, for 6 hours. IL-1b or IL-18 concentrations were measured by ELISA. [Results] IL-1b concentration tended to increase in dermcidin knockdown cells compared to control cells under NLRP3 inflammasome activation, but no difference was observed in IL-18 concentration. [Conclusions] Dermcidin binds to NLRP3 inflammasome and inhibits IL-1b secretion, but does not affect IL-18 secretion.

W108-2

Two cases of myositis fasciitis syndrome in identical twins with the V585I homo variant of the CARD14 gene successfully treated with infliximab

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Conflict of interest: None

CARD14 variants give rise to autoinflammatory skin diseases, such as CARD14 mediated psoriasis (CAMPS), but hitherto there have been no case reports of non-dermatological conditions associated with this genetic anomaly. Case 1: A 46-year-old female patient with an identical twin sibling was admitted with severe, acute pain in the extremities. Myositis fasciitis syndrome was diagnosed on the basis of MRI and muscle biopsy findings. High-dose glucocorticoid (GC) therapy was effective, but multiple immunosuppressants were ineffective. Infliximab (IFX) therapy led to long-term remission without GC. Six months after IFX was discontinued, the myositis flared again but promptly resolved after a single IFX dose. Case 2: The patient's sibling was admitted with severe pain in the extremities 18 months after the onset of symptoms in her sister. Myositis fasciitis syndrome was diagnosed on the basis of MRI and muscle biopsy findings. The patient responded only to high-dose GC. However, after IFX was introduced, the GC dosage was able to be tapered off. A genetic analysis of autoinflammation revealed a V585I homo variant of *CARD14*. Neither patient had development of CAMPS, suggesting that the CARD-14 variant in their case may be associated with NFκB-mediated myositis fasciitis syndrome.

W108-3

A case of Familial Mediterranean Fever (MEFV) Gene-related Enteritis

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Conflict of interest: None

(Case) A 15-year-old female. At age 6 she presented with erythema multiforme exudativum, stomatitis, and arthritis. Genetic testing revealed a MEFV mutation (G304R), and was diagnosed with atypical familial Mediterranean fever. Since abdominal pain persisted even after starting colchicine, lower endoscopy was performed. She had an ulcer in her terminal ileum and had a well-marginal ulcer along the ileocecal valve. Capsule endoscopy revealed an ulcer in the terminal ileum and erosion in the jejunum. Lower endoscopy after 6 doses of canakinumab showed no improvement in terminal ileal ulcers and ileocecal ulcers, so the patient was switched to adalimumab. On subsequent endoscopy, the terminal ileum as well as the ileocecal valve ulcer were scarred. Pathological examination revealed severe erosion of the ileal mucosa and chronic active inflammatory cell infiltration accompanied by neutrophils, which improved to mild chronic inflammatory cell infiltration 6 months after switching to adalimumab. (Summary) Canakinumab was used for atypical MEFV. All symptoms except abdominal pain were relieved. Lower endoscopy revealed MEFV Gene-related Enteritis in the ileocecal region. Disappearance of abdominal pain and tissue scarring were observed after switching to adalimumab.

W108-4

Diagnostic treatment with pamidronate is effective in Chronic Recurrent Multifocal Osteomyelitis in children

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Conflict of interest: None

[Purpose] Chronic Recurrent Multifocal Osteomyelitis (CRMO), a rare disease, has no specific markers and is often difficult to diagnose definitively. [Methods] Patients under 16 years of age who were diagnosed with CRMO and started treatment at our hospital over a 14-year period from April 2008 to March 2022 were selected and divided into two groups: a group with no change in diagnosis (CRMO group) and a group with a final change in diagnosis (non-CRMO group). [Results] Nine patients (male: female = 4:5, median age at onset = 8 years) were initially diagnosed with CRMO and started treatment (median age at start of treatment = 11 years). Subsequently, the final diagnosis was changed in 3 cases, resulting in 6 cases in the CRMO group and 3 cases in the non-CRMO group. There were no apparent differences between the CRMO and non-CRMO groups in age of onset or initial blood tests and imaging studies. Pamidronate was used as initial treatment in 6 patients in the CRMO group and 3 patients in the non-CRMO group. No pain resolution was achieved in the non-CRMO group. [Conclusion] In all cases of CRMO with low efficacy of pamidronate in the initial treatment, the final diagnosis was changed in all cases. The efficacy of pamidronate is useful as a diagnostic treatment in CRMO.

W108-5

A case of IL-36Ra deficiency with systemic symptoms and persistent chronic inflammation

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Conflict of interest: None

A 17-year-old man was admitted to our hospital with fever and abdominal pain. His papules persisted mainly on the face at 0~1 years of age, and skin symptoms gradually improved. From the age of 15, abdominal pain, diarrhea symptoms appeared, and fever were observed intermittently. Fever persisted at 38~39°C for 2 days and was 1~2 times a month. At fever, abdominal pain, arthralgia in the knee and ankle joints was noted. Lower gastrointestinal endoscopy showed scattered redness mucosa and aphtha from the sigmoid colon to the rectum, but no ulcer findings. Genetic testing for autoinflammatory diseases (400 genes) showed no variants in *MEFV* and heterozygous nonsense variants in *IL-36RN*, which led to a diagnosis of IL-36Ra deficiency. Colchicine was started after consultation and was effective for fever, but not for other clinical symptoms and inflammatory findings. Many pustular psoriasis patients who develop with gen-

eralized pustular psoriasis have been reported to have IL-36Ra deficiency. In addition, IL-36Ra deficiency with heterozygous *IL-36RN* variants such as this case that is not *IL-36RN* homozygous variants has been reported. This case of IL-36Ra deficiency without skin eruptions since childhood and persistent systemic symptoms and chronic inflammation are rarely reported.

W108-6

Clinical significance of TCR repertoire analysis in multisystem inflammatory syndrome in children (MIS-C) in Japan

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Conflict of interest: None

[Introduction] Multisystemic inflammatory syndrome in Children (MIS-C) is a systemic inflammatory syndrome that develops several weeks after the onset of coronavirus disease 2019 (COVID-19). Although MIS-C cases in Europe and the United States are known to show a specific proliferation pattern by T-cell receptor (TCR) repertoire analysis, it is unknown in Japanese cases. [Methods] Four cases of MIS-C and 1 case of *Yersinia pseudotuberculosis* infection (Ypt) and 2 cases of toxic shock syndrome (TSS) were included in the study. TCR-Vβ repertoire of peripheral blood T cells and serum cytokine analysis (CXCL9, IL-18, sTNF-RII, IL-6, IL-10) were performed. [Results] In 3 of 4 MISC cases, there was a significant proliferation of TCR-Vβ21.3 positive cells in both CD4 and CD8 positive cells. On the other hand, Ypt showed a different pattern with a significant proliferation of Vβ3, and TSS showed a significant proliferation of Vβ3-positive and Vβ18-positive cells. Serum cytokines showed an increase in CXCL9. During the recovery period, the abnormal findings seen in the acute period normalized. [Conclusions] TCR repertoire analysis is useful for the diagnosis and assessments of the disease activity in MIS-C.

W109-1

Synovial osteochondromatosis mimicking juvenile idiopathic arthritis in a boy

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Conflict of interest: None

[Introduction] Synovial osteochondromatosis (SOC) is a rare benign condition in children that have joint pain. We describe the case of a boy with SOC suffering from chronic left shoulder pain and limited range of motion mimicking JIA. [Case] A 9-year-old boy presented with chronic left shoulder pain during exercise for 4 months. There was a swelling of the left shoulder with tenderness. Range of motion limitation of 30°of elevation and 30°of abduction of the left arm was observed. Antinuclear antibody, rheumatoid factor, anti-CCP antibody were all negative. X-ray image showed calcified lesion in the left shoulder, and ultrasonography showed synovial thickening. Range of motion was improved by methotrexate, and adalimumab. Bisphosphonate was administered due to elevation of bone resorption markers and thinning of the left humeral head, which resulted in worsening of range of motion limitation. More than 30 calcified masses were removed by arthroscopic surgery. Since then, there was improvement in the movement. [Discussion] SOC is a rare disease of chronic joint pain in children. SOC was suspected from the imaging examination of this child, but anti-inflammatory treatment was preceded by synovitis, which temporarily improved the limitation of range of motion.

W109-2

Remission Rates and Drug Withdrawal Status of Articular Juvenile Idiopathic Arthritis in our Department

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Conflict of interest: None

[Objective] Some subtype of articular juvenile idiopathic arthritis (JIA) can achieve clinical remission off medication (CR). [Methods] To research the rate of remission and drug withdrawal status, we conducted retrospective observational study on the patients who had visited our department from 2013 to 2022, and who developed articular JIA by 2017. [Results] There were 16 polyarticular JIA (PJIA) patients, including 7 RF-positive PJIA (RF+PJIA) and 9 RF-negative PJIA (RF-PJIA), and 33 oligoarticular JIA (OJIA). CR was achieved in 14% of RF+PJIA, 56% of RF-PJIA, 67% of OJIA. Clinical remission off medication (CRM) was achieved in 86%, 44% and 12%, respectively. In either subtype, patients achieving CR did not receive biologic agents (bDMARDs). 6 (86%), 4 (44%), and 7 (21%) patients was administered bDMARDs, and 0, 2, and 2 patients withdrew bDMARDs, respectively. 2 RF-PJIA and 1 OJIA who withdrew bDMARDs relapsed and required restarting of bDMARDs. 50% of RF+PJIA and RF-PJIA patients had maintained CRM on bDAMRDs monotherapy. [Conclusions] The remission rate varied by subtype of JIA. Some OJIA cases could withdraw bDMARDs, but many PJIA cases, bDMARDs withdrawal was difficult even if CRM was maintained with bDMARDs monotherapy. Further study is desirable on drug withdrawal.

W109-3

Comparisons of clinical features between adult patients with childhood-onset and adult-onset systemic lupus erythematosus

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Conflict of interest: None

[Objective] We aimed to cross-sectionally compare the clinical features between adult patients with childhood-onset and adult-onset systemic lupus erythematosus (SLE). [Methods] The data of Japanese adult patients with SLE at enrolment were retrieved from a large observational cohort database. The clinical features were cross-sectionally compared between the adult patients with childhood-onset and adult-onset SLE. Patients diagnosed under the age of 18 were defined as childhood-onset. [Results] The numbers of the patients, median ages at diagnosis, median ages at enrollment, median disease durations at enrollment of the childhood-onset and adult-onset SLE patients were 18 and 104, 16 and 30 years, 36 and 43 years, and 22 and 12 years, respectively. The daily dosages of glucocorticoids, the SLE Disease Activity Index 2000, the Physician Global Assessment, and the frequency of active lupus nephritis were significantly higher in the childhood-onset SLE patients than those in the adult-onset SLE patients. The Systemic Lupus International Collaborating Clinics Damage Index values were not significantly different between the two groups. [Conclusions] The disease activities of the childhood-onset SLE patients were higher even in their adulthood than those in the adult-onset SLE patients.

W109-4

Comparison of clinical characteristics between prepubertal-onset and pubertal-onset systemic lupus erythematosus: results from prospective cohort study of young patients with systemic lupus erythematosus in Japan (PLEASURE-J)

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Akane Watanabe[16], Kenji Oku[17], Yuko Kaneko[14], Yoshiya Tanaka[13], Keishi Fujio[12], Masakazu Matsushita[18], Nobuyuki Yajima[4], Takashi Wada[6], Atsuko Murashima[3], Ayako Nakajima[19]
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Conflict of interest: None

[Objective] The aim of our study was to investigate influence of age at onset in clinical characteristics of pediatric SLE (pSLE). [Methods] We compared the clinical characteristics of age at disease onset (prepubertal-onset (onset<12 years) and pubertal-onset (onset≧12, <18 years)), using PLEASURE-J study. [Results] Of 263 patients in PLEASURE-J study, pSLE were 47. The median age at diagnosis (IQR) in pSLE were 15.0 (12.0, 16.5). The patients with prepubertal-onset and pubertal-onset were 10 and 37. The prepubertal-onset group had more patients with a urine protein/Cre ratio ≧0.5 g than the pubertal-onset group (44% vs 17%, p= 0.02). Renal biopsies were performed in 6 patients of pubertal-onset group and in 19 patients of pubertal-onset group. All patients showed evidence of lupus nephritis, with class II: 2/class III: 3/class IV: 1 in pubertal-onset group and class II (±V): 6/class III (±V): 4/class IV (±V): 6/class V: 2 in pubertal-onset group. The median levels (IQR) of anti-dsDNA antibodies were higher in pubertal-onset group than in pubertal-onset group (435 (230, 1036) vs157 (11, 400), p=0.09). SELENA-SLEDAI and initial treatment did not differ between two groups. [Conclusions] The proportion of renal impairment was higher in prepubertal-onset group. it is important to focus on age at onset in pSLE.

W109-5

Nationwide clinical epidemiological study of juvenile onset systemic sclerosis in Japan in 2021

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Conflict of interest: None

[Objective] To investigate clinical and epidemiological characteristic of Japanese patients with juvenile onset systemic sclerosis (SSc). [Methods] We conducted a nationwide survey of patients with juvenile SSc diagnosed before the age of 18 years between 2016 and 2020 in Japan and evaluated clinical and epidemiological features. [Results] A questionnaire was returned from132/200 (66%) institutions. We enrolled 137 patients (female, 78.1%, median age at diagnosis, 13.9 years, median disease duration, seven years). Patients with diffuse cutaneous SSc (dcSSc) were more common than those with limited cutaneous SSc (lcSSc) (62.7 vs. 29.1%). Raynaud's phenomenon was the most common feature (89.7%). The most common organ involvement was interstitial lung disease (40.1%), followed by gastroesophageal reflux disease (33.6%), arthritis (16%), myositis (12,4%), and pulmonary arterial hypertension (7.2%). ANA positivity was seen in 80% of the patients. Anti-Scl-70 and anticentromere antibody positivity were identified in 52.6% and 11.7% of patients, respectively. [Conclusions] Patients with juvenile SSc present more frequently diffuse subset. Clinical manifestations in juvenile onset SSc patients in Japan are similar to those of other pediatric populations.

W109-6

A case of primary angiitis of the central nervous system in which transcranial color-coded sonography was useful in determining therapeutic effect

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Conflict of interest: None

Primary angiitis of the central nervous system (PACNS) is a rare disease that causes localized vasculitis of CNS. A 10-year-old girl was suspected cerebral infarction and transferred to our hospital. She had mild right hemiplegia and motor aphasia. Blood and CSF test showed no abnormalities, and VZV-PCR in CSF was negative. MRI showed diffusion restriction in the left middle cerebral artery (MCA) region, wall thickening of the left internal carotid artery (IC), and stenosis of the left MCA. Contrast-enhanced MRI showed multifocal contrast enhancement effects in the left IC, left middle dural artery and branches of the left MCA. Aortitis was not found in CTA, she was diagnosed PACNS and treated with twice of IVMP, IVCY and 1 mg/kg/day of oral prednisolone. IVMP was added since vasculitis in other areas were found in MRI after 3 weeks. Transcranial color-coded sonography (TCCS) revealed left MCA blood flow undetectable at the onset in spite of MRA showed no change in left MCA stenosis after 5 weeks. There are no specific findings in PACNS, and MRI abnormalities may persist for more than 3 months, often making it difficult to determine the therapeutic effect. TCCS was useful in determining the efficacy of treatment to detect slight blood flow difficult to detect on MRI.

W110-1

Fibroblasts in the fascia of dermatomyositis are major CXCL10-expressing cells: RNA-seq analysis of fascial tissues in dermatomyositis

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Conflict of interest: None

[Objective] This study aimed to identify the localization and type of cells expressing CXCL10, which was found to have high expression level by RNA-seq analysis, in the fascia of patients with dermatomyositis (DM). [Methods] RNA-seq analysis was performed on biopsied fascia tissues in patients with DM and polymyositis (PM) before treatment. Next, in situ hybridization (IH) was performed using target probs for CXCL10 and vimentin to identify the localization and type of CXCL10-expressing cells in the fascia. We then quantified the number of CXCL10-expressing cells in the fascia of patients with DM compared with PM. In addition, serum CXCL10 levels were measured by ELISA, and the relationship between

the serum levels and the number of CXCL10-expressing cells in the fascia was analyzed. [Results] IH showed CXCL10 expression in fibroblasts. The number of CXCL10-expressing fibroblasts was significantly higher in patients with DM than PM. Furthermore, the numbers of CXCL10-expressing fibroblasts were positively correlated with the serum levels of CXCL10. [Conclusions] The number of CXCL10-producing cells were significantly higher in the fascia of patients with DM than PM. Our data suggests that fibroblasts in the fascia mainly produce CXCL10 in patients with DM.

W110-2

Development of a human muscle cytotoxic assay with human induced pluripotent stem cell derived CD8+ T cells and muscle cells

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Conflict of interest: Yes

[Objective] Cytotoxic CD8+ T cells (CTLs) play a crucial role in the myoinjury of polymyosits (PM). We aimed to develop a model of CTL-mediated myoinjury utilizing muscle cells and regenerative CTLs (rCTLs) derived from human iPS cells (hiPSCs). [Methods] hiPSCs were established from HLA-A*24: 02+ or HLA-A*24: 02- polymyositis (PM) patients and transfected with a doxycycline (Dox)-inducible MyoD vector. After the culture with Dox, hiPSCs highly expressing MyoD were sorted and re-cultured in undifferentiation medium without Dox. These cells were differentiated into muscle cells in a differentiation condition with Dox. hiPSC-derived rCTLs established from WT1-specific primary CTLs were activated by B cell line presenting WT1 and cocultured with the muscle cells pulsed with WT1. The cytotoxicity of rCTL was evaluated by fluorescence of calcein released from the pre-labeled muscle cells. [Results] HLA-A*24: 02-restricted and antigen-specific cytotoxicity of rCTLs against muscle cells were confirmed. The cytotoxicity was dependent on the number of rCTL and suppressed by tacrolimus. [Conclusions] We established a human cell-derived myoinjury model using hiPSCs. This model would facilitate the analysis on the mechanism of CTL-mediated myoinjury in human and dissect the pathophysiology of PM.

W110-3

Investigation of YKL-40 Involvement in Anti-SRP Antibody-Positive Immune-Mediated Necrotizing Myopathy

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Conflict of interest: None

[Background and Purpose] YKL-40 is involved in tissue repair, inflammation, and tissue injury. Anti-SRP antibody-positive immune-mediated necrotizing myopathy (IMNM) is a muscle disease characterized by myofiber necrosis. It has no lymphocytic infiltration. We have studied the possible role of YKL-40 in muscle destruction in PM/DM, but not in IMNM. In this study, we measured serum YKL-40 levels in IMNM patients and performed immunofluorescent staining of muscle biopsy specimens to verify the difference from PM/DM. [Methods] Serum YKL-40 levels were measured by ELISA and compared with those in healthy controls (HC) and PM/DM patients. Muscle biopsy specimens were stained with anti-YKL-40 antibody and anti-CD68 antibody. [Results and Discussion] The serum YKL-40 level of IMNM patients was 89 ng/mL, which was higher than that of HC patients, but similar to that of PM/DM patients. Immunofluorescence staining revealed YKL-40-positive cells, but CD68 was negative. However, the serum YKL-40 level was high in this study, suggesting that there may be a condition in which the serum YKL-40 level is elevated in IMNM. YKL-40-positive cells were also observed, suggesting the possibility that YKL-40 may be involved in the pathogenesis of IMNM. We need further research to ensure the results.

W110-4

Possible correlation between serum IL-8 levels and the activity of myositis in dermatomyositis

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Conflict of interest: None

[Objective] Anti-nuclear matrix protein 2 (NXP2) antibody-positive dermatomyositis (DM) is characterized by extensive and severe myositis. In this study, we evaluated which cytokines/chemokines involved with the activity of the myositis. [Methods] We performed quantitative immunoassays using the MILLIPLEX® Multiplex Assays Using Luminex to evaluate serum levels of IFN-γ, IL-1β, IL-6, IL-8, IL-12p40, and TNF-α in samples collected over time from a 9-year-old female with anti-NXP2 antibody-positive DM. Serum levels of IL-8 in samples from five patients with anti-NXP2 antibody-positive DM and five patients with anti-TIF1γ antibody-positive DM without both interstitial lung disease (ILD) and malignancy before starting treatments, along with five healthy controls, were also evaluate by ELISA. [Results] In our case, the serum level of IL-8 was elevated when the myositis worsened, and decreased in accordance with the improvement of myositis, suggesting that the serum IL-8 levels were correlated with the myositis activity. Furthermore, serum IL-8 levels were significantly elevated in anti-NXP2 or anti-TIF1γ antibody-positive DM patients with myositis but not ILD, than healthy controls. [Conclusions] It was suggested that serum levels of IL-8 correlate with the activity of myositis in DM.

W110-5

A case of dermatomyositis triggered by COVID-19 infection

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Conflict of interest: None

[Case] A 47-year-old man presented with fever, cough, and malaise after the COVID-19 infection. Eyelid edema, skin rashes, and both upper arms and mechanic's hands were also present. Chest computerized tomography showed interstitial pneumonia. He was admitted to our hospital. Blood tests showed elevated CK 3,380 U/L, anti-ARS antibodies 170.9 U/mL (positive for anti-PL-7 antibodies), and anti-SS-A antibodies >240 U/mL. Magnetic resonance imaging and muscle histopathology also suggested myositis, and a diagnosis of dermatomyositis (DM) was made. Prednisolone 60 mg and tacrolimus 3 mg tended to improve symptoms but failed to reduce CK levels, which were reduced by concomitant high-dose intravenous immunoglobulin treatment. [Clinical Significance] Although various autoimmune diseases are known to occur after COVID-19 infection, there have been few case reports of anti-ARS antibodies-positive DM. On the other hand, a lot of COVID-19 cases with elevated anti-MDA-5 antibody levels as myositis-specific antibodies have been reported. The mechanisms by which COVID-19 infection induces autoantibody, including anti-ARS antibodies, production have been unclear. Further case accumulation is expected.

W110-6

A case of Anti-TIF1-Gamma Antibody-positive dermatomyositis that developed after one dose of immune checkpoint inhibitor (ICI)

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Conflict of interest: None

[Case] The case was a man in his 70s. Pembrolizumab was adminis-

tered for lung cancer. Blood tests before administration showed a normal CK level, no muscle weakness, and no skin findings. However, the face was slightly reddish. Gottron's sign was not observed. Since immune-related adverse event (irAE) myositis was suspected, autoantibody measurements were performed, and prednisolone (PSL) was promptly administered at 1 mg/kg/kg. After the start of treatment, the CK level stopped declining at about 500 U/L. Anti-MDA5 antibody was positive. Steroid pulse therapy was performed because muscle weakness progressed and the CK level increased, and the CK level remained within the normal range., and muscle weakness was improved. [Clinical Significance] We experienced a case of dermatomyositis after ICI administration. Nine cases of irAE myositis that developed at our hospital showed good steroid responsiveness and a rapid decrease in the CK level, but this case was intractable. In cases treated for irAE myositis and exhibiting steroid resistance, there is a possibility of general polymyositis/dermatomyositis, and autoantibody measurement and muscle biopsy are necessary. It is often complicated by myocarditis and requires immediate treatment.

W111-1

A fatal case of anti-MDA-5 antibody-positive rapid progressive interstitial lung disease with atypical symptoms including, arthritis and no skin involvement

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Conflict of interest: None

[Case] A 76-year-old woman visited our Department had joint pain 2 months prior to admission. RF, anti-CCP antibody, and anti-nuclear antibody were negative. After that, she visited our Department again because of mild shortness of breath on exertion. A CT scan showed ground glass opacity and reticular shadows predominantly on subpleural regions in both lungs, and she was admitted to our hospital. Respiratory condition was stable and oxygen administration was unnecessary. Serum CRP level was 0.56 mg/dL, serum ferritin level was 423 ng/mL. On the 7th hospital day, anti-MDA-5 antibody was found to be positive, and anti-MDA-5 antibody-positive rapid progressive interstitial pneumonia (RP-ILD) was diagnosed. She was treated with 1 mg/kg/day of oral glucocorticoid following glucocorticoid pulse therapy, oral tacrolimus, and intravenous cyclophosphamide. However, her respiratory condition deteriorated rapidly on the 43rd hospital day, and she died on the 53rd hospital day. [Clinical Significance] Anti-MDA-5 antibody-positive RP-ILD without skin involvement is rare. Since delayed diagnosis can lead to fatal outcome, chest imaging and anti-MDA5 antibody measurement should be considered in patients with arthritis and mild respiratory symptoms even in the absence of skin involvement.

W111-2

A case of juvenile dermatomyositis complicated with positive anti-MDA5 antibody treated with a triple combination therapy of mycophenolate mofetil (MMF)

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Conflict of interest: None

A 14-year-old female presented with a dermatomyositis specific skin rash and polyarticular pain. She was admitted to our hospital because laboratory studies demonstrated positive anti-MDA5 antibody and she also had respiratory distress and fever. Although she had no decrease in MMT and elevation of creatin kinase, a chest CT scan showed ground-grass opacities. She was diagnosed with clinically amyopathic dermatomyositis (CADM) with positive anti-MDA5 antibody. She was treated with mPSL pulses and then with PSL 1 mg/kg/day and Tac. The addition of cyclophosphamide (IVCY) was considered, but not introduced because the patient was young and the family was very concerned about the effect of IVCY on fertility. So MMF was started. After that, a chest CT scan showed improvement and anti-MDA5 antibody titer and ferritin were steadily declining. CADM has a very high rate of death and the effectiveness of a triple combination therapy with PSL, calcineurin inhibitor and IVCY is widely known. In this case, we first considered the introduction of IVCY. But her family were very concerned about the effect of IVCY on fertility, so we started MMF. There are few reports on the effectiveness of MMF in young CADM patients. MMF may also be an option in cases that side effects of IVCY are concerned.

W111-3

Treatment with baricitinib for anti-MDA5 antibody-positive dermatomyositis with interstitial lung disease: a case report

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Conflict of interest: None

We report a case of a patient with anti-MDA5 antibody (MDA5)-positive clinically amyopathic dermatomyositis (CADM) in whom baricitinib (BLM) was useful for interstitial lung disease (ILD). [Case] A 52-year-old man developed fatigue, dry cough, and exertional dyspnea along with Gottron's papule and mechanic's hands whilst no findings of musculoskeletal involvements, leading to the diagnosis of CADM. A radiographical examination showed ILD, and positivity for MDA5 was found. High-dose corticosteroid (CS) was administered concomitantly with tacrolimus and intravenous infusion of cyclophosphamide (IVCY) because of his progressively showing hypoxia. Exacerbation of respiratory symptoms and radiographical findings, including the appearance of mediastinal emphysema, was progressively found even though rituximab (RTX) was additionally administered. BLM was alternatively administered after ceasing RTX, resulting in remission. [Discussion] The usefulness of concomitantly administering high-dose CS, calcineurin inhibitor, and IVCY, as well as alternatively RTX, has been suggested for achieving remission in rapidly progressive ILD related to MDA5-positive CADM. Our report also suggests that BLM can be a useful agent for refractory patients with this disorder.

W111-4

Rituximab and subsequent belimumab in rapidly progressive interstitial lung disease-complicated anti-MDA5 antibody-positive dermatomyositis: A case report

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Conflict of interest: None

[Background] Rapidly progressive interstitial lung disease (RP-ILD) caused by anti-MDA5 antibody-positive dermatomyositis (DM) is a refractory disease. Guidelines recommends the use of immunosuppressive agents in addition to glucocorticoids (GC) for induction of remission, but little is known about maintenance therapy. [Case] The patient was a 49-year-old female who was reffered to us because of dyspnea and rash for one month prior to the visit. We made a diagnosis of anti-MDA5 antibody (+) DM with RP-ILD. Initial treatment was high-dose GC including steroid pulse therapy in combination with tacrolimus, and IVIG subsequently. The remission was achieved after the introduction of tofacitinib (TOF). Subsequently, the patient developed pulmonary embolism and TOF was discontinued. To maintain remission, rituximab (RTX) 375 mg/m^2 was administered for one cycle, followed by belimumab (BLM) 520 mg IV every 4 weeks and mycophenolate mofetil. The patient had no flare-ups for 2 years thereafter. [Clinical Significance] BLM after RTX has been investigated for treatment of SLE and Sjögren's syndrome, in which BAFF levels increase after B cell depletion. B cells are also considered to be a target in anti-MDA5 Ab+ DM. Then, BLM after RTX may be effective in maintaining remission in the disease.

W111-5

Anti-MDA5 antibody-positive dermatomyositis with Immune thrombocytopenia; a case report

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Conflict of interest: None

A 63-year-old man was referred to our hospital because of interstitial pneumonia. He suffered from worsening dyspnea lasting for 3 months. He was diagnosed with clinically amyopathic dermatomyositis (CADM) due to cutaneous symptoms such as Gottron's papule and polyarthritis without any muscle symptoms. He was positive for anti-MDA5 antibody, and noted severe thrombocytopenia; his platelet count was 5000/μL. No obvious secondary cause for thrombocytopenia was found, and the urea breath test was negative. Bone marrow puncture showed no abnormalities, leading to the diagnosis of immune thrombocytopenia (ITP). He was hospitalized urgently and treated with methylprednisolone 1 g/day for 3 days followed by prednisolone 55 mg/day (1 mg/kg/day) and tacrolimus. His platelets returned to baseline within 2 weeks, and the skin and lung lesions rapidly improved. Anti-MDA5-antibody positive CADM with ITP is rare, and the clinical course varied. The present case may be a rare one with good response to treatment.

W111-6

Sequential development of anti-TIF1-gamma antibody and dermatomyositis after the onset of rash complicated by sarcoidosis

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Conflict of interest: None

A 60-year-old woman with no history of malignancy developed erythema on her arms, and thereafter clavicular part and cheeks. She also had periungual erythema and papules on fingers. Though dermatomyositis was suspected, associated antibodies (anti-TIF1-γ, MDA5, Mi-2, ARS and RNP antibody) were negative. Two years later, she complained of erythema again, which was ameliorated by topical steroid. However, the symptom recurred, and she became anti-TIF1-γ antibody positive. Creatine kinase (CK) was normal, and she had no muscle weakness. CT showed no findings of interstitial pneumonia. 7 month later, she got necessity of rest for walking. She had myalgia on her arms and thighs, and CK significantly elevated to 275 U/L. CT revealed new nodules in lungs and hilar lymphadenopathy. Biopsy from the lymph nodes showed epithelioid cell granulomas. The findings of dermatomyositis do not necessarily develop at the same time, and it sometimes leads to the struggle to make the diagnosis. In this case, while anti-TIF1-γ antibody was negative at the onset of rash, it became positive and she presented the findings of myositis afterwards. Also, she had pathological evidence of sarcoidosis. We discuss the clinical course of this case and review the association between sarcoidosis and dermatomyositis.

W112-1

Relationship between Work Status, Disease Activity, and Drug Costs in Patients with Rheumatoid Arthritis - Analysis on NinJa database using Propensity Score Matching

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Conflict of interest: None

[Objective] To explore the relationship between work status, disease activity, and drug costs in patients with rheumatoid arthritis (RA). [Methods] RA patients data including work status were extracted from NinJa2020, and were classified into two groups: those engaged in labor (working group) and those unemployed non-working group (W-). Disease activity, HAQ-DI, medications, and drug costs were compared between the two groups of 1755 each after adjustment for age, gender, disease duration, BMI, and tender/swollen joint counts using propensity score matching. [Results] W- group had significantly higher DAS28CRP (2.24 ± 0.98 vs. 2.07 ± 0.93), SDAI (6.53 ± 6.63 vs. 5.44 ± 6.21), HAQ-DI (0.75 ± 0.86 vs. 0.34 ± 0.52), glucocorticoids use (37% vs. 28%), costs of bDMARDs (¥24,999 ± 45,701 vs. ¥19,179 ± 39,755/mo), and total costs of all DMARDs (¥38,856 ± 51,416 vs. ¥31,303 ± 45,650/mo) than working group, while MTX use (53% vs. 63%) was significantly lower in W-. There were no significant differences in b/ts DMARDs usage rate, and cs/ts DMARDs costs. [Conclusions] Unemployed RA patients had higher disease activity and more advanced physical impairment despite higher drug costs compared to employed patients.

W112-2

COVID-19 and patient behavior in our department

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Conflict of interest: None

Purpose We will understand how the Covid19 epidemic since January 2020 affected the medical care of our department, and find out the issues of medical care in the post Covid19. [Methods] We compared the clinical results (number of outpatients referred, total number of outpatients) in 2020 and 2021 with those in 2018 and 2019. [Results] The number of referred patients and the total number of outpatients were 131 and 5260 in 2018, 128 and 6033 in 2019, 134 and 6382 in 2020, 144 and 6630 in 2021 respectively. There was no decrease in the number of outpatient referrals and the total number, and the total number was on the increase. No significant change was observed during the Covid19 epidemic in our district, nor was the number of patients examined by month. [Conclusion] Although there was no significant change in patient behavior due to the Covid19 epidemic, there was a decline in hospital functions. In the future, it was considered necessary to further enhance cooperation between hospitals and clinics.

W112-3

Serial changes in anxiety related to corticosteroid from the initiation of therapy to discharge from the hospital

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Conflict of interest: None

[Object] We aimed to evaluate the serial changes in anxiety levels related to corticosteroid use. [Methods] This study included 18 patients treated with corticosteroids for autoimmune diseases. The degree of anxiety toward corticosteroid use was assessed by the visual analogue scale. Comprehension of drug characteristics and use was assessed using a Likert scale. The State-Trait Anxiety Inventory (STAI) was also surveyed. The surveys were conducted immediately before the initiation of corticosteroid therapy and just before discharge from hospital. [Results] Anxiety levels related to corticosteroids decreased before discharge when compared to the levels before initiation of therapy ($p < 0.001$). STAI scores were also decreased ($p < 0.05$). However, the change in anxiety levels related to corticosteroid use did not show a correlation with the changes in STAI. Contrastingly, patients who had a poor understanding of the drugs showed little or no changes in their anxiety levels related to corticosteroid use at discharge ($p < 0.05$). [Conclusions] Some aspects of anxiety related to corticosteroids may be groundless, which is caused by unsubstantiated assumptions without a complete understanding of corticosteroids.

W112-4

The clinical experience of nintedanib use for treatment of rheumatoid arthritis with Interstitial lung disease in our hospital

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Conflict of interest: None

Background: Rheumatoid arthritis with interstitial lung disease (RA-ILD) has not established clear evidence for diagnosis and treatment. In recent years, INBUILD trial showed that nintedanib suppresses respiratory function deterioration in interstitial lung disease with progressive fibrosis (PF-ILD). Methods: We retrospectively reviewed the clinical course of 3 patients treated with nintedanib for RA-ILD in our hospital, focusing on the following points. 1) age & gender, 2) imaging findings on HRCT, 3) VATS or BF, 4) duration and side effects of nintedanib administration, 5) treatment of RA, 6) changes in respiratory status. Result: Case 1: 1) 58 y.o., male, 2) alternative diagnosis pattern, 3) lymphocyte predominance in BF, 4) 1 year, decreased dose due to diarrhea, 5) tacrolimus + steroid, 6) home oxygen therapy introduction. Case 2: 1) 69 y.o., male, 2) possible UIP pattern, 3) diagnosed with IPF by MDD after VATS, 4) 2 years, decreased dose due to liver failure, 5) tacrolimus, 6) over time decline. Case 3: 1) 69 y.o., male, 2) possible UIP pattern, 3) macrophage predominance after BF, 4) 6 months, well tolerated, 5) tacrolimus + abatacept, 6) over time decline. Conclusion: The introduction of nintedanib for PF-ILD is also an option for RA patients with preceding ILD.

W112-5

Two cases of rheumatoid arthritis-related severe interstitial pneumonia that could be saved by drug therapy including JAK inhibitors and multidisciplinary treatment

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Conflict of interest: None

[Background] Acute exacerbation of interstitial lung disease associated with rheumatoid arthritis (RA-ILD) has a high mortality, but no treatment has been established. We report two cases of RA-ILD that could be saved by JAK inhibitors and multidisciplinary treatment. [Case 1] A 65-year-old woman who had a 25-year history of RA developed ILD 3 years ago. She stopped peficitinib (PEF) due to herpes zoster. She was hospitalized for aspiration pneumonia and had an acute exacerbation of RA-ILD. She did not respond to steroid pulse and intravenous cyclophosphamide (IVCY), and was started on intubation and ventilator management. She required catecholamine use and continuous hemodiafiltration. After PEF was resumed, the progression of lung lesions stopped. [Case 2] A 75-year-old man who developed RA 3 years ago and was taking methotrexate and PSL. He developed acute prostatitis and had an acute exacerbation of RA-ILD. He did not respond to steroid pulse, then was started on intubation and ventilator management. After tofacitinib and IVCY was started, he was extubated and discharged. [Conclusion] We considered JAK inhibitors as a potential treatment option for acute exacerbation of RA-ILD.

W113-1

A case of Sjögren's syndrome presenting with active sialadenitis and improvement of salivary gland ultrasound findings after glucocorticoid therapy

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Conflict of interest: None

[Case] A 28-year-old woman diagnosed with rheumatoid arthritis 5 months earlier was referred to our clinic because of parotid swelling for the past 3 months. An MRI at the referring hospital showed multiple small cysts in the parotid and submandibular glands, and Sjogren's syndrome (SS) was suspected. She had a history of parotid swelling a few years earlier, which resolved with antimicrobial therapy. She had no history of smoking or pregnancy. At the initial visit, she had no joint swelling or tenderness, and both parotid glands were enlarged and tender. She was unaware of ocular and oral dryness, and Saxon test was 2 g/2 min. Salivary gland ultrasound (SGUS) showed diffuse hypo/anechoic areas and vascular signals in both parotid and submandibular glands (OMERACT GS3/PD3). Blood tests were positive for anti-SS-A, RF, and anti-CCP, negative for anti-SS-B, no elevation of IgG or IgG4, and no hypocomplementemia. She was diagnosed with SS with active sialadenitis and started on prednisolone 20 mg every other day. Prednisolone was tapered off over 10 weeks, and follow-up SGUS showed an improvement in the hypo/anechoic areas and vascular signals. [Implication] The SGUS findings in this case suggest a reversible pathology of sialadenitis and may be useful for patient stratification.

W113-2

The impact of hypergammaglobulinemia on developing extraglandular lesion during the course of Sjögren's syndrome

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Conflict of interest: None

[Objective] To reveal whether the incidence of extraglandular lesions that develop during the course of Sjögren's syndrome (SS) was different between patients with/without hypergammaglobulinemia at the time of diagnosis. [Methods] This was a single, retrospective study enrolling patients who were diagnosed with primary SS from August 2005 to October 2021. Major extraglandular lesions were defined as joint, skin, pulmonary, and renal lesions, cytopenia, peripheral or central neuropathy, and development of lymphoma. We evaluated the risk of hypergammaglobulinemia using Kaplan Meier method, Cox proportional hazard models. [Results] A total of 306 cases were included, with an average age of 57.6 years and a median follow-up period of 1234 days. The cumulative incidence of major extraglandular lesions was 41% in the high-IgG group and 18% in the non-high-IgG group at 3 years. Cox regression analysis showed that hazard ratio in the high-IgG group was 2.45. In addition, hypocomplementemia was observed in the high-IgG group, but there was not significant difference between the low-C4 group and the non-low-C4 group about development of extraglandular lesions. [Conclusions] SS patients with hypergammaglobulinemia suggested to be carefully followed up to detect extraglandular lesions.

W113-3

Investigation of interstitial lung disease in primary Sjögren's syndrome

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Conflict of interest: None

[Background] Interstitial lung disease (ILD) is one of the most critical organ lesions in primary Sjögren's syndrome (pSS); however, it is often asymptomatic and non-progressive. [Methods] We retrospectively reviewed 20 pSS patients with ILD who attended our hospital or had been admitted between 2010 and 2022 and analyzed the data at the time of the initial examination. [Results] The mean age of the patients was 77 years, and the mean disease duration was 86 months. Of the 20 patients, 8 were in the advanced group, and 12 were in the non-advanced group. The patients in the advanced group required intervention with prednisolone combined with azathioprine or tacrolimus; six had an improvement in %FVC, one had no improvement, and one had a decrease in %FVC, which was not treated due to other serious complications. Retrospective analysis of the data from the first visit showed that the advanced group had higher IgG (2868 vs. 1916 mg/dl, $p< 0.01$), RF (187.5 vs. 13.1 U/mL, $p< 0.05$), and KL-6 (2211 vs. 979 U/mL. $p< 0.01$) than the non-advanced group. [Conclusion] While some pSS patients with ILD do not require therapeutic intervention, others should be treated with immunosuppressant. The treated patients had higher IgG, RF, and KL-6 levels at the time of the initial examination.

W113-4

Distinguishing Sjögren's Syndrome with Myopathy from Polymyositis with Sjögren's Syndrome

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Conflict of interest: None

[Objective] To investigate how to distinguish Sjögren's syndrome (SS) with myopathy from polymyositis (PM) with SS. [Methods] This is a retrospective study reviewing the medical records of patients with SS and those with PM. Evaluated items were age, gender, autoantibodies, maximum values of CK, and organ damage. Mi-2, Ku, PM-Scl100, PM-Scl75, SRP, Jo-1, PL-7, PL-12, OJ, EJ, Ro-52 were tested using the BML myositis-related autoantibody set. [Results] Six SS with myopathy (all females, 63 y.o. on average) and 6 PM with SS (5 females and a male, 66 y.o. on average) were involved in this study. SS patients were positive for anti-SS-A (3 cases) and Ro-52 (2 cases). All PM patients showed positive results for any myositis-related autoantibodies, and 3 patients were additionally positive for anti-SS-A. In CK levels, SS showed 235-6640 mg/dl, and PM 868-3930 mg/dl (no statistical difference). Pulmonary involvement developed in one SS and 2 PM. Cardiovascular involvement developed in one SS (pulmonary hypertension) and one PM (cardiomyopathy). All SS and PM patients were treated with PSL. Two PM patients used TAC. MTX was used for 2 SS and 2 PM. Two SS and 2 PM were treated with AZP. [Conclusions] The autoantibody pattern is the only item to distinguish SS with myopathy from PM with SS.

W113-5

Sjögren's syndrome with purpura due to IgA rambda monoclonal gammopathy secondary to thymic MALT lymphoma

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Conflict of interest: None

A 67-year-old woman presented with purpura of the lower extremities, dry mouth. Seven years before, purpura appeared and disappeared repeatedly on both lower extremities accompanied by pruritus, and she was referred to the dermatology department of our hospital. Four years before, she began to have dry mouth, was referred to our rheumatology clinic. Based on anti-SSA antibody positive and minor salivary gland biopsy findings. She was diagnosed with Sjogren's syndrome Hypergammaglobulinemia with IgAλmonoclonal gammopathy was also observed at the same time. Chest computed tomography revealed a thymic tumor. Two years before, a thymectomy was performed, and a diagnosis of thymic MALT lymphoma was made. She was admitted to the hospital due to an increase in purpura punctate of the lower extremities. On admission, laboratory examination showed that the elevated levels of IgG (2735 mg/dL), IgA (837 mg/dL), and CRP (0.25 mg/dL). A skin biopsy of the purpura revealed no obvious vasculitis. Oral prednisolone 30 mg/day was initially started, and the symptoms were alleviated. IgG and IgA normalized and monoclonal gammopathy disappeared. We herein reported a case of thymic MALT lymphoma with a series of rare complications.

W114-1

UBA1 screening of clinically suspected VEXAS cases in Japan: a multicenter prospective cohort study

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Conflict of interest: None

[Objective] To clarify the use of *UBA1* genetic testing in patients suspected with VEXAS syndrome. [Methods] Patients with clinically suspected VEXAS syndrome who underwent Sanger sequencing and PNA clumping PCR of *UBA1* gene at our institution were included in the study. Cases were divided based on the *UBA1* variant positivity. The association with clinical manifestations was analyzed. [Results] We accumulated 55 cases from April 2021 to September 2022. *UBA1* variant positive patients were 26 cases (47.3%): 13 with p. Met41Thr, 5 with p. Met41Leu, 3 with p. Met41Val and 5 with c. 118-1G>C. All *UBA1* variant-positive patients were male, with a mean age of onset of 71.2 ± 10.4 years. Common symptoms included skin rash (92%, $p<0.05$), fever (88%, $p=0.13$), and lung involvement (81%, $p<0.05$). Almost all patients had macrocytic anemia and bone marrow vacuoles. However, we observed a *UBA1* variant-negative cases clinically mimicking VEXAS syndrome. [Conclusions] The *UBA1* gene test was highly positive in nearly half of the suspected cases, but further case accumulation and analysis is needed because of the possibility of false positive and false negative results.

W114-2

Refractory Behçet's disease due to an acquired genetic abnormality (Trisomy-8, VEXAS syndrome)

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Conflict of interest: None

Acquired genetic abnormalities are involved in the inflammatory pathogenesis of refractory Behçet's disease (BD), and many cases of BD associated with myelodysplastic syndrome (MDS) have been reported. We report a group of patients with Trisomy-8 and VEXAS syndrome who presented with refractory BD experienced in our department and the problems in their treatment. [Case 1] A 58-year-old woman. She was diagnosed as MDS with intestinal BD with Trisomy-8, Trisomy-9, and X chromosome abnormalities. She also had secondary alveolar proteinosis. Her symptoms improved with allogeneic hematopoietic stem-cell transplantation (HSCT). [Case 2] An 18-year-old female. She was diagnosed with MDS with intestinal BD and Trisomy-8. She was refractory to conventional immunosuppressive therapy, but her symptoms rapidly improved with HSCT. [Case 3] A 60-year-old man. He was diagnosed with complete BD and MDS, and a somatic variant (c. 118-1G>C) in the *UBA1* gene was confirmed. The patient was treated with high-dose steroids, tocilizumab, and plasma exchange therapy, but his symptom did not improve, and death. [Conclusion] BD associated with genetic abnormalities is often refractory. Trisomy-8-positive patients have been successfully treated with HSCT, and it may be effective for VEXAS syndrome.

W114-3

Investigation of clonal hematopoiesis in Behcet's disease

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Conflict of interest: None

[Objective] The condition in which hematopoietic stem cells acquire somatic mutations in hematologic cancer-related genes and expand clonally is called clonal hematopoiesis (CH). CH is a risk factor for hematologic cancer and has been linked to inflammation. Behcet's disease (BD) is associated with MDS, but the association of CH in BD have not been reported. We investigated the frequency of CH in BD and its association with disease status. [Methods] Peripheral blood samples were collected from 47 BD patients at our department and Saga University Hospital, and DNA was extracted. The presence of CH was determined using a next-genera-

tion sequencer, and we investigated the clinical profile of patients with CH. [Results] The median age of patients was 65 years, and 5 of the patients had a history of hematologic cancers. 7 of 47 patients (14.9%) had CH-related somatic mutations. Comparing the frequency of CH in patients without hematologic complications to that in a previously reported healthy population by age, a trend toward a higher frequency of CH was observed in BD patients. In this investigation, there was no significant difference in clinical presentation depending on the presence or absence of CH. [Conclusions] The frequency of CH may be higher in BD compared to a healthy population.

W114-4

Long-term follow-up of two cases with VEXAS syndrome

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Conflict of interest: None

VEXAS syndrome is a disease with various autoinflammatory conditions and MDS caused by somatic *UBA1* mutations. Here we report a long-term follow-up of two patients with VEXAS syndrome. Patient 1 was a 58-year-old man with a 6-year history of myelodysplastic syndrome (MDS), neutrophilic dermatosis, and relapsing polychondritis. He was admitted with diffuse lung micronodules and diagnosed with VEXAS syndrome (UBA1 mutation: p. Met41Thr). Although anemia and autoinflammation initially responded to predonisolone (PSL) and cyclosporine A (CsA), they relapsed after dose reduction of PSL. As azacytidine and tofacitinib were ineffective and intolerant, CsA has been continued for two years with transfusion independence. Biologics will be added in future. Patient 2 was a 73-year-old man with a 13-year history of pancytopenia, neutrophilic dermatosis, arthritis, episcleritis, and ulcerative colitis with total colorectal resection. Four years ago, he developed tubulointerstitial nephropathy and was treated with PSL and golimumab (GLM). He was admitted with progressive anemia and diagnosed with VEXAS syndrome (UBA1 mutation: p. Met41Leu) with MDS. CsA was added to PSL and GLM. Combination therapy including CsA may provide long-term benefits for patients with VEXAS syndrome.

W114-5

Clinical status of Behçet disease and trisomy 8 myelodysplastic syndrome-associated enteropathy at our hospital

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Conflict of interest: None

[Objective] Concerning Behçet Disease (BD), there remain to be many issues, such as the handling of trisomy 8 myelodysplastic syndrome-associated enteropathy (Tri8^{+}MDSE). In the present study, we analyzed our department's clinical status of BD, including Tri8^{+}MDSE. [Methods] We surveyed and analyzed gender, age, disease classification, symptoms, HLA typing, treatment content, and the presence or absence of blood diseases in 82 patients with BD who had visited our department. [Results] Of a total of 82 patients, there were 23 males and 59 females. There were 13 patients with complete-type BD, 67 patients with incomplete-type BD, and 2 patients suspected of having BD. There were 82 patients with recurrent aphthous ulcer of the oral mucosa, 77 patients with skin symptoms, 27 patients with eye symptoms, 54 patients with genital ulcer, 27 patients with gastrointestinal lesions, 6 patients with vascular lesions, and 2 patients with central nervous system lesions. Two patients (2.4%) had hematological complications, both of whom had myelodysplastic syndrome (trisomy 8+). Of those, one patient died, while the other survived (azacitidine in one patient). [Conclusions] Valuable findings in the clinical practice of BD, including the frequency of Tri8^{+}MDSE, were obtained.

W114-6

VEXAS syndrome with EBV-associated T/NK lymphoproliferative disease successfully treated with etoposide and CHOP therapy: Case Report

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Conflict of interest: None

[Introduction] We report a case of VEXAS syndrome with EBV-associated T/NK-lymphoproliferative disease (EBV-T/NK-LPD) successfully treated with etoposide (ETP) and CHOP therapy. [Case] In year X, a man in his 50s presented with polyarthritis, generalized painful erythema, and multiple infiltrative shadows on chest CT. The patient did not improve with methotrexate, tacrolimus, and infliximab in year X+1. Fever, cytopenia, hepatosplenomegaly, and elevated LDH/ferritin occurred. He had macrocytic anemia, and bone marrow examination showed numerous vacuoles in the cytoplasm of myeloid and erythroblastic progenitor cells. MAS was diagnosed. The patient rapidly improved with high-dose prednisolone (PSL), and tocilizumab did not add any benefit. MAS relapsed at X+3 years. There was an increase in EB virus in peripheral blood and NK cells, and we considered EBV-T/NK-LPD. ETP was followed by CHOP therapy. For X+4 years, the patient was stable with mPSL 1 mg/day. In X+8 years, c. 118-1G>C was detected by *UBA1* gene analysis, and VEXAS syndrome was diagnosed. [Clinical Significance] This case suggests the possibility of efficacy of ETP/CHOP therapy for VEXAS syndrome resistant to various treatments.

W115-1

Identification of IL-1b downstream factors that regulate alternative splicing of the inflammasome component ASC

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Conflict of interest: None

[Objective] We have previously investigated inflammasome adaptor protein ASC in patients with palindromic rheumatism and found the dominant-active splice variant of ASC lacking exon2 (Δexon2 ASC) which increases IL-1β production compared to wild-type ASC (Suganuma Y et al., Asian Pac J Allergy Immunol, 2022). We also reported that IL-1β and the rs8056505G allele on this gene co-ordinately regulate Δexon2 ASC expression (Hattori M et al., JCR2021). In this study, we sought to identify the splicing factors that affect the expression of Δexon2 ASC *via* IL-1β. [Methods] The transcriptome of IL-1β-stimulated THP-1 cells was analyzed by RNA-seq. [Results] We identified 131426 transcripts and detected 41 down-regulated and 11 up-regulated genes upon IL-1β stimulation. In particular, mascRNA (MALAT1-associated small cytoplasmic RNA), which is one of the tRNA-like small ncRNAs was most significantly up-regulated. [Conclusions] It is suggested that mascRNA may be involved in the expression of Δexon2 ASC, as MALAT1 has been reported to regulate splicing *via* SR protein. We will confirm the effect of MALAT1 (mascRNA) on Δexon2 ASC expression by using siRNA.

W115-2

Successful Canakinumab Treatment for Familial Mediterranean Fever Patient with Insufficient Response to Colchicine

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Conflict of interest: None

Familial Mediterranean fever (FMF) is characterized by recurrent episodes of fever and serositis. We report here a case of FMF refractory to colchicine, in which canakinumab was introduced and resulted in remission. A 52-year-old woman had recurrent attacks with fever, headache, and vomiting. The attacks of fever lasted two to three days and had fully recovered. She was admitted to the hospital for repeated similar episodes. Spinal fluid examination showed increased cell counts and diagnosed with meningitis. The patient's symptoms resolved within a few days, and she was discharged from the hospital. She was clinically suspected of FMF by recurrent attacks of fever, so she was referred to our hospital. Colchicine was started and the attack interval was prolonged but did not disappear. *MEFV* gene analysis revealed heterozygous mutation on Exon2 (L110P-E148Q), leading to a diagnosis of FMF atypical case. After introduction of canakinumab, the attacks completely resolved. We present this case because it is the first report of canakinumab use in aseptic meningitis associated with FMF.

W115-3

Impact of the presence of multiple MEFV variants of unknown significance in familial Mediterranean fever

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Conflict of interest: Yes

[Objective] We often encounter patients with suspected familial Mediterranean fever (FMF) and multiple *MEFV* variants of unknown significance (VUS). We aim to examine the impact of multiple VUS on the diagnosis and symptoms of FMF. [Methods] Patients who fulfilled Tel-Hashomer criteria and had variants in exons other than exon 10 were included. Patients were divided into two groups according to the number of variants [single-variant group (SG) and multiple-variant group (MG)]. We analyzed the diagnosis, clinical symptoms, and treatment between the groups. [Results] A total of 271 patients were included (133 patients in SG and 138 patients in MG). At the 1-year survey, 96 patients (72.2%) in the SG and 106 (76.8%) in the MG were diagnosed with FMF, showing no association between the number of variants and the diagnosis of FMF (p=0.38). There was no association between clinical symptoms and the number of variants, however, the proportion of patients who responded to colchicine was significantly lower in the MG (p=0.034). [Conclusions] The presence of multiple variants other than exon10 did not contribute to the diagnosis of FMF. It was also suggested that the presence of multiple variants may affect the efficacy of colchicine, but there was no involvement in clinical symptoms.

W115-4

A case of familial Mediterranean fever with a MEFV M694I homozygote in which pregnancy was an exacerbating factor

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Conflict of interest: None

The patient is a 32-year-old woman. She presented with pain and swelling in both ankle joints a few times a year during her childhood. She was hospitalized for peritonitis in year 0, which resolved spontaneously within 3 days. She continued to have the same symptoms associated with menstruation. In year 1, *MEFV* gene analysis revealed homozygous for M694I, and a diagnosis of Familial Mediterranean fever (FMF) was made. Treatment was initiated with colchicine. Tocilizumab was introduced in year 4, which was discontinued in year 6 due to secondary ineffectiveness. Three months later, she became pregnant with her first child, and colchicine was discontinued. Around 20 weeks gestation, abdominal pain began to occur, and colchicine was resumed. Her second child was conceived in year 8, and colchicine was stopped at 11 weeks' gestation. At 22 weeks gestation, peritonitis occurred and colchicine was resumed. Thereafter, she continued to have abdominal pain every 1 to 2 weeks, and mildly elevated CRP levels persisted even during intermittent attacks of abdominal pain. After delivery, she had no abdominal pain, and her CRP had normalized. This case suggests that pregnancy may be an exacerbating factor for FMF in patients homozygous for *MEFV* M694I.

W115-5

A case of intestinal and vascular Behcet's disease with the diagnosis of chronic progressive neuro-Behcet's disease following the onset of infective endocarditis

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Conflict of interest: None

[Case] The patient developed rheumatoid arthritis in X-16 and was treated with abatacept, but in X-3, oral aphthous ulcer, vulvar ulcer and subcutaneous thrombophlebitis, HLA-B51 positive, ulcerative lesion in ileocecal area, and pseudoaneurysm of brain were observed, so he was diagnosed of vascular and intestinal Behçet's disease and changed from abatacept to colchicine and Adalimumab. The patient was hospitalized with fever, hearing loss, lightheadedness, and disorientation since June X. After admission, blood culture was positive for Str. Gordonii, and TEE showed verrucae on the aortic and mitral valves, he was diagnosed IE, and ABPC 8 g was administered for 6 weeks. Since the patient had hearing loss, staggering, and disorientation, CSF examination revealed elevated CSF IL-6, and MRI images, diagnosis of neuro-Beichet's disease. To treatment of IE was prioritized, no immunosuppressive treatment for neuro-Beichet's disease was given. [Discussion] We experienced a case of Behçet's disease complicated with all three special types. The special type of Behçet's disease cause severe sequelae and affect the prognosis of life. Although the incidence of special type Behçet's disease is low. So we report the patient with all three special types of the disease.

W115-6

Two cases of adult-onset Still's disease manifested by ruptured Baker's cyst detected with musculoskeletal ultrasound

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Conflict of interest: None

[Backgroud] Adult-onset Still's disease (AOSD) includes a group of patients with chronic arthritis. Baker's cysts (BC) are bursae located in the knee fossa. Although arthritis is considered a risk factor for ruptured BC, there have been no reports of ruptured BC in AOSD. [Case 1] A 72-year-old woman presented with fever, arthralgia in both hands, and eruption. She was suspected of having AOSD because of liver dysfunction, leukocytosis, and hyper-CRP/ferritinemia. Two days before admission, she noticed edema and pain in the left lower leg, and MRI showed gastrocnemius

fasciitis. She was diagnosed with AOSD, and musculoskeletal ultrasound (MSKUS) found polysynovitis and bilateral ruptured BCs. Treatment with prednisolone (PSL; 30 mg/day) resulted in remission. [Case 2] A 73-year-old man presented with fever, knee arthralgia, edema in lower legs, and eruption. Lymphadenopathy, splenomegaly, liver dysfunction, leukocytosis, and hyper-CRP/ferritinemia were observed. He was diagnosed with AOSD, and MSKUS found polysynovitis and left ruptured BC. Treatment with PSL 55 mg/day and intravenous tocilizumab resulted in remission. [Discussion] Bursitis, including ruptured BC in AOSD, may be overlooked because they are considered edema or myalgia. MSKUS is helpful in the diagnosis of ruptured BC.

W116-1

The effectiveness of hydroxychloroquine for SLE complicated pregnancy

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Conflict of interest: None

[Objective] Family planning in SLE patients need to be taken care about disease activity and risk of medication. Uncontrolled disease activity leads to obstetric complications or fetal adverse events. There were some reports show that HCQ could depress the flare rate during pregnancy or disease activity after delivery. We retrospectively reviewed the effectiveness of HCQ in SLE complicated patients. [Methods] We retrospectively reviewed the medical record of SLE complicated patients from Jan 2015 to May 2022. We set the delivery outcome and SLEDAI for the primary outcome, and amount of corticosteroid during pregnancy, use of immunosuppressant, course of pregnancy, outcome of delivery for the secondary outcome. Statistical analysis was performed with Mann-Whitney's U test. [Results] There was no significant difference in patient characteristics. Rate of normal delivery was significant higher, and hypertensive disorders in pregnancy, fetal growth restriction were tended to be lower in HCQ group. SLEDAI showed no significant difference within HCQ group and non-HCQ group or before and after delivery. [Conclusions] HCQ may improve delivery outcome in SLE complicated pregnancy. SLEDAI showed no significant difference before and after delivery in both group, but further study should be needed.

W116-2

Hydroxychloroquine and low-dose aspirin use in relation to pregnancy outcome in lupus pregnancy

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) has an increased risk for pregnancy complications. The aim of this study was to evaluate the efficacy of HCQ and ASA on pregnancy outcomes. [Methods] All pregnant woman with SLE under PSL 20 mg or less during the first trimester who were managed at Tama Medical Center or St. Luke's International Hospital from April 2010 to Aug 2022, were retrospectively enrolled. We analyzed the relationships between the use of HCQ and ASA during the first trimester and pregnancy outcomes. [Results] Total of 120 pregnancies were enrolled. Overall, 2.5% pregnancies and 4.2% pregnancies resulted in miscarriages and intentional abortions, respectively, and 93.3% pregnancies were live births. HCQ was used in 37.5% and ASA was used in 31.7%. 15% pregnancies and 14.2% were resulted in hypertensive disorders of pregnancy (HDP) and small-for-gestational age (SGA), respectively. The odds ratio (OR) for HDP was 0.60 (95% CI: 0.15-1.96) in HCQ use and 1.45 (95% CI: 0.43-4.57) in ASA use. The OR for SGA was 0.46 (95%CI: 0.10-1.64) in HCQ use and 0.61 (95%CI: 0.13-2.19) in ASA use. [Conclusions] The efficacy of HCQ and ASA on pregnancy outcomes in SLE needs to be examined in a large prospective study.

W116-3

A retrospective study of bisphosphonate use in female patients with systemic lupus erythematosus and its effect on bone mineral density during pregnancy

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Conflict of interest: None

[Objective] In SLE patients on steroid therapy who are planning pregnancy, adequate osteoporosis prophylaxis is necessary, so we continue bisphosphonates (BPs) in some cases until conception. The purpose was to clarify the effects of BPs on bone mineral density (BMD) during pregnancy. [Methods] The subjects were 34 patients who had live births after the onset of SLE and performed DEXA within 1 year before the last menstrual period and within 6 months after delivery. Medications and changes in lumbar frontal BMD values were analyzed retrospectively. [Results] Of the 34 patients, 19 were on BPs until conception (group with BPs). In the group with BPs, BMD was maintained from 0.888±0.117 g/cm^2 to 0.8911±0.128 g/cm^2 after delivery, with a mean change of +0.2%. Meanwhile, in the group without BPs, BMD decreased significantly from 0.954±0.121 g/cm^2 to 0.895±0.127 g/cm^2 (p=0.003), and the mean change was -6.1% (p=0.005). The BMD change rate was negatively correlated (r=-0.55, p=0.0006) with total days of hospitalization during pregnancy. Even after adjusting for heparin use during pregnancy, period of hospitalization and BPs were associated with the rate of BMD change. [Conclusions] Continuation of BPs until conception is possibly effective in maintaining lumbar spine BMD during pregnancy.

W116-4

Analysis of adverse pregnancy outcomes (APO) and predictors in pregnancies complicated with systemic lupus erythematosus (SLE)

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Conflict of interest: None

[Objective] To investigate pregnancy outcomes and predictors for APO in pregnancies with SLE. [Methods] For all pregnancies with SLE at our hospital from Jan 2017 to Sep 2022, we examined 1) maternal background and treatment, 2) development of APO, and 3) comparison of maternal clinical features between APO and non-APO groups, retrospectively. [Results] 1) 46 pregnancies were analyzed, the mean age at delivery were 32.1±4.1 years, 15 mothers had lupus nephritis, 25 had anti-SS-A antibody (Ab), and 21 had antiphospholipid Ab. For treatment, corticosteroids were administered in 45 mothers, tacrolimus in 24, belimumab in 3, and low-dose aspirin in 23 during the pregnancy. 2) Among all pregnancies, live birth was obtained in 36 (78.3%) pregnancies, and APO developed in 20 (43.5%) (11 preterm deliveries, 5 fetal deaths, 14 low birth weight, 9 hypertensive disorders, including duplicates). 3) The APO group had significantly lower C3, platelet (Plt) count, and BMI, while significantly higher urine protein in the 1st trimester than non-APO group (p<0.05). Multiple logistic regression analysis showed that Plt count in the 1st trimester was independently associated with APO (OR: 0.963, p=0.0231). [Conclusions] The Plt count in the 1st trimester was suggested

to be a predictor for APO.

W116-5

The Analysis of risk factors for adverse pregnancy outcomes in SLE patients who have attained LLDAS at the conception

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Conflict of interest: None

[Objective] We analyze the risk factors for adverse pregnancy outcomes (APOs) in SLE patients who have attained LLDAS at conception. [Methods] We used the data of SLE patients who have been treated at the planning for pregnancy. We selected the patients who had attained LLDAS at conception and analyzed the risk factors for APOs from autoantibodies, therapeutic agents, and serum immunological parameters. [Results] In 66 pregnancies, 42 cases attained LLDAS at conception. APOs were occurred in 19 cases, including spontaneous abortion and stillbirth in 4 cases, preterm birth in 5 cases, low birth weight in 12 cases, and gestational hypertension in 2 cases. In cases which have attained LLDAS, mean glucocorticoid (GC) dose during pregnancy was extracted as a risk factor for all APOs ($p<0.01$). It also became a risk factor for preterm birth. In addition to GC, the positivity of anti-SS-A antibody (P=0.04), unused hydroxychloroquine (P=0.04), low values of C3 and CH50 (P=0.045, 0.02, respectively) were extracted as risk factors for low birth weight. [Conclusions] The mean GC dose during pregnancy is a risk factor for APOs in SLE patients who have attained LLDAS at conception. Even when disease activity is controlled during pregnancy, it is important to control GC dose strictly.

W116-6

Pregnancy and Outcome Differences in Women with Systemic Lupus Erythematosus Before and After Pregnancy Support Treatment- Preconception care and support enables patients to think more realistically about pregnancy

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Conflict of interest: None

[Objective. Method] There are few guidelines regarding support for collagen disease affected women who actually wish to become pregnant. To investigate the differences in pregnancies and their outcomes in SLE women before and after the outpatient department of maternal medicine was established at our hospital. Target cases From April 2003 to October 2022, 123 SLE women who underwent pregnancy management at our hospital's collagen disease department. [Results] There were 44 subjects (group 1) before the opening of the outpatient clinic, and 79 subjects after the opening (group 2). 70 (88%) in group 2 gave birth (p: 0.0004). On the other hand, miscarriage occurred in 9 (20.5%) in group 1 and 3 (3.9%) in group 2 (p: 0.0031). Prednisolone dosage during pregnancy was 12.8 mg/d in group 1, 11 mg/d (p: 0.023) in group 2. Regarding disease activity, exacerbation during pregnancy occurred in 12 cases (27%) in group 1 and 8 cases (10%) in group 2. [Conclusions] By sharing a life plan between medical staff and patients through preconception care and planning treatment before pregnancy, patients who wish to become pregnant can think about pregnancy more realistically. Adequate disease management during pregnancy leads to better outcomes for both mother and baby.

W117-1

A Study of Risk Factors for the Development of Cardiovascular Disease in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] It has been reported that RA patient are getting older as well as the Japanese population is aging. In particular, CVD is an important disease group that influences the prognosis of life. We aimed to evaluate the incidence of CVD in RA patients attending Nagoya University Hospital. [Methods] We included 969 patients who were outpatients attending Nagoya University Hospital from 2018 to 2022 and who received anti-RA drugs. CVD requiring hospitalization was defined as myocardial infarction, heart failure, and stroke. Cox proportional hazards analysis was used to examine risk factors for the occurrence of events. [Results] During the observation period of 969 patients, there were 19 cases of CVD requiring hospitalization and 21 deaths. The combined event of CVD and death was considered as the outcome, and the results showed that there were no significant differences between men HR: 3.82, $p<0.001$), older age (HR: 1.07 p=0.001), Charlson's Comorbidity Index high (HR: 1.26 CI 1.07-1.49 p=0.007), anemia (HR: 2.12 p=0.023), MTX (HR: 0.30p=0.003), biologic agent (HR: 3.02p=0.009) were risk factors. [Conclusions] Risk factors suggest that patients who are elderly, have difficulty receiving MTX due to comorbidities, and require biologic therapy are at higher risk of CVD and death.

W117-2

Evaluating glomerular filtration rate slope for patients with rheumatoid arthritis

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Conflict of interest: None

Object: This study aimed to investigate the glomerular filtration rate slope for patients with rheumatoid arthritis in real clinical practice. Methods: 969 RA patients who were attending Nagoya University Hospital as outpatients and treated with any DMARDs drugs from 2018 to 2022. The eGFR slope was conducted from fixed and random effects by mixed effect model analysis. We performed multiple regression analysis to identify the baseline characteristic factor associated with eGFR slope. Results: The overall patients' mean age ± SD was 60.6±15.1 years, 24.2% were male. Baseline renal function categories were as grade 1 (eGFR≧90) or grade 2 (90>eGFR≧60): 81.5%, grade 3 (60>eGFR≧45): 16.8%, grade 4 (30>eGFR≧15): 1.8%. The estimation of mean eGFR slope by the mixed effect model was -1.47±3.32 per year with 78.8% showing a decreasing trend. We identified that the associated factors with declined eGFR were higher titer of eGFR at baseline (Odds ratio (OR)=1.05, 95% confidence interval [CI], 1.03-1.06, $p<0.001$) and higher titer of CRP at baseline (OR=1.10 CI: 1.01-1.20, p=0.033) by multivariable regression analysis. Conclusions: Elevated CRP level was a significantly associated factor with eGFR decline, suggesting that control of disease activity is important in renal function decline.

W117-3

A retrospective study of methotrexate-associated lymphoproliferative diseases associated with rheumatoid arthritis at Juntendo University

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Conflict of interest: None

[Objective] To determine the clinical course of methotrexate-related lymphoproliferative disease (MTX-LPD) that develops in rheumatoid arthritis (RA) patients. [Methods] We extracted clinical data of RA patients who discontinued MTX treatment from January 2016 to December 2020

at Juntendo University Hospital. [Results] Of the 830 patients who discontinued MTX, the median age at the time of discontinuation was 62 years. Reasons for discontinuation were patients' wish to discontinue 87 (10.5%), 82 (9.9%) due to other diseases, 78 (9.4%) did not respond to MTX, and 69 (8.3%) for MTX-LPD, 59 with infectious disease (7.1%), 56 with interstitial pneumonia (6.7%), 52 with liver failure (6.3%), 50 pregnancy wishes (6.0%), 46 patients with gastrointestinal symptoms (5.5%), bone marrow suppression 37 (4.5%), rashes 34 (4.1%), stomatitis 26 (3.1%), renal failure 23 (2.8%), malaise 9 (1.1%), allergy 6 (0.7%), 5 due to old age (0.6%) and unknown in 142 (17.1%). Diffuse large B-cell lymphoma (DLBCL) was the most common histopathology among patients with MTX-LPD, and 55 of 69 MTX-LPD patients (79.7%) spontaneously regressed after discontinuation of MTX. [Conclusions] A wide variety of factors are involved in the clinical course of MTX-LPD, and further analysis is required.

W117-4

Carpal tunnel syndrome in a rheumatic disease clinic

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a risk factor of carpal tunnel syndrome (CTS). Since symptoms of CTS are similar to those of musculoskeletal manifestations and digital vasculopathy, patients with CTS can be referred to rheumatic disease clinics. The aim of this study is to investigate clinical practice of CTS in our rheumatic disease clinic. [Methods] The source population comprised of patients who received treatment for rheumatic diseases at Tama Namub Chiiki Hospital or those who were referred for suspected rheumatic diseases between April 2019 and March 2022. [Results] Twenty-three patients were diagnosed with CTS. Of these, 12 patients had pre-existing diagnoses of RA. Four patients were referred because of suspected rheumatic diseases, but they were diagnosed with CTS alone. Seventeen patients received local carpal tunnel corticosteroid injections, and 11 of them improved. [Conclusions] Rheumatologist should be familiar with clinical manifestations and physical examinations of CTS because they are in charge of care of patients with CTS. Local carpal tunnel corticosteroid injections can be performed with the application of musculoskeletal ultrasound technique.

W117-5

Efficacy of biologics and JAK inhibitors for chronic airway lesions in patients with rheumatoid arthritis in our hospital

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Conflict of interest: None

[Objective] However, there is no consensus regarding its effectiveness against chronic airway lesions. Therefore, we investigated the efficacy of Bio and JAK inhibitors against chronic airway lesions associated with RA at our hospital. [Methods] We registred RA patients with chronic airway lesions in our hospital medical records, and analyzed the biologics groups (TNFα inhibitor group: 10 cases, IL-6 receptor inhibitor group: 8 cases, T cell-selective co-stimulatory modulator group 6 cases) and JAK inhibitors (5 patients). We analyzed changes in respiratory function and KL-6 levels after the treatment for 12 and 24 weeks retrospectively. [Results] There were no significant differences in age, sex, disease duration, disease activity, etc. among the four groups., FVC improved during both 12 and 24 weeks except for the TNFα group (TNFα inhibitor group Δ-0.03 L/ 24 weeks Δ0.08 L, IL-6 receptor inhibitor group 12 weeks Δ0.15 L/ Δ0.18 L at 24 weeks, T cell selective co-stimulatory drug group at 12 weeks Δ0.003 L/24 weeks Δ0.02 L, JAK inhibitor group at 12 weeks Δ-0.04 L/24 weeks Δ0.06 L) [Conclusion] There is a possibility that biologics and JAK inhibitors can be expected to be effective for chronic airway lesions in RA.

W117-6

Spontaneous regression of lymphoproliferative disorders in rheumatoid arthritis: 5-year-clinical course of three cases

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Conflict of interest: Yes

[Objective] Lymphoproliferative disease (LPD) associated with rheumatoid arthritis (RA) is an unknown pathophysiology. [Cases] Case 1 was a 55-year-old woman who had an abnormal shadow on chest X-ray 16 years after starting MTX. Case 2 was a 63-year-old woman who had multiple infiltrative shadows in both lungs associated with cold symptoms. She had a definitive diagnosis of LPD on bronchoscopic biopsy. Case 3 was a 44-year-old woman who happened to have bilateral axillary lymphadenopathy on chest CT taken at the time of anaphylaxis after administration of infliximab BS. After discontinuation of MTX, LPD disappeared in all 3 cases, and no recurrence of LPD was observed for the next 5 years. [Discussion] All 3 patients were female, RF positive, anti-CCP antibody high titer positive, average age at onset of RA was 24 years old, age at onset of LPD was 54 years old, mean soluble interleukin-2 receptor was 2731 U/mL. The average MTX treatment period was 8 years, the average maximum dose of MTX was 13.3 mg/week, and biologics were used at the onset of LPD in 2 cases. After the onset of LPD, RA treatment was based on steroids and salazosulfapyridine, but RA relapsed in 2 patients. [Clinical Significance] We reported the 5-year clinical course of 3 patients with RA-related LPD.

English Poster Session

EP1-01

Regulatory effects of autoantibody IgG on osteoclastogenesis

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Conflict of interest: None

Inflammatory arthritis is common in both systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), and eventually leads to bone homeostasis disorders. However, RA patients generally have severe bone destruction, which is rare in SLE patients. Recent studies have demonstrated that anti-citrullinated protein antibodies are important factors leading to bone destruction in RA. On the other hand, SLE patients present deposition of autoantibodies in the joints, our studies demonstrat that SLE IgG plays an important role in bone protection through occupation of FcgammRI and inhibition of osteoclastogenesis. These different phenomena occur because of the effects of the autoantibodies on the monocytes/macrophages during osteoclastogenesis, and the mechanisms underlying these effects differ between SLE and RA patients.

EP1-02

Mechanism of metabolic disorder of MSC in MDS blocking HSC differentiation

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Conflict of interest: None

[Objective] Myelodysplastic syndrome (MDS), as a precancerous diseases, has become an elderly disease significantly. The blocked differentiation of hematopoietic stem cells (HSCs) is closely related to abnormal mesenchymal stem cells (MSCs) in the bone marrow microenvironment, but the mechanism remains to be explored. Studies have shown that metabolism can affect the function of MSCs. Therefore, this paper aims to explore the mechanism of why MSCs with metabolic disorders in bone marrow affect the differentiation of HSCs in patients, so as to provide new targets for the diagnosis and treatment of MDS. [Methods] MDS-MSCs were isolated and cultured in vitro. The abnormalities of MDS-MSCs were evaluated by Cell Counting Kit, apoptosis assay, qRT-PCR, and Western Blotting. After co-culture of MSCs with HSC, the regulatory effect of MSCs on HSCs differentiation was evaluated by flow cytometry, colony-forming experiment, and apoptosis assay. [Results] Compared with the control group, the proliferation of MDS-MSCs was slow and the apoptosis was increased, the hematopoietic ability of HSCs was decreased, the expression of intracellular glucose metabolism related enzymes was abnormally low, and the expression of lipid metabolism related enzymes was abnormally high. After targeted inhibition of CPT-1A, a key enzyme related to lipid metabolism, the ability of MSCs to support HSCs differentiation was restored. [Conclusions] MDS-MSCs overexpress CPT-1A, a key enzyme related to lipid metabolism, to block the differentiation of HSCs and affect the disease progression of MDS.

EP1-03

Abnormal HOXB axis in MSC promotes MDS progression

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Conflict of interest: None

[Objective] Bone marrow mesenchymal stem cells (MSC) play a role in the progression of myelodysplastic syndrome (MDS). However, due to the extremely heterogeneous disease of MDS, it is difficult to explore the common targets in the limited sample size study. In this study, we analyzed the genetic differences between MDS-MSC and healthy controls (HC) through dataset enrichment, and verified the key molecules, so as to provide a new target for clinical MSC-targeted adjuvant therapy of MDS. [Methods] Screening GEO database GSE107490, GSE140101 and GSE 61853; limma package, DAVID, String, and Cytoscape were used to search for Hub genes. Correlation analysis and survival curve were used to evaluate Hub genes, and key regulatory mirnas were screened and enriched. MDS-MSCs were further isolated and cultured in vitro, and the functional recovery of MDS-MSCs and MDS-HSCs were evaluated by cell proliferation, apoptosis and differentiation experiments. [Results] Big data screening analysis and in vitro experimental verification showed that the overexpression of HOXB3 and HOXB7 in MDS-MSC could be regulated by the key molecule hsa-miR-125a-3p, hsa-miR-671-3p, hsa-miR-1207-5p, hsa-miR-4433b-3p, hsa-miR-6819-5p, and the interference of HOXB3 and HOXB7 expression could enhance the cell proliferation and differentiation ability of MDS-MSC, inhibit cell apoptosis, and support the hematopoietic differentiation ability of HSCs. [Conclusions] The dysregulation of MDS-MSC growth and development is closely related to the pathogenesis of MDS. The overexpression of differential genes HOXB3 and HOXB7 can be regulated by hsa-miR-125a-3p, hsa-miR-671-3p, hsa-miR-1207-5p, hsa-miR-4433b-3p, hsa-miR-6819-5p and significantly inhibit the hematopoietic ability of MDSs, suggesting that targeting HOXB signaling axis can assist the treatment of MDS.

EP1-04

Protocatechuic acid and cinnamic acid combinational approach attenuates collagen-induced rheumatoid arthritis through modulation of gut microbiota in rodents

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Conflict of interest: None

Objective: Procatechuic acid and cinnamic acid are natural phenolic compounds isolated from *Prosopis cineraria* has been demonstrated to possess strong anti-inflammatory effects. Traditionally, *Prosopis cineraria leaves* have also been used for rheumatism treatment. The present work was designed to explore the potential of a combination of protocatechuic acid and cinnamic acid [PA+CA] on type II collagen-induced rheumatoid arthritis in rats via assessing possible underlying mechanisms such as inflammation and gut microbial communities. Methods: Thirty rats were utilized to induce rheumatoid arthritis via intradermal injection of bovine type-II collagen (BTC-II; 100 µg) in Freund's complete adjuvant (0.1 ml) on day 2 and 3 as a first and booster injection, respectively. After 5 days of a booster dose, animals were randomly divided into five groups and treated with their respective drug regimen, i.e., vehicle (0.2 ml distilled water), [PA+ CA] (10, 20 and 40 mg/kg b.w.) and ketoprofen (5 mg/kg b.w.), were orally administered once a day for next 21 days. At the end of study, the anti-rheumatoid arthritis activity of [PA+ CA] was investigated by observing the degree of paw swelling, arthritis index scores, as well as pro-inflammatory cytokine levels in serum and gut microbiota. Results: Results revealed that [PA+CA] group has statistically alleviated the swelling of the paw, arthritis score index and different pro-inflammatory serum markers of rheumatoid arthritis as compared to vehicle group. Moreover, [PA+CA] was able to significantly modulate the gut microbial inhabitants by decreasing the relative abundance of Helicobacter, Lachnospiraceae and Mucispirillum. Conclusion: The current study concludes that [PA+ CA] exhibited beneficial anti-inflammatory potential in arthritic model via modulation of gut microbiota and this combinational therapy can be utilized as a beneficial anti-rheumatic arthritis tool for the management of arthritis.

EP1-05

A case of Japanese pianist Kazuko Yasukawa, who was suffered from rheumatoid arthritis -A historical view of rheumatic disease-

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Conflict of interest: None

[Objective] To clarify the treatment of rheumatoid arthritis (RA) two or three decades ago, when neither biological agents nor Janus kinase inhibitors was used. [Methods] Pathography of a Japanese pianist Kazuko Yasukawa, who was suffered from RA, are shown here according to Izumiko Aoyagi's description, who followed after Yasukawa. [Results] Yasukawa was born in 1922 and brought up in France and graduated from Par-

is National Music School. In 1978, she felt general joint pain, and diagnosed as RA. She was retired because of extensor tendon rupture in 1983. During those period, she was treated with prednisolone and gold. In 1991, methotrexate was started, but she was suffered from fractures and infectious diseases. In 1996, she died of pulmonary emboli in the morning on the planned discharge day. [Conclusions] Non-steroidal anti-inflammatory drugs, oral steroid and gold injection were popular treatment for RA in those days. Anti-inflammatory effect of those drugs was insufficient, therefore marked deformity and fracture caused by osteoporosis were often occurred.

EP1-06

Complicated rheumatoid arthritis combined with tuberculosis and malignant tumor: a case report

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Conflict of interest: None

Objective: To improve clinicians' understanding and rational use of medication in patients with complicated rheumatoid arthritis (RA) with tuberculosis and malignant tumor. Methods: The treatment process of a patient with complicated RA who also had tuberculosis and cervical cancer were reviewed to summarize the clinical features, diagnosis, medication process, and prognosis. Results: The patient presented with painful wrist swelling in 2006, which gradually involved both knees, metacarpophalangeal and proximal interphalangeal joints of both hands, with symmetrical pain and morning stiffness of about 2 hours. Methotrexate, sulfasalazine, leflunomide, non-steroidal anti-inflammatory drugs, and low-dose prednisone were used selectively in combination for oral administration. In 2015, the patient developed a low fever, night sweats, cough, and was diagnosed with pulmonary tuberculosis, after treatment, the tuberculosis was well-controlled. In 2018, the patient presented with a 3rd/4th/5th PIPJ buttonhole deformity in both hands, especially in the little finger. The patient was diagnosed with cervical cancer in the same year and underwent surgery followed by regular chemotherapy. The tumor was controlled in 2020 when the patient added Iguratimod in the continuing treatment. Up to 2022, the patient achieved low disease activity. Conclusion: Patients with complex RA combined with tuberculosis and malignancy should have a clear relationship between the diseases, differentiate the treatment sequence and focus, thoroughly assess the efficacy and risk, and strengthen multidisciplinary cooperation so that patients can be optimally diagnosed and treated. The clinical implications: Patients with combined tuberculosis or tumor should pay attention to the clinical use of medication, and should continue anti-rheumatic attainment therapy after tuberculosis and tumor have been controlled, using a combination of multiple immunosuppressive agents to achieve better therapeutic results.

EP1-07

The efficacy and safety of HIF-PH inhibitors in patients with RA-CKD anemia. Is disease activity related the efficacy?

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of HIF-PH inhibitors in patients with RA-CKD anemia. [Methods] In retrospective, from 2021 January to 2022 August, 14 patients with RA-CKD anemia are treated by HIF-PH anemia. The patients are evaluated the efficacy and safety. [Results] At baseline all patients are below 10.0 g/dL Hemoglobin. The patient characteristics are from 52 to 78 years, female 10, male 3, DAS28 from 2, 4-6.8. 9 patients are EPO failure. [Results] At 3 months after HIF-PH inhibitors, the anemia are improvement (from 0.7 g/dL to 1.4 d/dL). There is no relation that between improvement and disease activity, age, baseline anemia level in statistically. However 2 patients who have high disease activity (DAS 28>5.1) are very significantly improvement anemia (>1.0 g/dL). All patients have no serious adverse events. [Conclusions] The efficacy and safety of HIF-PH inhibitors in patients with RA-CKD anemia are good despite EPO.

EP1-08

Risks and optimal therapeutic solutions in a patient with Osteoporosis, Osteogenesis Imperfecta and Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Optimal treatment of osteoporosis can sometimes be difficult when several conditions of the osteoarticular system co-exists and whose treatment may interfere. [Methods] 57 old female patient is admitted to our Clinic in December2020, for polyarticular pain, swelling, morning stiffness, accompanied by marked functional impotence. She is known with osteogenesis imperfecta, corticodependent rheumatoid arthritis (2007), diffuse osteoporosis of complex etiology, complicated, fracture of the femoral neck and right ankle (May 2016) At that time, the patient was undergoing treatment with Infliximab, Methotrexate 20 mg sc/week, folic acid, Leflunomide 20 mg/day, methylprednisolone 8 mg/day, Alendronate 70 mg/week, Calcium and Alfa D3 1 mcg/day. Following the clinical, imaging and biological evaluation of December2020, we decided to change the biological treatment for RA with Adalimumab and to discontinue Methotrexate therapy, maintaining Leflunomid Also at that time is also performed DXA which shows a T score in the lumbar spine of -3.1 and hips -3.2. In December 2011, DXA exam is repeated and revelas worse scores than the previous ones The patient also told that, she still was undergoing cortisone therapy. We decided to stop bisphosphonate therapy and start Denosumab 60 mg at 6 months. This therapeutic option was decided, despite the potential risk of strong immunosuppression (2 associated biological molecules). [Results] In October2022, the patient repeats the DXA exam, which shows an improvement of the T scores, lumbar spine a T score = -2.5, and in the hips = -2.7 [Conclusions] Treatment of osteoporosis can sometimes be difficult, especially among patients with multiple comorbidities, non-adherent to the recommendations of the physician. Although now, we have multiple therapeutic options for osteoporosis and rheumatoid arthritis, less for osteogenesis imperfecta, the choice of the optimal treatment must be made carefully, taking into account the risks/benefits and possible drug interactions.

EP1-09

The influence of aging on functional capacity in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] This study aims to clarify the influence of aging on functional capacity in patients with rheumatoid arthritis (RA). [Methods] RA patient was monitored with simplified disease activity index (SDAI), health assessment questionnaire disability index (HAQ-DI), pain score using a visual analog scale (PS-VAS), EuroQol-5th dimension with 5 lines (EQ5D-5L), and measured Sharp/van der Heijde score (SHS) from the beginning of treating (baseline). Patients were classified by age at baseline and at last observation; Group-YY: less than sixty-five-year at last observation, Group-YO: less than sixty-five-year at baseline and more than sixty-five-year at last observation, and Group-OO: no less than sixty-five-year at baseline. RA patients who were followed up for more than one year were picked up in the study. Association between HAQ-DI and other parameters such as gender, age, SDAI, PS-VAS, and SHS was statistically evaluated at baseline, at sixty-five-year old, at last observation, and change between the two periods. [Results] A total of 538 patients, in these, 143 in Group-YY, 88 in Group-YO, and 307 in Group-OO, were included in the study. The female gender rate was 75.5, 72.7, and 72.6%, and mean values in each group at baseline were 12.5, 12.1, and13.0 (SDAI), 29.7, 55.4, and 56.3 (SHS), 35.5, 31.1, and 36.6 (PS-VAS), 0.281, 0.353, and 0.627 (HAQ-DI), and 0.807, 0.761, and 0.724 (EQ5D-5L) for Group-YY, Group-YO, and Group-OO, respectively. SHS in Group-YY was significantly less than those in Group-YO and Group-OO. HAQ-DI and EQ5D-5L were significantly different between the two of each groups. HAQ-DI correlated

significantly with age, SDAI, SHS, and PS-VAS at baseline, PS-VAS at age sixty-five, and age, SHS, and PS-VAS at the last observation. Change of HAQ-DI from sixty-five to the last observation correlated significantly with age, SDAI, and SHS. [Conclusions] HAQ-DI was influenced by aging when the patient's age exceeded sixty-five.

EP1-10

Success rate of short-term glucocorticoid treatment in patients with early rheumatoid arthritis

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Conflict of interest: None

[Objective] The aims of this study were to evaluate the success rate of short-term (less than 3 months) glucocorticoids treatment in patient with early rheumatoid arthritis and to determine factors associated with success rate of short-term glucocorticoids treatment. [Methods] The prospective descriptive study was conducted among patients who were newly diagnosed rheumatoid arthritis by 2010 ACR/EULAR criteria, had symptoms less than 1 year and had Disease Activity Score (DAS28ESR) more than 3.2 between July 2020 and May 2021. All patients were treated with combination DMARDs (methotrexate, sulfasalazine and hydroxychloroquine). Patients were received low dose glucocorticoids (10 mg/day) at the initial treatment and tapered if their DAS28ESR less than 3.2 (low disease activity). The medical records about treatment with glucocorticoids were collected for 6 months after initial treatment. [Results] There were only 3 of 10 patients (30%) with rheumatoid arthritis who had moderate to high disease activity that succeeded in short-term (less than 3 months) glucocorticoids treatment. The Health assessment questionnaire (HAQ) score > 0.5 at 3 months and ESR > 30 mm/hr. at 3 months were associated with failure in short-term glucocorticoids treatment. [Conclusions] The success rate of short-term glucocorticoid treatment in patients with early rheumatoid arthritis was 30%. This low success rate showed that most of clinical practice guidelines for treatment rheumatoid arthritis with short-term glucocorticoids are difficult to do in real-life practice especially patients with moderate to high disease activity.

EP1-11

Factors that influence the quality of life in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] This study aims to clarify the influence of clinical parameters on the quality of life in patients with rheumatoid arthritis (RA). [Methods] RA patient was monitored with simplified disease activity index (SDAI), health assessment questionnaire disability index (HAQ-DI), pain score using a visual analog scale (PS-VAS), EuroQol-5th dimension with 5 lines (EQ5D-5L), and measured Sharp/van der Heijde score (SHS) from the beginning of treating (baseline). Association between EQ5D-5L and other parameters such as gender, age, SDAI, PS-VAS, SHS, and HAQ-DI was statistically evaluated at baseline and at last observation, and change between the two periods. [Results] A total of 538 patients were included in the study. The female gender rate was 73.4%, and mean values at the baseline and at the last observation were 67.2 and 73.2 (age), 12.7 and 4.4 (SDAI), 49.3 and 46.4 (SHS), 35.4 and 24.5 (PS-VAS), 0.487 and 0.498 (HAQ-DI), and 0.755 and 0.825 (EQ5D-5L), respectively. All of these parameters were significantly different between the two periods EQ5D-5L at baseline correlated significantly with HAQ-DI and PS-VAS, and their beta values were -0.604 and -0.444, respectively. EQ5D-5L at the last observation correlated significantly with SDAI, HAQ-DI, and PS-VAS at the last observation, and their beta values were -0.04, -0.623, and -0.099, respectively. When the last values of these parameters were divided by value at the baseline and the change from the baseline to the last observation, EQ5D-5L at the last observation correlated significantly with both of baseline and the change of all of SDAI, HAQ-DI, and PS-VAS, and their beta values were -0.439, -0.493, -0.143, 0.547, 0.605, and 0.139 for SDAI, HAQ-DI, PS-VAS at the baseline, and those change from the baseline to the last observation, respectively. [Conclusions] Quality of life in RA patients depends on disease activity control, pain control, and functional capacity. These variables could be controllable by treatment.

EP1-12

Methotrexate-Related Osteopathy: A Rare Complication of Long-term Methotrexate Therapy in Rheumatoid Arthritis

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Conflict of interest: Yes

[Objective] Methotrexate-related osteopathy (MRO) is a rare adverse effect of therapy that presents with the classic triad of osteoporosis, lower extremity pain, and atypical fractures. As these symptoms overlap with classic symptoms of rheumatoid arthritis, clinicians should have a high degree of suspicion and awareness for MRO to prevent morbidity. This literature review aims to discuss the pathophysiology, clinical features and risk factors for developing methotrexate-related osteopathy. [Methods] A literature review was conducted using OVID Medline, OVID Embase, and Pubmed to identify the mechanism, clinical characteristics, and risk factors for the development of methotrexate-related osteopathy. Furthermore, cases identified through literature review were summarized to highlight typical features. [Results] Methotrexate has been shown to suppress bone formation by inhibiting early osteoblastic cell differentiation. It typically presents as a classic triad of osteoporosis, pain, and atypical fractures. Specifically, fractures associated with MRO involve the lower extremity most commonly the distal and proximal tibia. Risk factors for the development of MRO include longstanding rheumatoid arthritis, duration of methotrexate therapy, and post-menopause. MRO is misdiagnosed as rheumatoid arthritis related pain or synovitis. Methotrexate withdrawal leads to improvement in symptoms. [Conclusions] Methotrexate-related osteopathy is a rare but devastating complication of methotrexate therapy. The risk of MRO is more pronounced in patients with rheumatoid arthritis. As MRO often overlaps with symptoms of rheumatoid arthritis, early recognition is important as methotrexate withdrawal can prevent morbidity.

EP2-01

Two cases of onset and severe course of MCTD induced by Covid-19

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Conflict of interest: None

[Case 1] A 41 yo woman was treated with a diagnosis of "Chronic tubulointerstitial nephritis" for 3 years. Within 6 months after undergoing Covid-19, she developed MCTD with a predominant manifestation of SSc and DM, positive for IB: ANF, anti-dsDNA, nucleosome, histone, SmD1, SS-A/Ro60kD, Scl70, U1-snRNP antibodies. Moreover, the disease proceeded with signs of MIS-C. Despite ongoing pulse therapy (GCS), she developed polyglandular syndrome type III with severe hypothyroidism and adrenal insufficiency. The patient's condition stabilized after prolonged use of corticosteroids and complex symptomatic therapy. [Case 2] A 50 yo man suddenly fell ill 3 months ago after suffering Covid-19: fever, shortness of breath, cough. On IB: sharply positive anti-Ro-52, anti-SS-A antibodies. Along with MCTD, the patient had all the signs of MIS-C. His condition steadily worsened despite the pulse therapy of GCS and symptomatic treatment. The patient died 4 months after the onset of the disease. [Clinical Implication] Both cases are associated by the rapid and severe course of MCTD after Covid-19. There were symptoms of polyserositis, multi-organ damage, high titers of transaminases and inflammatory markers. Commonly the manifestation of an autoimmune disease can be observed after an acute viral infection, Covid-19 as a trigger is no exception. However, only a few such case reports have been described so far and MIS-C in the outcome of Covid-19 is more typical than autoimmune disease. These two clinical cases had features of MIS-C both in terms of the timing of development and the clinical criteria, but MIS-C is characterized

by a favorable course with timely therapy. Here we saw the development of severe, polysymptomatic disease, involving many organs and systems despite glucocorticoid pulse therapy. It is possible that MCTD developed subclinically, but Covid-19 and its complication in the form of MIS-C became a trigger and determined a severe course.

EP2-02

COVID-19 associated vasculitis

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Conflict of interest: None

BACKGROUND: Coronavirus disease 2019 (COVID-19) is a syndrome primarily presenting as a pulmonary disease, but can involve any or all of the organ systems. We report a case of superior mesenteric artery (SMA) vasculitis in a patient with COVID-19. **METHOD**: Case Report **CASE:** A 49 year old female admitted due to acute onset generalized abdominal pain. She had no other symptoms aside from history of nonproductive cough 1 week prior to admission. On work-up, she had normal CBC, elevated CRP at 24 mg/L (<6), ESR 28 mm/hr, ALT 68 U/L (<49), AST 35 U/L (<34) and positive for COVID-19 confirmed by PCR. CT scan of the abdomen showed fat stranding densities surrounding the SMA extending to the celiac trunk region suggestive of vasculitis. SMA vasculitis was confirmed with CT angiogram and revealed circumferential wall-thickening of the SMA with resultant mild luminal narrowing. Further workup showed negative ANCA and hepatitis profile. The patient was managed as a case of post COVID-19 vasculitis not related to any systemic connective tissue disease. Supportive treatment was done with subsequent resolution of symptoms. **CONCLUSION:** Patients with COVID-19 may have atypical presentations such as gastrointestinal symptoms. Few reports of mesenteric vasculitis associated with COVID-19 have been described among adults. Determining the presence of COVID-19 and its relationship to a patient's clinical course is important for making diagnoses and determining subsequent therapeutic strategies.

EP2-03

Tocilizumab-Associated Ileal perforation in a Patient with Rheumatoid Arthritis in SARS-Cov-2 Infection

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Conflict of interest: Yes

Introduction Tocilizumab, a monoclonal antibody of the IL-6 receptor, is a therapeutic option for the patients with moderately to severely active rheumatoid arthritis. Gastrointestinal perforation is a rare but critical complication that occurs in patients treated with tocilizumab. In the COVID-19 pandemic, tocilizumab has been recently highlighted for its beneficial effect in reducing the risk of death in severely ill COVID-19 patients. In this current study, we report the ileal perforation in a COVID-19 confirmed patient who had received tocilizumab for the treatment of rheumatoid arthritis. **Case presentation** A 57-year-old woman with a medical history of rheumatoid arthritis and hypertension presented to emergency room with abrupt onset of severe abdominal pain. Physical examination revealed direct and indirect tenderness of the whole abdomen. She had a history of COVID-19 infection 1 month ago and recovered without complications. She also has been treated for rheumatoid arthritis, and the disease activity has been maintained low with the administration of tocilizumab since 2019. The latest administration of tocilizumab to the patient was 2 weeks ago. The plain radiograph of the abdomen showed pneumoperitoneum. The abdominal computed tomography was also conducted to find the origin of free extraluminal air, and it revealed heterogenous wall enhancement of the ileal loop and the mesenteric haziness. The emergency surgery was performed, and the ileal perforation was noted. The small bowel segmental resection was performed through the surgical procedure. **Conclusions** COVID-19 has been founded to cause gastrointestinal inflammation. The use of tocilizumab in COVID-19 patients should be carefully conducted because it could act as a permissive of gastrointestinal perforation. Furthermore, the physician should be aware of the possible complication of tocilizumab because early diagnosis and timely management are crucial to preventing high mortality complications.

EP2-04

Neutrophil extracellular traps as a marker in diagnostic and prognostic prediction of adverse effects of nCoV-19 vaccine

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Conflict of interest: None

[Objective] Pathogens including SARS-CoV2 can induce NETosis. The spike protein has been shown to directly promote inflammation through NFκB and IL-6 induction. Whether biomarkers of NETosis can be implicated in adverse effects (AEs) due to COVID-19 vaccine has not been confirmed. [Methods] We analyzed serum myeloperoxidase-DNA (MPO-DNA) and citrullinated histone H3 (citH3), and B-cell activating factor (BAFF) in patients with rheumatic diseases (discovery cohort, n=16) and healthy participants (validation cohort, n=34) receiving mRNA and ChAdOx1 nCoV-19 vaccines. Ex vivo NET-forming capacity was also performed. [Results] CitH3 in patients with more than Grade 1 AEs including cutaneous vasculitis, autonomic dysfunction etc. is significantly increased (p=0.009, n=16). Treatment with belimumab (n=6) and cyclophosphamide (n=3) resulted in almost full recovery from AEs for probable or definite lupus patients. CitH3 in serum (p=0.005) and supernatant in *ex vivo* stimulation (n=6, p=0.13) both decreased after treatment. For healthy participants, higher citH3 are associated with longer duration of malaise, headache, rash and diarrhea but not fever through hierarchical-clustering analysis. In addition, Elecsys anti-spike assay but not total IgG are significantly correlated with MPO-DNA after two doses of ChAdOx1 nCoV-19 vaccine (n=34, r=0.39, p=0.02 for S assay; r=-0.07 for IgG) and after mRNA booster vaccination (n=34, r=0.35, p=0.04; r=-0.09 for IgG). We speculated that the relationship between anti-spike antibodies and NETosis is bidirectional. NETs are a known source of autoantigens, and B-cell activating factor could also release upon neutrophil activation. BAFF, which turns B cells into antibody-producing cells, could facilitate both anti-spike and other pathogenic antibodies secretion. [Conclusions] Biomarkers of NETosis showed promise in diagnostic and prognostic prediction of nCoV-19 vaccine-related AEs.

EP2-05

Disease flare-ups after SARS-COV -2 Vaccination among patients with rheumatic and musculoskeletal diseases in a Rheumatology Specialized Care Center- Sri Lanka

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Conflict of interest: None

[Objective] To evaluate the patterns of disease flare-ups following Covid -19 vaccination in patients with rheumatic and musculoskeletal diseases (RMDs). [Methods] This cross-sectional analytical study was conducted at Ragama Rheumatology and Rehabilitation Hospital, Sri Lanka involving 248 clinic patients using a structured questionnaire. [Results] The mean age of the study population was 52.69 and 75.4% were females. 12 patients (4.7%) reported flare symptoms following 1st dose of vaccination. Of them, 67% were females and 41.7% were within the 40-45 years age group. 75% of patients have experienced the onset of the flare symptoms following 1 week of the vaccination and 41.7% of symptoms have lasted more than 8 weeks. 66.7% who got this flare have received Sinopharm, while 25% received Covieshield. In this flare 58.3% got polyarthritis, 16.7% monoarthritis, 8.3% oligoarthritis and 16.7% generalized rash. By contrast, 42 (16.9%) patients who received the 2nd dose of the vaccine got flare symptoms, the majority in the form of polyarthritis (53.4%). 90.5% of this population were females and 38.1% were within the 50-59

years age group. 42% got flare following 1st week of the vaccination and 57% of symptoms have lasted more than 8 weeks. 5 patients who got flare symptoms following the first dose reported having flare after the 2nd dose too. None of the flare symptoms following 1st or 2nd dose of the vaccinations needed hospitalization. Interestingly gender (p=0.012), use of methotrexate (p=0.043), and the presence of flare to the first dose (p=0.02) were found to be significantly correlated with the occurrence of flare symptoms following 2nd dose of vaccination. [Conclusions] This study reveals a considerable incidence of non-severe RMD flare-ups following Covid vaccination, mainly with the 2nd dose. Further studying the effects of repeated and periodic Covid vaccination among patients with RMDs is timely to reassure and improve vaccine acceptance in this group of patients.

EP2-06

The prevalance of ultrasonographic images of 1st MTP joint in patients with hyperuricemia who have not attack history

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Conflict of interest: None

[Objective] The prevalance of ultrasonographic images of 1st MTP joint in patients with hyperuricemia who have not attack history. [Methods] From 2020 September to 2022 August, we have checked the ultrasonography at 1st both MTP onits in patients with hyperuricemia (>7.0 mg/dL) who have no attack history. [Results] 133 patients, 108 male, 59.2 years, 7.2-10,2 mg/dL were included, Only 2 patients have double contour signs, and its signs are very subtle. [Conclusions] The prevalance of ultrasonographic uric signals of 1st MTP joints in patients with hyperuricemia who have not attack history are very low. We might not treat the hyperuricemia who have not attack history for reduce the prevent joint damages.

EP2-07

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome associated with a paravertebral mass encasing vertebral artery

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Conflict of interest: None

[Objective] SAPHO syndrome is a rare disorder characterised by chronic inflammation of anterior chest wall, axial skeleton, peripheral joints and presence of acneiform and neutrophilic dermatoses. [Result] A 54-year-old man presented with sternoclavicular joint swelling, and acneiform rash over forearms for over a year. Computed tomography of his chest showed sclerosis and hyperostosis and joint erosions of the sternoclavicular and manubriosternal joints, thickening and hyperostosis of the anterior aspect of the manubrium and upper sternum and flowing syndesmophytes in the cervical and thoracic spine. Triphasic bone scan confirmed chronic inflammation in bilateral sternoclavicular joints, sternum. Erythrocyte sedimentation rate (ESR) was 32 mm/hour and C-reactive protein (CRP) was 9.4 mg/L (0.2-9.1 mg/L). He was diagnosed with SAPHO and commenced on methotrexate. However, patient preferred to stop methotrexate after 6 months as he felt asymptomatic. He reported development of a left supraclavicular swelling a year later. Computed tomography revealed 6.1 cm by 1.6 cm left paravertebral soft tissue mass arising from C5-6 and T1-2 vertebrae, associated with contiguous erosions into the intervening disc spaces as well as the left first and second costovertebral joints, partially encasing the left vertebral artery and mildly displacing the left scalene muscle and esophagus. ^{18}FDG PET/CT scan showed that the uptake of the mass was equal to blood pool and malignancies and indolent infections were not suggested. Due to the tortuous nature of the paravertebral mass encasing the left vertebral artery, biopsy could be performed. ESR rose to 44 mm/hour and CRP 15.1 mg/L. The patient was re-commenced on DMARD. [Conclusion] Prevertebral soft tissue masses in SAPHO are reported sparsely in the literature. Although rare, prevertebral masses are part of the inflammatory manifestations of SAPHO and alternative diagnoses such as infections and malignancies should be out ruled.

EP2-08

A Japanese long-term nationwide observation study investigating chronic renal dysfunction, complications of malignancy, glucocorticoid toxicities, and mortality in immunoglobulin G4-related kidney disease

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Conflict of interest: None

[Objective] This study aimed to clarify the long-term renal prognosis, complications of malignancy, glucocorticoid toxicities, mortality, and factors related to those outcomes in IgG4-RKD. [Methods] The medical records of 95 patients with IgG4-RKD were reviewed. We investigated clinical and pathological features at baseline and course of renal function, complications of malignancy, cardiovascular events, glucocorticoid toxicities, and mortality during the long-term follow-up (median 73 months). The crude incidence rates (IR) of outcomes were calculated. Cox regression analyses were performed to assess factors related to outcomes. The standardized incidence ratio (SIR) of malignancy and standardized mortality ratio (SMR) were calculated using national Japan statistics. [Results] At diagnosis, the median eGFR was 46 mL/min/1.73 m^2. Prednisolone led to a reasonable initial improvement. The IR of chronic kidney disease (CKD) was 30.6/100 person-years, and 68%, 17%, and 3% of the patients had CKD, >30% eGFR decline, and end-stage kidney disease, respectively, during the clinical course. Age- and sex-adjusted Cox regression analyses indicated that eGFR (per 10 mL/min/1.73 m^2, hazard ratio [HR] 0.71), hypertension (HR 1.81), and pathologically extensive fibrosis (HR 2.58) at treatment initiation had a significant impact on the time to CKD. Ten patients (11%) died during follow-up due to malignancy, infection, or cardiovascular events. A SMR was 0.94. Cox regression analyses showed that the best eGFR within 3 months after treatment initiation and malignancy were associated with mortality (HR 0.67 and 3.27, respectively). The IR of malignancy, cardiovascular events, severe infection, and fracture were 2.93, 1.61, 1.80, and 0.88/100 person-years, respectively, and the SIR of malignancy tended to be high (1.52). [Conclusions] This study suggests that early treatment for preservation of renal function and periodical screening of malignancy may improve patient prognosis in IgG4-RKD.

EP2-09

Efficacy of early and repeated use of high-dose intravenous immunoglobulin (IVIG) in a super-elderly onset anti-transcriptional intermediary factor1-γ (TIF1-γ) antibody-positive dermatomyositis (DM) with severe dysphagia

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Conflict of interest: None

[Case] A 96-year-old, female patient with a history of hypertension and osteoporosis was admitted with a three-month history of eczematous lesions followed by progressive dysphagia. Her vital signs were normal. Physical examination revealed characteristic skin changes. Severe, symmetrical, proximal muscle weakness, elevated serum muscle enzymes, and the presence of anti-TIF1-γ antibody were noted. Magnetic resonance imaging (MRI) of the lower limbs demonstrated hyperintensities on T2-weighted imaging. A muscle biopsy revealed staining of myxovirus-resistance protein A. Computed tomography (CT) of whole body revealed no

interstitial pneumonia or tumors. No malignancies were detected by an upper or lower endoscopy, mammography or gynecological examination. Videoendoscopic evaluation demonstrated a minimal swallowing reflex. The diagnosis of DM was made, and methylprednisolone (mPSL) pulse therapy followed by IVIG (0.4 g/kg/day) for five days, oral tacrolimus, and oral PSL treatment resulted in rapid improvement of the muscle weakness, skin eruptions, and abnormal muscle enzymes. However, the severe dysphagia persisted. Additional IVIG (administered four times in total at one-month intervals) together with extensive rehabilitation resulted in full recovery of the swallowing function. At day 120 after admission, videoendoscopy demonstrated no aspiration, and the patient was discharged with the ability to ingest food orally. However, she presented two months later with hematochezia and subsequently received the diagnosis of duodenal cancer. [Clinical Significance] Dysphagia is a debilitating and potentially life-threatening complication, frequently associated with anti-TIF1-γ antibody. Early and repeated IVIG therapy for severe dysphagia may be beneficial in these patients, as shown in our case. Malignancies are also associated with anti-TIF1-γ antibody, of which majority are detected within 1 year of myositis diagnosis. Therefore, detailed screening for cancer is advocated.

EP2-10

Multi-target therapy avoiding cyclophosphamide for anti-MDA5 antibody-positive juvenile dermatomyositis with interstitial lung disease

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Conflict of interest: None

Objective Recently, the clinical characteristics and prognosis of juvenile dermatomyositis (JDM) have been clarified depending on the type of myositis-specific autoantibody. Of these, JDM positive for anti-MDA5 antibody is known as JDM with a poor prognosis due to rapidly progressive interstitial lung disease (ILD). There is still no consensus about an optimal treatment for anti-MDA5 antibody-positive JDM (aMDA5$^+$JDM). We investigated what kind of treatment is desirable for aMDA5$^+$JDM based on our own experience. **Methods** We experienced a 13-year-old girl with aMDA5$^+$JDM who firstly developed arthritis. She had already had ILD when she visited our hospital. The use of CY is usually considered, but CY has side effects such as gonadal disorders and is difficult to use for adolescent females. Therefore, treatment was started with multi-target therapy including tacrolimus (Tac) and mycophenolate mofetil (MMF). After starting treatment, ILD and skin symptoms gradually improved, and the use of CY could be avoided. Glucocorticosteroids were stopped after one year and then Tac and MMF are continued for another year without recurrence. In addition, we conducted a literature search and review of aMDA5$^+$JDM cases treated with calcineurin inhibitors (CNI) in combination with inosine 5'-monophosphate dehydrogenase (IMPDH) inhibitors. **Results** Sixteen references, 26 cases were identified. Of these cases, 22 cases were alive and there were 4 deaths. Fourteen cases were treated with CY and 15 with rituximab. Many side effects were not described, but among those we could find, susceptibility of infection and increased blood pressure were observed. **Conclusion** The combination of CNI and IMPDH inhibitors, especially Tac and MMF, is a relatively safe and potentially effective treatment for aMDA5$^+$JDM. In view of the side effects of CY, starting with multi-target therapy may be an option.

EP2-11

The EQ5D score is not influenced by aging yet correlated with the HAQ score

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Conflict of interest: None

[Objective] EuroQol-5th dimension score (EQ5D) is a most popular index for measuring the quality of life in patients with rheumatoid arthritis (RA). In this study, an association between EQ5D and aging using retrospective cohort data. [Methods] RA patients who had been followed up for more than 3 years were picked up. Patients' simplified disease activity index score (SDAI), HAQ, pain score using a visual analog scale (PS), Sharp/van der Heijde score (SHS), and EQ5D were monitored since the start of treatment (BL). Patients were divided into 3 groups; G-YY, who initiated to treat as younger than 65 and lasted until younger than 65; G-YO, who initiated as younger than 65 and lasted until older than 65; G-OO, who initiated as older than 65. Mean EQ5D during treating of the G-YY and G-OO were compared using crude and after SHS or HAQ were matched. Moreover, EQ5D of G-YO between younger than 65 and older were compared statistically. [Results] There were 538 patients in those 143 of G-YY, 88 of G-YO, and 307 of G-OO. Mean values were 49.9, 61.2, 76.9 for age, 12.5, 12.1, 13.0 for SDAI, 0.281, 0.353, 0.627 for HAQ, 29.7, 55.4, 56.3 for SHS, 35.5, 31.1, 36.6 for PS, and 0.807, 0.761, 0.724 for EQ5D in the G-YY, G-YO, and G-OO, respectively. The mean EQ5D score in the G-YY was significantly higher than that in the G-OO using crude data, however, there was no significant difference between the two groups after SHS or HAQ was adjusted. When the mean EQ5D score was compared in the G-YO between before 65 and after 65, there was also no difference between the two-term. The HAQ score was correlated significantly with age using whole patients' data. [Conclusion] The HAQ score was significantly correlated with aging, and the EQ5D score was significantly correlated with the HAQ score, however, the EQ5D score was not correlated with aging. This explains the EQ5D score is independent of aging. This would be beneficial for calculating cost-benefit evaluation in elderly people.

EP2-12

Septic arthritis associated with closed extraarticular glenoid fracture: A Case Report

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Conflict of interest: Yes

[Objective] Septic arthritis associated with closed fractures has not yet been reported. This is a case of a 73 year old male presented with septic arthtritis on left shoulder after a closed extraarticular glenoid fracture. [Methods] Our patient is an 73 year old Filipino Male presented 4 days history of left shoulder swelling and pain associated with fever with no history of previous infection and trauma. No history of previous PTB infection. [Results] MRI results revealed Type 1 extraarticular glenoid fracture with moderate fluid on glenohumeral joint space. Arthroscopic debridement was done. Synovial tissue specimen was sent for culture studies and revealed positive for Staphylococcus aureus and Mycobacterial Tuberculosis. Antibiotics and Anti Koch's treatment was started. [Conclusions] Although Septic arthrtitis associated with closed intraarticular fracture is rare, Prompt diagnosis and treatment is needed to prevent further complications.

EP2-13

Application of intra-soft tissue antibiotics perfusion after removal of THA with MRSA infection: a case report

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Conflict of interest: None

[Objective] Continuous local antibiotics perfusion (CLAP) is a treatment for infections of traumatic bone and soft tissue injury that uses continuous infusion of high-concentration antibiotics to perfuse the wound with it. We report a case in which CLAP was successfully used to control infection after removal of hip arthroplasty with MRSA infection. [Case] An 81-year-old man had suffered rheumatoid arthritis 15 years ago. He was introduced to dialysis due to chronic renal failure 5 years ago. Two months ago, he underwent left total hip arthroplasty (THA) with KT plate and allogeneic bone graft for left hip disorder due to rheumatoid arthritis. He was transferred to another hospital for rehabilitation one months after

his left THA. Three weeks after his transfer, he developed fever and wound dehiscence. MRSA was detected in his blood culture. Based on the patient's and family's wishes, the decision was made not to perform revision surgery, but only to remove the joint prosthesis. The prosthesis was removed and performed debridement in the hip joint as much as possible. Intra-soft tissue antibiotics perfusion (iSAP) tubes were placed in the hip joint and femoral marrow cavity, and gentamicin was administered at 2 ml/h with a concentration of 60 mg/50 ml. CLAP was performed for 2 weeks, and vancomycin was administered intravenously until 4 weeks postoperatively, after which the patient was switched to oral minocycline. There were no further signs of infection such as redness or dehiscence of the wound. [Conclusions] CLAP was used in combination to control MRSA infection and the dead space, resulting in containing of the infection, because complete removal and debridement of the bacterial components after removal of the hip prosthesis seemed difficult to achieve. CLAP may be a useful adjunctive therapy after joint removal with MRSA infection.

EP2-14

Prevalence of shoulder pain and associated risk factors among farmers in Jeju

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Conflict of interest: None

[Objective] Work-related injuries and musculoskeletal disorders are common among farmers due to high physical strain and repetitive laborious activities associated with agricultural work. One of the most common complaints related to musculoskeletal disorders is shoulder pain. This study aimed to investigate the prevalence of shoulder pain and analyze the socio-demographics, agricultural work-related conditions, and biomechanical factors associated with shoulder pain. [Methods] We used initial survey data from the Safety for Agricultural Injury of Farmer's cohort study of adult farmers in Jeju Island. The presence and characteristics of shoulder pain, socio-demographics, agricultural work-related conditions, and biomechanical factors were assessed using semi-structured questionnaires. [Results] The overall prevalence of shoulder pain was 17%. In the multivariate logistic regression analysis, stress level (occasional: OR, 1.581; 95% CI, 1.079 to 2.318; frequent: OR, 1.964; 95% CI, 1.205 to 3.200; extreme: OR, 2.999; 95% CI, 1.480 to 6.074 versus rarely), type of farming (orchard: OR, 0.82; 95% CI, 0.597 to 1.124; livestock: OR, 0.225; 95% CI, 0.079 to 0.641 versus field), and agricultural damage within one year (yes: OR, 2.078; 95% CI, 1.269 to 3.405) were significantly related to shoulder pain. Multivariate logistic regression analysis adjusting for a set of covariates (farming duration, sex, stress level, farming type, agricultural injury within a year) revealed three biomechanical factors significantly related to shoulder pain: shoveling, pickaxing, hammering; repetitive use of particular body parts; constant elevation of the arm above the head. [Conclusions] Some occupational and biomechanical risk factors contribute to shoulder pain. Therefore, postural education, injury prevention, and psychological support will be needed to prevent shoulder pain.

EP2-15

Giant cell arteritis in an elderly filipino female

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Conflict of interest: None

BACKGROUND: Giant cell arteritis (GCA) is a systemic vasculitis of the medium and large-size vessels and can lead to irreversible visual loss in the elderly patients. GCA is rare among Asians. We report a case of GCA in a 79-year-old Filipino patient presenting with headache and blurred vision. **METHOD:** Case Report **RESULTS:** A 79 year old female, with a significant history of recurrent strokes, was admitted due to a 1 year history of bitemporal and occipital headache accompanied by bilateral blurring of vision. She had occasions of proximal lower extremity muscle weakness and morning stiffness. There was noted prominent, enlarged and tender bilateral superficial temporal arteries. On work-up, she had an elevated ESR at 130 mm/hr. Color flow doppler ultrasound (CFDU) revealed tortuous bilateral superficial temporal arteries with associated intimal thickening. Likewise, bilateral axillary arteries were also noted to have intimal thickening and showed a characteristic "halo sign", signifying vessel wall inflammation. The patient was managed as a case of Polymyalgia Rheumatica (PMR) with GCA and was started on Prednisone 20 mg daily with significant improvement of symptoms. **CONCLUSION:** GCA is a rare form of vasculitis among Asians most commonly presenting as headache. In the absence of biopsy, CFDU is a promising diagnostic modality in GCA and could be proposed as an added skill to the diagnostic armamentarium of Filipino rheumatologists. Prompt recognition and treatment with steroids and immunosuppression can appropriately manage GCA and prevent its dreaded complications such as permanent loss of vision.

EP2-16

Revisiting the diagnostic challenges of cranial giant cell arteritis mimickers: A case report

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Conflict of interest: None

[Case] An 87-year-old man with essential hypertension and dementia was referred to us for possible giant cell arteritis (GCA). He presented at another hospital with a one-week history of general malaise, two-day history of a 38°C fever, bilateral temporal scalp pain, and jaw claudication. Laboratory results revealed elevated inflammatory markers. The findings of a chest X-ray, echocardiogram, and contrast-enhanced computed tomography (CT) of the neck to pelvis were unremarkable. Brain CT showed a hypodense, left, subdural hematoma. Results from two sets of blood culture (BC) returned negative. Despite treatment with ceftriaxone (CTRX) for seven days, the patient remained febrile and was subsequently referred to our facility for testing for GCA. On arrival at our hospital, the patient was unaware of the time. Physical examination revealed tortuous, bilateral temporal arteries with tenderness on palpation. Two sets of BC, a lumbar puncture, and a temporal artery biopsy (TAB) were performed. CSF contained 48 WBCs per mm^3 (predominantly monocytes); thus, acyclovir therapy was begun for suspected viral meningoencephalitis. A herpes simplex virus polymerase chain reaction test returned negative three days later, but the patient's consciousness status remained altered. Brain magnetic resonance imaging (MRI) revealed multiple brain abscesses. Three additional sets of BC and brain abscess drainage were performed, and vancomycin with metronidazole therapy was begun. TAB showed no signs of vasculitis, and one bottle of BC returned positive for *Capnocytophaga sputigena*. The antibiotics were switched to CTRX, and follow-up brain MRI demonstrated regression of the brain abscesses. Treatment was concluded after eight weeks. [Clinical Significance] Numerous disorders, including serious infections, can mimic the clinical picture of cranial GCA. The present case highlights the importance of a thorough clinical examination to avoid misdiagnosis of a GCA-mimicker and incorrect treatment.

EP2-17

Knowledge of disease among filipino patients with spondyloarthritis

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Conflict of interest: None

[Objective] The objective of this study was to determine the level of knowledge of patients with spondyloarthritis (SpA). [Methods] All consecutive patients seen at the UP-PGH 19 years old and above (in-patient and out-patient) from June 2021 to March 2022 diagnosed with SpA specifically axial spondyloarthritis (axSpa) and Psoriatic Arthritis (PsA) only were recruited in this study. Informed consent was secured and patient confidentiality was observed. The Philippine General Hospital Arthritis Knowledge Questionnaire (PGH-ArKQ) was designed to reflect the Filipino participants' knowldge on basic information about their disease and to identify specific areas to address in patient education. Means, standard deviations, and proportions will be used to describe and summarize the data. T-test was used to test the differences in mean values. [Results] There were 45

adult Filipino patients with spondyloarthritis recruited in the study (38 PsA, 7 axSpa). The mean age was 42.16 (±11.07) years and ranges from 20 to 70 years old. There were 22 (48.9%) females. The mean duration of years of disease was 6.18 (±5.56) years. The mean duration of follow-up at current HCP was 4 (±3.41) years. there were 16 (35.6%) employed, 18 (40%) college graduates, mean consultations per year was 3.6 (±1.98). The usual source of information about spondylarthritis was their physician. The mean knowledge score was 5.23 out of perfect score of 9. Most patients know their diagnosis and non-communicable nature of SpA. Majority of the participants (80%) have inadequate knowledge on their disease. [Conclusions] Majority of our SpA patients had low knowledge scores with poor health-seeking behavior. This study may be used to improve on our role as physician on patient education by integrating relevant clinical knowledge leading to treatment adherence and better quality of life.

EP3-01

Avascular necrosis of bone in a patient with systemic lupus erythematosus without corticosteroid use: A case report

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Conflict of interest: None

[Objective] Avascular necrosis of bone [AVN] can cause significant disability and limitation of mobility in systemic lupus erythematosus [SLE] patients. Risk factors of AVN include a longer disease duration, high LDL-C, positive aCL IgG and anti-dsDNA, cushingoid body habitus, and the use of corticosteroid. In the absence of steroid use, AVN is extremely rare. Herein, we present an experience of AVN in an SLE patient without use of corticosteroid. [Methods] The patient was a 39-year old female, diagnosed at 17 with SLE. She had taken medicines irregularly but her disease status had been relatively stable. She visited our hospital with left hip joint pain. At that time she was taking hydroxychlorquine 200 mg/day, losartan 50 mg/day, aspirin 100 mcg/day and NSAID from another hospital. She denied a history of steroid use. On laboratory testing, ANA was 1:320, anti-ds-DNA Ab, anti-Ro/La Ab, and anti-Smith Ab were negative. CBC, liver, and kidney function test were in normal range. LDL-C was 79 mg/dL, ESR was 36 mm/hr, CRP was 0.79 mg/dL. Anti-phospohlipid antibodies were positive (aCL IgG 79.0 GPL, anti-β2 glycoprotein IgG 142.0 G units, confirmative lupus anticoagulant 1.42). X-ray of hip joint demonstrated marginal irregularity and sclerotic change with central lucency in the head of left femur. We started conservative management of joint pain. After 10 months, she newly complained of bilateral knee pain. X-ray of knee joint demonstrated joint space narrowing in both knees on medial aspect and severe bony sclerotic changes in both lateral condyles of femur. [Results] The risk factors for AVN in SLE have been reported by several studies. There is a strong causal relationship between corticosteroid intake and AVN development in SLE patients. However, in this case, the patient had never taken corticosteroid since diagnosis of SLE. [Conclusions] The pathophysiology of AVN is not clear yet, however SLE itself should be considered an important risk factor of AVN.

EP3-02

Protein losing enteropathy as a manifestation of lupus in a 19-year-old Filipino female: A case report

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Conflict of interest: None

Introduction: Systemic lupus erythematosus is a disease which may initially present with different symptoms, most commonly photosensitive rash and arthritis. Gastrointestinal symptoms are a recognized but rare presenting manifestations of SLE. Protein-losing enteropathy in SLE presents as profound pitting edema, pleural, pericardial effusion, ascites, nausea, vomiting, and diarrhea and associated hypoalbuminemia in the absence of nephrotic range proteinuria. **Objective:** This paper reports a case of SLE initially presenting with gastrointestinal symptom, chronic diarrhea. Diagnosis, management, outcome, prognosis and response rate of treatment were also discussed. **Case:** A 19-year old Filipino female presents a two-month history of watery, non-bloody diarrhea then with noted progressive generalized edema, difficulty of breathing and orthopnea. Protein losing enteropathy was entertained and diagnosis of SLE was made after exclusion of other causes of hypoalbuminemia. Pulse therapy was done which showed improvement in the condition of the patient. **Conclusion**: SLE-related gastrointestinal involvement is clinically important because most cases can be life threatening if not treated promptly. It is important therefore to rule out infectious, inflammatory and malignant processes. Lupus-related protein-losing enteropathy generally responds well to treatment with glucocorticoids. Timely diagnosis is very critical for the timely management providing resolution of symptoms.

EP3-03

Diffuse alveolar haemorrhage in lupus: A rare favorable outcome to therapeutic plasma exchange plus rituximab: A case series

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Conflict of interest: Yes

INTRODUCTION: A case of two systemic Lupus erythematosus (SLE) Filipino female patients who were diagnosed with Diffuse alveolar haemorrhage (DAH), which is a rare and devastating complication of SLE with a mortality rate as high as 86%, characterized by decreasing hemoglobin, hemoptysis, dyspnea, diffuse pulmonary infiltrates, desaturation, and respiratory failure. This report highlights the rarity of reported cases with good outcome to treatment given for DAH with SLE. **OBJECTIVE:** We aim to present two cases of Filipino women with severe lupus activity with life-threatening DAH that had good response to combination of Rituximab and Therapeutic Plasma Exchange (TPE). **CASE SUMMARY:** The first patient is 19 years old with one month history of progressive bipedal edema, oliguria, orthopnea and easy fatigability. Tests revealed anemia, azotemia, and hyperkalemia. Tests showed positive ANA and elevated anti-dsDNA. Pulse therapy was given. Bronchoscopy revealed friable mucosa. BAL culture showed *A. baumannii.* Findings were consistent with DAH, hence TPE with Rituximab was given. Patient's symptoms resolved; unfortunately, central-line infection and nosocomial pneumonia developed leading to septic shock. Family opted to bring the patient home. The second patient is a 28-year-old with progressive dyspnea and is a known case of ITP. She presented with tachycardia, bibasal crackles and bipedal edema. Bronchoscopy revealed petechial hemorrhages and plaques with consideration of vasculitis and infection. BAL culture showed *A. baumannii.* Findings were consistent with DAH. TPE with RTX were given. Patient was discharged improved. **CONCLUSION:** DAH is said to be one of the most severe forms of pulmonary involvement in SLE, us clinicians should be prompt in identifying the earliest signs and symptoms of this condition and to formulate and provide immediate medical strategies to prevent further complications and mortality in patients with this condition.

EP3-04

Efficacy of abatacept on treatment of flares in patients with systemic lupus erythematosus arthritis: a meta-analysis

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Conflict of interest: None

[Objective] Systemic Lupus Erythematosus (SLE) has various manifestations which may range from mild to life threatening. The most common manifestations include mucocutaneous lesions and arthritis or musculoskeletal complaints. Current studies on SLE have been aiming to develop targeted biologic treatments used to target different aspects of the immune response in patients with SLE. This study was conducted to determine the efficacy of abatacept in treating flares among patients with SLE presenting with systemic polyarthritis. [Methods] Search engines were used to identify studies on the efficacy of abatacept on systemic lupus erythematosus arthritis such as Pubmed, Cochrane and Google Scholar. Two authors extracted data independently using a standard data extraction form and agreed data before entry into review manager. Two independent authors assessed risk of bias for each study. A fixed-effect model for meta-analysis was used. Two reviewers independently rated the quality of the evidence for each outcome. [Results] The data from three studies were assessed. Re-

sults show that the efficacy of abatacept in preventing flares among patients with SLE polyarthritis is equivalent to that of the current standard of care: oral steroids. Analysis of adverse events demonstrated that there were more adverse events noted in the steroid group as compared to the abatacept group. However, it is important to note that in the abatacept group low dose steroids were also being given as an adjunct, thus the adverse effects of abatacept alone were not measured. [Conclusions] Abatacept is as effective as current standard treatment for recurrence of flares in patients with systemic lupus erythematosus polyarthritis, thus it may be an option of treatment for those with refractory disease unresponsive to steroids. Furthermore, it may be a better treatment option due to less severe adverse effects as compared to the use of chronic steroids.

EP3-05

Treatment with lysophosphatidic acid (LPA) improves glomerulonephritis in MRL/lpr mice

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Conflict of interest: None

[Objective] Our previous report suggested that treatment with LPA suppressed depressive-like behavior and microglial activation in MRL/lpr mice. However, the effects of LPA on glomerulonephritis in SLE model mice have not yet been evaluated. In the present study, we determined whether the treatment with LPA affects glomerulonephritis in MRL/lpr mice. [Methods] 18-week-old MRL/+ and MRL/lpr mice were treated intraperitoneally with vehicle or LPA (1 mg/kg) for 3 weeks. After the blood and urine samples were collected, the renal tissues were isolated after perfusion. [Results] Treatment with LPA decreased plasma creatinine, and significantly decreased IL-18 and dsDNA antibody titer in MRL/lpr mice. The treatment decreased urinary albumin and increased the urine volume in MRL/lpr mice. In addition, the treatment significantly decreased both CD68-positive cells and PAS-positive area in the glomerulus of MRL/lpr mice. [Conclusions] Treatment with LPA improved glomerulonephritis in MRL/lpr mice. Since we revealed that the treatment improved splenomegaly in MRL/lpr mice, we will talk about additional results about the effects of LPA on systemic immunity.

Poster Session

P1-001

Investigation of the period from onset to consultation of early arthritis patients who were referred to Rheumatology for early joint pain and their initial diagnosis and diagnosis after 1 year in a community hospital in Japan

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Conflict of interest: None

[Objective] Early diagnosis and intervention are important for inflammatory diseases such as rheumatoid arthritis (RA), and the delay from onset to diagnosis is problem. Diagnosis tends to be more difficult in the early stages, and the diagnosis may change later. We will grasp the current situation at a community hospitals and reflect it in future medical care. [Methods] We retrospectively observed a patient with undiagnosed arthritis within 2 years of onset who was referred to our hospital from April 1, 2015 to March 31, 2021. We verified the period from onset to consultation, and the diagnosis name at the beginning and one year later. [Results] There were 344 patients. The mean time from onset to consultation with a specialist was 18.6 weeks, and the mean time from onset to consultation at a medical institution was 15.0 weeks. Early diagnosis was RA 36%, polymyalgia rheumatoid arthritis 13%, spondyloarthritis 10%, antinuclear antibody-related disease 8%, crystal arthritis 12%, infection 3%, primary vasculitis 1%, unclassified arthritis (UA) 15%. The follow-up rate of hospital visits after 1 year and the concordance rate of diagnosis names after 1 year were UA 58.5%/65%. [Conclusions] There is a long period between the onset of symptoms and consultation at a medical institution.

P1-002

Consultation status of rheumatoid arthritis patients from onset to diagnosis and treatment

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the status of consultations, from the manifestation of RA symptoms to consultation, diagnosis, and treatment. [Methods] The subjects were 262 patients (53 males, 209 females, average age 67.7±13.3 years) who were undergoing RA treatment at our department or other hospitals. Age at onset of RA, painful joints, time from onset of symptoms to hospital visit, first hospital/clinical department, whether the patient was an RA specialist, name of diagnosis at first visit, period until diagnosis of RA, and RA A questionnaire survey was conducted regarding the department in which the patient was diagnosed, whether the patient was a specialist in RA, the length of time until the first RA drug was prescribed, and the prescribing doctor. [Results] The age at onset of RA was 54.1±16.0 years old. Painful joints were mostly fingers and wrists. rice field. Time from first visit to diagnosis of RA was 17 days (median), time from diagnosis to medication was 7 days (median), 1 day (median) for RA specialists, 7 days (median) for non-specialists. [Conclusions] The majority of patients underwent orthopedic surgery, and the period from diagnosis to the start of treatment was shorter in patients who consulted an RA specialist.

P1-003

Development of machine learning models for severe infection in rheumatoid arthritis patients treated with anti-TNF agent and clustering using Japanese electronic medical record database

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Conflict of interest: None

[Objective] To evaluate prediction models for severe infections in rheumatoid arthritis (RA) treated with anti-TNF agents. [Methods] Japanese electronic medical record (EMR) database was used. Patients with anti-TNF agents on/after RA diagnosis were included and the outcome was time-to-event for severe infections. Age, sex, laboratory results, use of

glucocorticoid (GC), and use of DMARDs were used as covariates. The high-dimensional variables obtained from the database were also leveraged. Regularized cox proportional hazard (rCoxPH), gradient boosting (GBT), random survival forest (RSF), survival support vector machine (SSVM), and three deep-learning models were developed. The developed model was evaluated with the Shapley additive explanations (SHAP) method and clustering. [Results] A total of 2593 patients were included. The SSVM showed the greatest metric (time-dependent concordance 0.743). The evaluation of SHAP values and clustering showed the use of GC, comorbidities such as diabetes, histories of admissions, and frequency of hospital visits were associated with the outcome. [Conclusions] SSVM was the most efficient machine learning model in the study. Machine-learning models using EMR database may be useful to help clinical decisions and identify a meaningful patient population.

P1-004

Protocol of Late-onset Rheumatoid Arthritis Registry Study

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Conflict of interest: None

[Objective] The evidence for pharmacological treatment of RA is mainly based on RCTs for patients under 65 years of age, forcing the primary care physician to proceed with the initial treatment of elderly patients in a hands-on manner. We constructed a registry of patients with elderly-onset rheumatoid arthritis (RA), which is expected to increase rapidly in the future, and proposed optimal treatment strategies tailored to patient backgrounds. [Methods] Patients aged 65 years or older with RA who are newly initiating anti-rheumatic drug therapy or molecular targeted therapy will be included in the registry. [Results] Enrollment began on January 13, 2022, and 89 patients were enrolled by October 30, 2022. Of the 85 patients with complete baseline data, 30.6% were male. [Conclusions] Drug selection and baseline characteristics will be verified for patients enrolled until the end of December of this year.

P1-005

Survey on Rheumatoid Arthritis Medical Cooperation in Tottori

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Conflict of interest: None

[Objective] We conducted an awareness survey of physicians involved in RA practice in Tottori Prefecture regarding current RA medical collaboration. [Methods] A questionnaire with the following questions was sent to rheumatologists and rheumatology foundation registered physicians in Tottori prefecture. Question 1: Are there any problems with medical collaboration in RA treatment? Question 2: In what situations do you need medical collaboration? Question 3: What is needed to further promote medical collaboration? [Results] Seven were from clinics (all orthopedic surgeons) and 21 were from hospitals (6 internists and 15 orthopedic surgeons). Hospital physicians were more aware of issues such as regional disparities and reverse referrals in RA medical collaboration in Tottori Prefecture. The need for medical collaboration was higher when diagnosing, dealing with complications, and administering drug therapy. Many respondents thought it was important to improve the level of medical care through study groups, to promote communication among doctors, to share medical information, and to understand the RA treatment capabilities of each medical institution. [Conclusions] It was suggested that if medical collaboration is promoted, more facilities may be more proactive in RA treatment.

P1-006

Characteristics of BAFF/APRIL signaling and circulating B cells in ANCA-associated vasculitis

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Conflict of interest: None

[Objective] To investigate the signaling pathways of BAFF and APRIL in antineutrophil cytoplasmic antibody-associated vasculitis (AAV). [Methods] We used blood samples from 24 patients with active AAV (a-AAV), 13 with inactive AAV (i-AAV), and 19 healthy controls (HC). BAFF/APRIL receptors, including BAFF-R, TACI, and BCMA, on circulating B cells, as well as serum levels of BAFF, APRIL, and interleukin (IL)-6, were analyzed in this study. [Results] Higher frequencies of plasmablasts/plasma cells (PB/PC) and serum levels of BAFF, APRIL, and IL-6 were significantly observed in a-AAV than in HC. Serum levels of BAFF and APRIL were significantly higher in i-AAV than in HC. Expression of BAFF-R on memory B cells was significantly lower, whereas that of TACI on CD19+ cells, immature B cells, and PB/PC were significantly higher in a-AAV and i-AAV than in HC. Expression of memory B cells was significantly associated with serum APRIL levels and BAFF-R expression. [Conclusions] Decreases in BAFF-R on memory B cells, increases in TACI on CD19+ cells, immature B cells, PB/PC, and increased serum levels of BAFF and APRIL were persistently observed even in remission AAV. Persistently enhanced signaling of BAFF/APRIL may be implicated in disease relapse.

P1-007

Comprehensive analysis of post-translational modifications of neutrophil-derived myeloperoxidase obtained from MPO-ANCA-positive patients with ANCA-associated vasculitis

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Conflict of interest: None

[Objective] Mechanism of MPO-ANCA production, especially how myeloperoxidase (MPO) acquires the antigenicity, is still unknown. To address this issue, we analyzed post-translational modifications (PTMs) of MPO from MPO-ANCA-positive patients. [Methods] MPO was purified from neutrophil lysates obtained from 8 MPO-ANCA-positive patients with ANCA-associated vasculitis and 8 healthy individuals, then digested with trypsin. Ion intensity and amino acid sequences including PTMs of MPO peptides were comprehensively analyzed by nano-LC MS. [Results] Ion intensity of 38 MPO peptides were increased in the MPO-ANCA group compared to that in the control group ($p<0.05$). 9 out of 38 peptides included oxidation of Met, Phe, and Trp. Conversely, ion intensity of 10 MPO peptides were decreased in the MPO-ANCA group compared to that

in the control group ($p<0.05$). 4 out of the 10 peptides included glycosylation. Oxidized mouse MPO-immunized mice produced not only anti-oxidized MPO antibodies but also anti-MPO antibodies, whereas no preferential production of both antibodies was found in non-oxidized MPO-immunized mice. [Conclusions] PTM profile of MPO of MPO-ANCA-positive patients was different from that of healthy individuals. The oxidation of MPO may be a trigger of MPO-ANCA production.

P1-008

Bone strength and its related factors in the metacarpal head of rheumatoid arthritis patients: The first report

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Conflict of interest: Yes

Objectives: The bone quality is thought to be related to bone strength, but the relationship in rheumatoid arthritis (RA) patients is unclear. We measured the bone strength of the metacarpal head and investigated influencing factors. **Methods:** Using 105 resected metacarpal heads removed during implant arthroplasty at the metacarpophangeal joint, a bone structure analysis by micro-computed tomography (μCT), bone strength measurement by a compression test, and bone morphometry were performed, and the patient backgrounds were evaluated. **Results:** In a univariate analysis, the factors affecting bone strength were the prednisolone dose, Rooney score by synovial histopathology, percent of the young-adult mean (%YAM) and T score. A high Larsen grade decreased the %YAM but increased the cancellous trabecular width (Tb. Th). In a multiple regression analysis, the bone mass volume ratio (BV/TV) influenced bone strength. **Discussion:** RA can be a secondary osteoarthritic change. Cases with a high Larsen grade have a preserved bone strength, as bone regeneration progressed after the inflammation subsided at the time of surgery. **Conclusions:** To maintain bone strength, it is important to suppress local inflammation and deterioration of bone structure for a long period after RA onset.

P1-009

Investigation about the fluctuations and clinical significance of citrullinated ITIH4 in arthritis

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Conflict of interest: None

[Background] We have previously shown that citrullinated Inter-alpha-trypsin inhibitor heavy chain 4 (cit-ITIH4) is increased in blood and joints of peptide GPI-induced arthritis (pGIA) and rheumatoid arthritis (RA). We investigated its source, therapeutic response, and clinical significance in this study. [Methods] 1) Neutrophil extracellular traps (NETs) in pGIA joints were evaluated. 2) IL-6 inhibitors were administered to pGIA. Changes in arthritis, NETs and serum citrullinated protein were evaluated. 3) Plasma citrullinated protein expression before and after IL-6 inhibition for RA were examined. 4) Anti-cit-ITIH4 antibody was measured in plasma of RA and healthy control (HD) by ELISA using citrullinated recombinant ITIH4. [Results] 1) Specific expression of NETs was detected in pGIA joints on day14. 2) Arthritis and NETs expression was improved after treatment with IL-6 inhibitor. Serum cit-ITIH4 tended to decrease. 3) Cit-ITIH4 expression in RA plasma significantly decreased after treatment with IL-6 inhibitor. 4) Anti-cit-ITIH4 antibody in plasma of RA tended to increase compared to HD. [Conclusions] NETs were suggested as a source of cit-ITIH4, and treatment with biologic agents reduced its production. Plasma anti-cit-ITIH4 antibody might be elevated in RA specifically.

P1-010

CD14+ dendritic-shaped cells in synovial tissue of rheumatoid arthritis may be derived from circulating blood

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Conflict of interest: None

[Objective] CD14+ dendritic-shaped cells are very unique cells that possess immune response capacity, phagocytosis, and a mesenchymal phenotype. These cells play a key role in the pathogenesis of rheumatoid arthritis (RA), but their origin and function are still unknown. We reported that CD14+ dendritic-shaped cells express CD90 around blood vessels in highly active synovial tissue. In this study, we investigated CD14+CD90+ cells in the peripheral blood of RA. [Methods] Peripheral blood samples were collected from 7 untreated, active RA patients, 9 RA patients in remission, and 4 patients with osteoarthritis (OA) as control. The percentage of CD14+CD90+ cells in the peripheral blood was analyzed by flow cytometry, and the correlations with clinical data were examined. [Results] There were significantly more CD14+CD90+ cells in the untreated RA group. There was no significant difference between the RA group in remission and the control OA group. The percentage of CD14+CD90+ cells in blood in the untreated RA group correlated with the levels of CRP and rheumatoid factor. [Conclusions] The CD14+ dendritic-shaped cells found in RA synovial tissue may be derived from circulating blood, and involved in the pathogenesis of RA.

P1-011

Analysis of autophagy-related molecules in synovial macrophage subtypes of rheumatoid arthritis

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Conflict of interest: None

[Objective] We investigated autophagy-related molecules in rheumatoid arthritis (RA) synovial macrophages and analyzed the relationship between autophagy and inflammation. [Methods] 1) Histological evaluation: Synovial tissue sections from RA/OA patients (n=5) were HE-stained, and the degree of synovitis was evaluated by the Krenn classification. 2) Flow cytometry: Cells were isolated from synovial tissue and evaluated with fluorescent antibodies for M1, M2. and autophagy-related molecules LAMP1. [Results] 1) Histological evaluation showed that the degree of synovial inflammation was 5.4±2.3 in RA and 2.6±1.8 in OA on average. 2) Flow cytometric analysis showed that the percentage of M2-positive cells isolated from RA and OA was inversely correlated with the degree of inflammation. On the other hand, the population of M1/2-positive cells was observed, and its proportion positively correlated with the degree of inflammation. The MFI of LAMP1 was higher in M1/2, when compared to that of M1 and M2. The expression of LAMP1 in M1/2 cells was positively correlated with inflammation. [Conclusions] The appearance of M1- and M2-positive cells reflects the degree of inflammation, suggesting macrophage mobilization and its response correlated with the degree of inflammation in RA and OA synovitis.

P1-013

Evaluation about the abnormal doppler signals ultrasonography (US) of the shoulders in rheumatoid arthritis (RA) and polymyalgia rheumatica (PMR): especially correlation with rotator cuff tears (RCT)

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Conflict of interest: None

[Objective] We examined the PD signal and Gray scale (GS) score of

the shoulder in RA patients and PMR patients. And considered about the relation between PD signal and RCT, evaluated difference between RA and PMR. [Methods] We enrolled 45 untreated patients (RA: 35 patients, PMR: 10 patients). 90 shoulders were scanned according to a standardized scanning method. In addition, scanned rotator cuff (SSpT, subspinatus tendon, SScT), CHL. [Results] 1) 10 patients (13 shoulders) in the 35 RA had the US findings of RCT, and they were older than RCT negative RA patients significantly. 2) In RCT positive RA (13 shoulders), PD scores for the LHB, SScB, SScT were more frequently positive and higher grade than RCT negative RA significantly. 3) There were no RCT positive patients in PMR. In the PMR patients, the positivity and grading score were particularly higher for LHB, HV of the anterior aspect of the SScT significantly than the RCT negative RA.4) In the patients who had the HV of the anterior aspect of the SScT, we found the PD strongly for GHJ, CHL, SSpT in RCT negative RA. ON the other hand, we found less PD in PMR. [Conclusion] It is important to consider the distribution and strength of PD area, and consider of the presence of RCT for the diagnosis of RA and PMR.

P1-014

Relationship between Leeb's disease activity score and ultrasound findings of shoulders in polymyalgia rheumatica

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Conflict of interest: None

[Objective] This study aimed to assess the relation between ultrasound (US) findings in shoulders and disease activity after the treatment of polymyalgia rheumatica (PMR). [Methods] 19 untreated PMR patients with tenosynovitis at biceps brachii muscle by US examination were analyzed. All patients were treated with 15 mg/day of prednisolone equivalent. At baseline, 6 months, 12 months after the treatment and at the time of exacerbation, thickness and the doppler activity surrounding long head biceps (LHB) were examined. Relationship between Leeb's disease activity score (Leeb's DAS) and US findings after the treatment were also analyzed. [Results] At the time of the diagnosis, 73.3% of the patients showed positive doppler signal surrounding LHB and mean thickness of synovium surrounding LHB was 1.89±0.83 mm. 12 months after the treatment, 89.5% of the patients had achieved low disease activity of Leeb's DAS and negative doppler signal. Mean thickness of synovium surrounding LHB were 1.20±0.93 mm in patients who achieved low disease activity and 2.30±0.95 mm in patients who didn't achieve low disease activity, which tended to be corelated with Leeb's DAS. [Conclusions] US follow-up examination of shoulders after treatment is useful for evaluation of the disease activity of PMR.

P1-015

Investigation of elderly-onset RA in which musculoskeletal ultrasonography was useful for differentiation from PMR

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Conflict of interest: None

[Objective] Seronegative rheumatoid arthritis (SNRA) is account for about 20% of RA, and it is known that the proportion of SNRA is high in elderly-onset rheumatoid arthritis (EORA). On the other hand, polymyalgia reumatica (PMR) is a rheumatic disease with an average age of onset of 70 years or older, which often occurs in elderly people. In our department, treatment was initially started as PMR, and later 3 patients presented with RA-like peripheral arthritis. We will examine cases in which remission can be maintained by starting RA treatment relatively early after diagnosis. [Cases] Two of the three cases had pain in both shoulders, upper arms, and hip joints and thighs at the first visit. No pain was observed in the peripheral joints of the fingers and wrists with seronegative, high CRP and ESR. At the first visit, we suspected PMR and started oral PSL. One patient was initially diagnosed with PMR-like symptoms such as neck pain and thigh pain, and was seronegative. MTX was started becose peripheral joint synovitis was observed on MSUS in all three cases, and since then the symptoms have improved, and the PSL dose can be reduced. [Conclusion] PMR may be difficult to differentiate from EORA, MSUS is useful for their differentiation.

P1-016

Evaluation of synovitis before and after SARAH in patients with low-disease active (LDA) rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] Evaluate the increase in pain and synovitis after exercise load (EL) in patients with LDA-RA and consider optimal EL. [Methods] 10 RA patients (60% female, 76 years, symptom duration 4.9 years, all ACPA positive, CDAI 6.0, CRP 0.22 mg/dL) were included, who had been treated with MTX 7 cases, PSL 4 cases, and bsDMARDs 4 cases (ADA 1, GLM 1, TCZ 2). First, resting synovitis (the second/third PIP and MCP joints, intercarpal joint, and radiocarpal joint) of the dominant hand was evaluated by musculoskeletal ultrasonography. EL had been performed using SARAH, and synovitis after 10 min of EL was evaluated. The primary outcome was the increase of PD signal after EL of SARAH, and the increase of pain VAS as the secondary outcome. [Results] GS1PD0 case did not change, 1 out of 3 GS1PD1 cases increased to PD2, and 5 out of 6 GS2PD1 cases increased to PD2, but pain VAS did not increase. Healthy individuals did not increase PD signal and pain VAS in all cases. [Discussion] This study is an evaluation of EL after 10 min using SARAH for a short time, but it is a future study issue whether the increase in PD signal affects the long-term prognosis. [Conclusions] PD signal after 10 min of EL with SARAH increased in patients with LDA-RA in 6 of 10 patients, but pain VAS did not increase.

P1-017

Evaluation of extensor tendons by wrist ultrasonography in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Although remission rates for rheumatoid arthritis (RA) have improved with advances in therapeutic agents, extensor tendon ruptures are still encountered. Although there have been reports of abnormal bone morphology on X-ray or simple CT as a risk factor for tendon rupture, there have been few reports evaluating tendon rupture using ultrasonography. In this study, we evaluated extensor tendon rupture at the dorsal level of the wrist joint and bone morphology of the ulnar head. [Methods] 19 patients with RA (16 women) were included in the study. X-rays and ultrasonography evaluation were performed. [Results] Mean age was 70.6 years, mean duration of RA was 22.1 years. Larsen grade 1: 2, 2: 4, 3: 2, 4: 8, and 5: 2. Carpal height ratio (CHR) averaged 41.2 and dorsal subluxation ratio (DSR) was 18.1. Scallop sign was observed in 11 patients. Tendon rupture by ultrasonography showed Grade 0-1 changes in the second through fourth compartments, Grade 3 changes in the fifth compartment in 6 patients, and Grade 2 rupture in the sixth compartment in 1 patient. Dorsal convex deformity of the ulnar head was seen in 6 cases, 4 of which were accompanied by tears of the extensor digitorum profundus. [Conclusions] We considered that bony wear was one of the causes of tendon rupture.

P1-018

Application of bone marrow edema scoring system derived artificial intelligence in rapid radiographic progression rescue study

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Conflict of interest: None

[Objective] We demonstrated new bone marrow edema (BME) scoring system in X-ray (specificity 90%, sensitivity 65-70%) using deep learning with artificial intelligence (AI) reflects MRI BME in previous JCR late breaking abstract. In this study, to ascertain whether BME score in this system by X-ray film might reflect MRI BME, we retrospectively applied this system to the rapid radiographic progression rescue study previously reported. [Methods] RA patients inadequate response with MTX who have extensive BME in single or bilateral wrist joints and DAS28-ESR >3.2 were treated by enhanced group, of conventional synthetic (cs) DMARDs (26 patients) or by biologics (23 patients). X-ray film of two groups after 3-6 months treatment applied to BME scoring system (cut off: 0.4) and compared with MRI BME. [Results] In biologics group, number of BME score positive rate reduced from 65.3% to 15.3% after treatment in MRI BME improvement group and reduced 78.5% to 57.1% in MRI BME unchanged group. In csDMARDs enhanced group, number of BME score positive rate reduced from 75% to 25% after treatment in MRI BME improvement group and reduced 59.7% to 53.1% in MRI BME unchanged group. [Conclusions] AI-derived bone marrow edema score may reflect bone marrow edema in MRI.

P1-019

Development of a New Diagnostic Tool for Collagen Vascular Disease by Facial Recognition using Artificial Intelligence

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Conflict of interest: None

[Objective] In this study, we constructed an Artificial Intelligence (AI) model to see if it can discriminate between polymyositis (PM), dermatomyositis (DM), and non-PM/DM. The purpose of this study was not to promote discrimination against patients with collagen vascular diseases, such as in random primary screening, but rather to assist in diagnosis for obtaining early treatment opportunities. [Methods] Age, sex, medical history, and family history, laboratory data were examined. Still images of the subject's eyes (eyebrows, eyelids, and eyeballs) were taken, and each part's positional relationship and shape were quantified from the image data for analysis using AI. Since the number of each disease in the original data was disproportionate and small, the number of pieces was expanded when building the AI model and analyzed with the cooperation of Vareal Corporation. [Results] The AI model predicting 2-class classification of PM/DM or non-PM/DM was constructed using XAI technology and attempted to judge the images of PM/DM. The model showed a 55% correct response rate and tended to be based on the skin around the eyes. [Conclusions] Although the accuracy rate is still low, future research is expected to develop this model as a tool to assist physicians in diagnosis.

P1-020

Study of Interstitial pneumonia CT images in 47 cases of anti-U1-RNP antibody positive patients

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Conflict of interest: None

[Objective] To study interstitial pneumonia (IP) image of anti-U1-RNP antibody positive patients. [Methods] We extracted anti-U1-RNP antibody positive patients seen from 2017 to 2022 on our medical records retrospectively and studied the relationship between the CT pattern of IP and clinical diagnosis. [Results] We extracted 47 anti-U1-RNP antibody positive patients: 8 cases of mixed connective tissue disease (MCTD), 4 systemic scleroderma (SSc), 3 polymyositis/dermatomyositis (PM/DM), 4 systemic lupus erythematosus (SLE), 4 overlap syndromes of SSc/SLE and 24 others. The antibody value was higher significantly in MCTD and lower in SSc (median: 131.6, 12.1 U/mL respectively). IP was complicated in 24 cases: 6, 3, 1, 0, 2, 12 cases by disease respectively. Lower lobe predominant ground glass opacity (GGO) or reticular opacity was seen in 12 cases: 5, 2, 0, 0, 1, 4 by disease respectively. Peribronchovascular predominant opacity was seen in 15 cases: 4, 1, 1,0, 2, 7 by disease respectively. [Conclusions] Half of anti-U1-RNP antibody positive patients showed IP, while none in SLE. Lower lobe predominant GGO or reticular opacity was frequently seen in MCTD or SSc. Peribronchovascular predominant opacity was seen frequently in not only PM/DM, but also MCTD and overlap syndrome of SSc/SLE.

P1-021

Functional analysis of inflammatory osteoclasts using intravital imaging techniques

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Conflict of interest: None

[Objective] Inflammatory bone destruction is a major pathology of rheumatoid arthritis (RA) and is known to progress from an early stage of RA. In this study, we compared osteoclasts involved in pathological bone destruction with osteoclasts involved in physiological bone remodeling, and clarified the differences in dynamics and functions. [Methods] We induced collagen-induced arthritis in the reporter mice, administered a pH-sensing fluorescent probe to detect acidification created by osteoclasts, and quantitatively analyzed the changes over time of the bone resorption dynamics of osteoclasts by intravital two-photon microscopy. [Results] In the bone marrow, there were two functionally different types of osteoclasts, and osteoclasts destroyed only part of the covered bone. In contrast, under the inflamed joints, osteoclasts form bone erosions, destroy bones for long periods of time, and dissolved the entire covered bone. [Conclusions] Intravital imaging suggested that osteoclasts formed under two microenvironments (i.e., bone marrow and inflamed joints) may differ in terms of movement and function. This approach would be useful for developing a novel treatment for RA that prevents only pathological bone destruction, starting from the early stage of RA.

P1-022

Pathophysiological analysis of collagen-induced arthritis phenotype in Inter alpha trypsin inhibitor heavy chain 4 (ITIH4)-deficient mice

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Conflict of interest: None

Background: Inter alpha trypsin inhibitor heavy chain 4 (ITIH4) is a variable protein after rheumatoid arthritis (RA) onset and inhibits neutrophil migration. Citrullinated ITIH4 (cit-ITIH4) is specifically found in RA patients' blood and joint fluids. However, its detailed function in the arthritis-induced phenotype is unknown. Objective: To clarify the role of ITIH4 in collagen-induced arthritis (CIA) phenotype. Methods: 1) CIA was induced in C57BL/6 mice (WT) and the expression of ITIH4 and cit-ITIH4 in serum was examined. 2) ITIH4-deficient mice (ITIH4-KO) were generated, and organ damage was examined. 3) CIA was induced in WT and ITIH4-KO, and the arthritis score and joint's infiltrated cells were compared. 5) CIA was induced in WT and ITIH4-KO, and the lung's pathological findings were examined. Results: 1) ITIH4 and cit-ITIH4 in serum tended to increase after CIA induction. 2) ITIH4-KO exhibited no spontaneous organ phenotype. 3) Arthritis score was not different, although neutrophils and macrophage tended to increase in joint of ITIH4-KO. 5) Inflammatory cell infiltration in the lungs tended to be exacerbated in ITIH4-KO. Conclusion: ITIH4-KO tended to increase neutrophils and macrophages in the CIA-joints and exacerbate CIA-Lung lesions.

P1-023

Mechanism of Tef gene-downregulation by TNF alpha in RA synovial cells: a study of 3'UTR-binding miRNA

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Conflict of interest: None

[Objective] We have previously reported that TNFα decreases the expression of clock-controlled gene *Tef* (thyrotroph embryonic factor) in RA synovial cells and proliferative activities of those are increased under the condition of Tef mRNA silencing. In this study, we focus on microRNAs (miRNAs) that bind to the 3'UTR (untranslated region) in *Tef* gene to clarify their roles on RA synovial cells. [Methods] Primary cultured RA synovial cells established from 5 RA patients were used in this experiment. 50% horse serum medium was used to synchronize the expression cycle of clock genes in the cells, followed by stimulation in the presence of TNFα (10-100 ng/mL) for 24 hours. Total RNA was extracted and expression levels were analyzed for miRNA-22, -25, -32, -92, -125b, -137 by TaqMan miRNA assays, and for *Tef* mRNA by TaqMan Gene Expression Assays. [Results] Consistent with previous experiments, TNFα decreased the expression of *Tef* mRNA in a dose-dependent manner ($P<0.05$). The expression of miR-25, -125b showed an increasing trend by TNFα, but no significant difference was observed. Also, expressions of miR-22, -92, -137 were not increased. [Conclusions] In RA synovial cells, miRNA-22, -25, -32, -92, -125b, and -137 are not involved in the suppression of *Tef* mRNA expression by TNFα.

P1-024

Lipidome analysis in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We conducted this study to clarify correlation of lipidome profiles with the disease activity of rheumatoid arthritis (RA). [Methods] 229 females and 49 males were enrolled. Lipids were extracted from plasma, and analyzed by liquid chromatography and mass spectrometry. [Results] 329 lipids were detected. Correlation analysis revealed 37 and 2 lipids in females and males, respectively, were positively correlated with disease activity score (DAS) 28-erythrocyte sedimentation rate (ESR) and that 6 and 102 lipids correlated negatively in females and males, respectively. Stearic acid, palmitate acid, some phosphatidyl cholines and lysophosphatidyl cholines were negatively correlated in both genders, while many other different lipids were correlated to DAS28-ESR in either females or males. Analyses adjusted for drugs, age, and BMI using partial correlation coefficients also showed similar results. [Conclusions] It was demonstrated that several lipids in plasma had positive or negative correlations with DAS28-ESR. Difference in lipids correlated with the disease activity between genders may contribute to the gender difference in the pathogenesis of RA such as incidence and severity.

P1-025

Factors associated with renal involvement in rheumatoid arthritis patients with high disease-activity

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) are prone to renal dysfunction due to amyloidosis, nephrotoxicity of therapeutic agents, and other reasons. In addition, the aging of RA patients and the older age of onset of disease also exacerbate their renal involvement, and this make treatment more difficult. Therefore, we investigated the factors involved in renal function decline in RA patients with high disease-activity. [Methods] We included 233 RA patients who were started treatment with a biologic agent by the rheumatologist in our department, and were followed for 3 years from the start of evaluation. Patients with a decrease in estimated glomerular filtration rate (eGFR) of 30 or more were included in the renal function decline group, and factors related to renal function decline were compared. [Results] Patients with reduced renal function were older and had higher disease activity (DAS28 (CRP), DAS28 (ESR), SDAI, CDAI) at the time of initiation of biologic therapy. In addition, patients were more likely to have decreased renal function if the disease activity was still present 6 months after. [Conclusions] Good control of disease activity in RA may be useful not only to reduce joint destruction but also to protect the kidney.

P1-026

Relationship between muscle volume and time to start treatment in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] Investigate the influence that the difference of the period required for until start of therapy gives quantity of muscle from the onset during a contraction of a disease period. [Object] 12 women in her 60s and 70s who enforced the quantity of muscle measurement in RA patients. [Method] We measured the weight, quantity of muscle using the body composition meter of the multi-frequency BIA method. During a contraction of a disease period of RA, We investigated time to start of therapy from the onset. It was within one year and divided it into two groups more than one year each and compared the muscle quantity per weight. [Result] It was 5.8 years (from 2 months to 22 years) for 10.6 years (from 6 months to 32 years), the mean time to start of therapy during average age 70.3 years old (62-79 years old), a mean contraction of a disease period. By the comparison between two groups, there were significantly in comparison with groups more than it many arms ($p=0.022$), muscle quantity of lower limbs ($p=0.036$) for one year for one year. [Conclusion] In the group which did start of therapy to under onset one year in RA patients, there were more arms, muscle quantity of lower limbs than the group which started it one year later.

P1-027

Correlation analysis of patient profile during initial rheumatoid arthritis treatment and disease activity up to 52 weeks after treatment

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Conflict of interest: None

Objective: To identify predictors of response to RA treatment, we performed a correlation analysis of patient profiles at initial treatment and trends in disease activity up to 52 weeks posttreatment. Methods: We analyzed data from 264 patients who received MTX as initial therapy for RA at our hospital between 2010 and 2020. Statistical analysis was performed on the correlation between the number of days from RA onset to the start of treatment, RA disease activity at the start of treatment, and disease activity at 13, 26, and 52 weeks after the start of treatment. Results: Correlation analysis of SDAI (0 w/13 w/26 w/52 w) over time with the number of days from the onset of RA to the start of treatment showed a correlation

coefficient of (-0.06/0.08/0.17/0.05), respectively, with significant differences only at 26 weeks ($p < 0.01$). Correlation analysis of SDAI at the start of treatment and subsequent SDAI over time (13 w/26 w/52 w) showed significant differences at all time points with correlation coefficients of (0.34/0.16/0.21), respectively ($p < 0.01$). Conclusions: Early diagnosis and early treatment may contribute to good control of RA treatment.

P1-028

Clinical indices that correlate with each of three factors in Joint Index Vector

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Conflict of interest: None

[Objective] To search for clinical indicators that correlate with the Joint Index Vector (JIV) in treating rheumatoid arthritis (RA). [Methods] Simplified disease activity index (SDAI), health assessment questionnaire disability index (HAQ-DI), EuroQol-5th dimension (EQ5D), and pain score with visual analog scale (PS) at the first visit (BL), 1 year after the initiation (1Y), and its change (c_) in RA patients treated for more than 1 year since August 2014, were divided into independent and dependent variables, and the correlations were statistically evaluated including the 3-axis elements (3AEs) of JIV. [Results] 419 patients joined. All 3AEs for BL, x at BL and c_x for 1Y, and the all c_values of the 3AEs and x value at BL for c_SDAI were significantly correlated as SDAI as dependent variable (DV). All 3AEs for BL, values at BL and c_values of all 3AEs for 1Y, and c_x for c_PS were significantly correlated as PS as a DV. Values of all 3AEs for BL, x value at BL for 1Y, and c_values in x and y axis for c_HAQ-DI were significantly correlated as HAQ-DI as a DV. No element of JIV for BL, c_x for 1Y, and x at BL and c_x for c_EQ5D were significantly correlated as EQ5D as a DV. [Conclusion] These results suggest that the triaxial indices of JIV are closely correlated with clinical indices.

P1-029

Study of the Efficacy of Adalimumab in Antinuclear Antibody-Positive Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To compare the difference in the efficacy of anti-TNFα antibody therapy in patients with rheumatoid arthritis (RA) between anti-nuclear antibody-positive and negative patients. [Methods] In 74 RA patients who started adalimumab (ADA) at our hospital from 2018 to 2021, we divided them into antinuclear antibody (ANA)-positive and negative cases, and evaluated age, gender, Stage, Class, smoking history, methotrexate (MTX) dose at first, RF level, MMP-3 level, and at first and 24 weeks about DAS28ESR, DAS28CRP, SDAI, CDAI, and HAQ were compared. [Results] There were 38 ANA-positive cases and 33 negative cases. Into the positive cases, 12 were positive for anti-SS-A antibodies and 26 were negative for specific antibodies. CDAI and SDAI at 24 weeks were significantly lower in the ANA-positive patients (median ΔCDAI 29, $p=0.0211$; median ΔSDAI 13.84, $p=0.0369$), and MMP-3 at 24 weeks was significantly lower in the ANA-positive group than in the negative group (median 31.4 ng/mL, $p=0.00907$). [Conclusion] In patients with RA who are positive for ANA, disease activity may be significantly reduced six months after the start of adalimumab treatment, compared to the negative group.

P1-030

Association between biomarkers and disease activity in rheumatoid arthritis patients

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Conflict of interest: None

[Background] In 2021, we conducted the FLAIR Study, which sought to identify predictors of disease relapse following biologic drug discontinuation in 36 patients with rheumatoid arthritis who were clinically in remission. Comparing 20 patients who relapsed with 16 patients who did not relapse, reported a correlation between sTNFR1 and IL-2 levels in remission, helping predict disease relapse did. [Objective] Clarifying changes in biomarkers over time during remission and disease relapse to clarify what can be a more sensitive indicator of disease activity. [Method] We analyzed the behavior of biomarkers in 20 patients who relapsed after remission, after relapse, and after resuming the original treatment. [Result] Compared to remission, IL-8, IL-10, sTNFR1, VEGF, and IL-6 increased significantly during relapse. Investigation of the correlation between sTNFR1 and disease activity at relapse showed that sTNFR1 correlated with ESR at relapse ($r^2=0.3$). In addition, regarding the correlation of sTNFR1 in the remission period, there was a weak correlation with DAS28ESR ($r^2=0.17$). [Conclusion] In the relapsed group, sTNFR1 levels were high from the time of remission, but sTNFR1 increased with relapse. On the other hand, the correlation with disease activity remained weak.

P1-031

Predictive factors for the relapse of patients with rheumatoid arthritis (RA) in ultrasound imaging remission (USIR)

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Conflict of interest: None

[Object] To examine 2 year - clinical outcome of patients with RA in USIR. [Method] 76 patients with RA, fulfilling following requirements were enrolled; disease duration≧ 6 months, maintaining same RA treatment at least 6 months, low disease activity confirmed by DAS28 CRP or SDAI or CDAI, and USIR. USIR was defined as absence of joint synovitis, tenditis, tenosynovitis in bilateral wrist, 2nd-5th MCP and PIP joints, and any tender or swollen joints. Clinical dates, US were evaluated at the time of baseline, 1 year and 2 years. US was additionally examined if the patients showed clinical manifestations of relapse in any period. The relapse was defined by either requirement: receiving additional treatment, US flare. Baseline factors for the shorter time to relapse was analyzed by multivariate COX regression analysis. [Result] Over 2 years, 31 patients had the relapse and mean time to the relapse was 19.1±7.5 months. The change of DAS28-CRP from baseline to 1 and 2 years was -0.1±0.7, -0.1±0.7. An association of Stage 3 (HR=4.0, $p=0.007$), CRP (HR=127, $p=0.005$), csDMARDs with MTX (HR=0.28, $p=0.007$) on the shorter time to the relapse was revealed. [Conclusion] This study revealed the clinical course and predictive factors for the relapse in USIR patients.

P1-032

Examination of recurrence factors and treatment response after discontinuation of biologics in patients with rheumatoid arthritis

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Conflict of interest: None

In a study to predict relapse in patients with RA in remission who had discontinued bDMARDs, we investigated relapse factors and post-relapse treatment responsiveness. We prospectively enrolled RA patients who maintained an SDAI of ≦3.3 for more than 3 months during outpatient visits to our hospital and who discontinued bDMARDs. We investigated the DAS28-ESR and each endpoint before and after relapse, as well as the response to treatment after relapse. Of the 36 patients enrolled, 20 relapsed. The time to relapse was 43-651 days (median 115 days), and the median values of DAS28-ESR before and after relapse were 2.43 and 4.09, respectively. The DAS28-ESR increased by 1.59, and each item showed an increase in the tender joints count by 2, and the swollen joints count by 3 compared to the values before relapse. The contribution rate of each item to the DAS28-ESR increase was 41%, and 23%, respectively. 18 of 20 (90%≦) patients resumed bDMARDs after relapse. All patients who re-

sumed treatment showed a trend toward improvement in DAS28-ESR, and 15 (83%) of these patients had low disease activity or remission within approximately 3 months. At the time of relapse, all of the DAS28-ESR evaluation items increased. In addition, rapid improvement was observed by resuming bDMARD after relapse.

P1-033

Correlation between Composite Measure and Toe Joint Symptoms in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Objective: The assessment of disease activity in daily practice using composite measures (CM) has become common in rheumatoid arthritis practice, and while DAS28, SDAI, and CDAI are simple and have been shown to generally reflect disease activity, they do not assess the joints of the toes. Therefore, they may not be adequate for some patients with particularly prominent joint symptoms in the toes. In this study, we examined the correlation between composite measure (CM) assessment and foot joint symptoms. Methods: Correlations between DAS28 (ESR and CRP), SDAI, CDAI, and foot joint assessment were examined in 488 patients presenting to our outpatient department between January and December 2021, with the same evaluator. Results: There was a strong correlation between each CM. The correlation between the intensity of joint symptoms beyond the ankle joint and each CM was more positive for SDAI (r=0.719) and CDAI (r=0.700) than for DAS. Conclusions: There are both pros and cons of CM that does not include joint evaluation of the toes as an evaluation method for rheumatoid arthritis. However, both CMs showed some correlation with joint symptoms in the toes, and were considered useful, especially in the SDAI and CDAI, even when evaluation of the toes could not be performed.

P1-034

The persisting high MMP-3 level after normalization of CRP can be a predictor of joint destruction and its cut-off value is lower than current reference value

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Conflict of interest: None

[Objective] We examined whether sustained elevation of MMP-3 could be a predictor of joint destruction and whether the reference values are sufficient to prevent joint destruction. [Methods] 183RA patients were analyzed whose CRP became negative after MTX treatment. We evaluated their serum MMP-3 levels and change from the baseline modified Total Sharp Score (ΔmTSS) at 52 weeks. ΔmTSS between the groups with MMP-3 greater than or equal to the reference value (MMP-3+) and the group with MMP-3 less than the reference value (MMP-3-) were compared and ROC analysis was performed to determine the cut-off value for the suppressions of joint destruction progression. [Results] ΔmTSS after 52 weeks was significantly higher in the MMP-3+ group (0.98±1.98 vs 0.46±1.12 p=0.027) and the cumulative probability of ΔmTSS less than 0.5 was significantly lower in the MMP-3+ group (57.2% vs 77.5% p=0.013). Cut-off value for MMP-3 sufficient to suppress the progression of joint destruction is 49.90 ng/mL. [Conclusions] The persisting high MMP-3 level after normalization of CRP can be a predictor of joint destruction and the level of MMP-3 to suppress the progression of joint destruction is lower than current reference value.

P1-035

Only few patients suffered from radiologic progression in patients with recently diagnosed early-onset rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate what factors are involved in low rate of radiographic progression in recently diagnosed untreated early RA. [Methods] This study included 101 consecutive outpatients with early-onset rheumatoid arthritis (RA) with disease duration of <1 year between 2017 to 2020 (n=101, group A). Disease duration, disease activity at baseline and 12 months after the initiation of treatment as well as bone lesion were compared with those who were diagnosed between 2011 to 2016 (n=93, group B). [Results] At baseline, bone lesion was observed in 19.8% of the patients in group A, and the frequency was significantly lower than that in group B (32.3%, OR=0.9, 95%CI; 0.25-0.94). This difference might be due to shorter disease duration in group A (average, 3.3±2.4 months) compared with that in group B (average, 4.4±3.6 months, p<0.001). Furthermore, the frequency of the radiological progression at 12 months after the initiation of the treatment was only 2% of the patients in the group A whereas that in group B was 20% (OR=0.12, 95%CI; 0.035-0.43). There was no deference between group A and B for the rate of remission or treatment. [Conclusions] Lower frequencies for radiological progression would be due to intensive treatment towards high risk patients for radiographic progression.

P1-036

Similar effect of co-administration of methotrexate and folic acid for the treatment of rheumatoid arthritis compared to separate administration - A Single-Center Retrospective Study -

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Conflict of interest: None

[Objective] Methotrexate (MTX) is the first-line drug in the treatment of rheumatoid arthritis (RA). Supplementing with folic acid (FA) is recommended to lessen MTX side effects. The optimal timing of folic acid supplementation remain unclear. Therefore, we conducted a retrospective study to determine the impact of FA supplementation timing on MTX treatment efficacy. [Methods] We included 107 patients who were diagnosed with RA, started MTX treatment with FA at our department between April 1, 2018 and March 31, 2022, and who were followed up to 48 weeks. The patients were divided in two groups based on whether they received co-administration of MTX and FA (Co-FA) or not (non-Co-FA). The induction rates of biologic agents (Biologics) and JAK inhibitors (JAKi), as well as MTX treatment efficacy, were assessed. [Results] The mean DAS-28CRP was 3.29, the mean age was 58.3 years, and 76.6% of the patients were female. There were no significant differences in the patient's background, disease activity, or concurrent use of other csDMARDs. The DAS28-CRP trends and Bio/JAKi induction rates of the two groups were not significantly different. [Conclusions] Co-administration of MTX and FA may be less likely to reduce the efficacy of MTX than separate administration.

P1-037

Efficacy of Methotrexate in Elderly-Onset Rheumatoid Arthritis

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Conflict of interest: None

Objective: To compare efficacy of methotrexate (MTX) in patients with elderly-onset rheumatoid arthritis (EORA) to those with young-onset

RA (YORA). Methods: We included 175 patients who were enrolled in the multicenter early-onset untreated RA registry from June 2018 to March 2022 and were observable for 52 weeks. Patients were divided into two groups according to age of onset: EORA (65 years and older) and YORA (64 years and younger). Results: Of the 175 patients (104 EORA, 71 YORA), significantly fewer patients in EORA group received MTX (83.7% vs. 95.8%, P<0.05). MTX continuation rate was lower in EORA group (85.1% vs. 95.6%. P<0.05). SDAI was significantly higher in EORA group at the start of MTX but did not differ at 24 or 52 weeks (MTX start; 23.9±11.6 vs. 19.3±10.7, P<0.05. 24 weeks; 6.9±7.0 vs. 7.1±6.4, P=0.86. 52 weeks; 4.7±5.3 vs. 5.3±4.9, P=0.50). Conclusion: Although MTX administration rate was lower in EORA group, MTX administration was as effective in EORA group as in YORA group, and MTX continuation rate was good.

P1-038

Effect of cooperation between physicians and pharmacists in the treatment of rheumatoid arthritis in the immunopharmacist outpatient clinic

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Conflict of interest: None

[Objective] At Kameda Clinic, pharmacist outpatient clinics have been established for patients with immune diseases, and we retrospectively examined the usefulness of drug treatment and the effect of reducing the burden on doctors. [Methods] Patients with rheumatoid arthritis aged 18 years or older were included in the study, and the period of study was from December 2019 to March 2020, followed by 52 weeks of follow-up. The pharmacist outpatient clinic was conducted only on specific days of the week, and a comparison was made between a group that received only a doctor's examination (Pre) and a group that received both a pharmacist's outpatient clinic care and a doctor's examination (Post). [Results] The study included 426 target patients, of which 236 were in Pre and 190 were in Post. There were 1061 prescription proposals by pharmacists in the Post; another 71 were shared decisions made for pharmacotherapy. After follow-up, 32.1% of Pre and 47.0% of Post patients reported that their condition had improved. [Conclusions] A pharmacist assessed disease activity before the visit and provided a pharmacological perspective. The coordination between doctors and pharmacists was believed to be responsible for improved drug treatment.

P1-039

Survey of comorbidities affecting disease activity in elderly-onset rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the association between activity and comorbidity in elderly-onset rheumatoid arthritis patients aged 60 years or older at onset in the Akita Orthopaedic Rheumatology Group registry. [Methods] Of 166 EORA patients enrolled in the AORA registry with onset of less than 1 year during the 4-year period from 2015 to 2018, 77 patients who were followed up to 2020 were included. Patients were classified into remission/low disease activity group and intermediate/high disease activity group by DAS28-CRP at the last survey, and comorbidity was investigated. [Results] There were no significant differences in age, gender, or medications used at the time of the last survey, and only renal dysfunction was associated with a significantly higher percentage of intermediate and high disease activity. The use of medications by the presence or absence of renal dysfunction showed no difference between the two groups at less than 1 year of onset, but at the final survey, the group with renal dysfunction had a lower rate of MTX use and a higher rate of PSL use. [Conclusions] In the treatment of EORA, renal dysfunction was associated with poor disease activity control of RA. Patients with renal dysfunction were difficult to intensify treatment with MTX, and PSL were used instead.

P1-040

Treatments for elderly-patients with rheumatoid arthritis

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Conflict of interest: None

Objective Because distribution and onset of the age in patients with RA have shifted older, treatment diversities arose in daily practice. **Methods** Three RF- and ACPA-positive patient groups (< 65 years, 65-74 years, and ≧75 years: n=114, 101, and 98) and the EORA group (n=108) being diagnosed with and developed RA over 65 years were statistically analyzed. **Results** (1) These groups distributed around age of 70 years and peaked at onset age of 60 years. (2) DAS28-CRP was 2.3, 2.57, and 3.13 in three age groups, respectively, with poor disease activity (P<0.001). (3) MTX was used in 81.6%, 68.3%, and 58.2% (P<0.001) and ST mixture was taken in 41.2%, 45.5%, and 59.8%, respectively (P=0.021). Sarilumab was effective in patients with large joints lesion over ≧75 years. (4) DAS28-CRP>2.7 (P<0.001), ST mixture (P=0.005), and Non-EORA (P=0.019) were significantly involved in the VAS difference over 20 mm between physician and patient, and patient-VAS and DAS28-CRP were correlated in the < 65 and ≧ 75 age groups (P=0.019). (5) In ≧75 years, RA phenotype with PMR might present and JAK inhibitors were effective. **Conclusion** Treatments for elderly-patients with RA will be performed by remission or low disease activity but safety should be prioritized due to comorbidities, patient factors, and so on.

P1-041

A single-center study to assess the effectiveness of warmers on morning stiffness in Rheumatoid Arthritis patients

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Conflict of interest: Yes

[Objective] The progress in therapy for Rheumatoid Arthritis (RA) enables us to control disease activity. Yet many patients suffer from morning stiffness (MS), which impairs their quality of life. Though it is empirically known warming improves stiffness, the evidence is scarce. We conducted a clinical study to assess whether warming the wrists during sleeping improves MS with the originally developed warmers that generate heat at a lower temperature for bedtime use. [Methods] RA patients complaining MS were recruited at the Osaka University Hospital. Following 2 weeks of observation, they applied the warmers on both wrists for 2 weeks. Throughout the study, patients recorded self-assessment of MS on a scale of 0 -10 (MS score) as well as the duration of MS on the diary. Disease activity, sonography of both hands, and adverse events were also assessed. The primary endpoint was the difference in MS score between the warming and observation period (jRCTs052210155). [Results] 15 patients were enrolled. The mean MS score during the observation and warming period was 4.47 and 3.83, respectively, and the difference was significant by paired t-test. No cases of burn were reported. [Conclusions] We showed

that warming wrists during bedtime alleviated the morning stiffness of RA patients.

P1-042

Clinical course after using glucocorticoid as initial treatment of rheumatoid arthritis-Results from KURAMA Cohort-

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Conflict of interest: Yes

[Objective] Although short-term glucocorticoid (GC) with DMARD are helpful for remission in active rheumatoid arthritis, they are often sustained once started. This study aims to reveal the clinical course after GC use as initial treatment. [Methods] We investigated the persistence rate of GC and disease activity a year after initial treatment at the Rheumatology Cener, Kyoto University Hospital. [Results] Among 36 patients treated with GC, 8 patients were treated due to extra-articular involvement such as interstitial pneumonitis. GC were administered with 55.6% of patients a year after initial treatment. Median DAS28-ESR at induction and in a year were 5.93 and 2.68, respectively. These activity scores were higher than those of the patients without GC. [Conclusions] Disease activity of patients with GC were higher than those without GC and many patients were treated with GC a year after initial treatment.

P1-043

Practice of nintedanib therapy for collagen disease-associated interstitial lung disease (CTD-ILD) in our hospital

Keisuke Ikeda[1], Tomoki Tanaka[1], Nao Tsugita[1], Yosuke Iwadate[1], Hirotomo Asakura[1], Kosuke Shimode[1], Yu Matsueda[1], Yoshiyuki Arinuma[1], Tatsuhiko Wada[1], Kenji Oku[1], Sumiaki Tanaka[1,2], Kunihiro Yamaoka[1]

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Conflict of interest: None

[Objective] Nintedanib treatment (NTB) is mainly adopted to patients with CTD-ILD with progressive fibrosis to control the progression of the disease. However, due to the side effects and its cost, the introduction of NTB is not always prompt, and treatment interruptions observed. The purpose is clarify the disease background with the reasons of the NTB discontinuation in patients with CTD-ILD. [Methods] The background factors, respiratory function, continuation rates and adverse events in patients with CTD-ILD with NTB at our department from April 2020 to August 2022 were analyzed. [Results] Thirty-seven patients (SLE 17, RA 10, PM/DM 7, MCTD 3, MPA 1) were selected. Age was 55 (40-83) years, mean follow-up was 14.9+/-6.5 months, %VC prior to NTB was 65.1±17.5% (n=30). The discontinuation was observed in 18 patients (gastrointestinal (GI) symptom 10, liver dysfunction 1, eruption 1 and death 6). GI symptoms were observed in 26 patients, of which in 16 patients who continued NTB, 7 were dose reduced and 4 were added symptomatic treatment. [Conclusions] The post-treatment VC reduction and the continuation rate of the NTB were similar to the previous reports. Adverse events, mainly GI symptoms, with some patients able to continue treatment with NTB dose reduction or with the symptomatic therapy.

P1-044

Drug Survival of Sarilumab in treatment of RA and Its Analysis

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Conflict of interest: Yes

[Objective] Sarilumab is one of interleukin-6 receptor inhibitors available for treatment of Rheumatoid Arthritis. Here, we report our real world experience at St. Luke's international Hospital (SLIH). [Methods] his is a retrospective chart review of patients who were treated with Sarilmab at SLIH. [Results] Total 49 patients (men:women=1:7) were analyzed. The median disease duration was 6 years (2.5-11). Thirty-eight patients (78%) were positive for RF and 36 (75%) for anti-CCP antibody. Nine patients (18%) had Interstitial Lung Disease. Fourty-four patients (92%) used a conventional synthetic DMARD. Twenty-two patients used glucocorticoids. Forty-three patients previously had used biological DMARDs (bDMARD) or targeted synthetic DMARDs (tsDMARD). The median dose of prednisone who were on prednisone at baseline was 5 mg/day and 2.5 mg/day at 3 months (P=0.0034). There was no decreased drug survival observed among the patients who had previously used three or more b/tsDMARDs compared to ones who used one or two b/tsDMARDs. Sarilumab drug survival was statictically lower among the patients who had used abatacept previously compared to ones who had not. [Conclusions] Sarilumab showed relatively good continuation rate. Prednisone dose was decreased significantly at 3 months after Sarilumab use.

P1-045

Efficacy and long-term administration of sarilumab for bio-naïve rheumatoid arthritis

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Conflict of interest: None

<Objective>To examine the efficacy of sarilumab on bio-naïve rheumatoid arthritis (RA). <Methods>We analyzed 45 bio-naïve RA treated with sarilumab between January 2018 and July 2022 at Tokai University Hospital. We collected data on DAS28 (CRP, ESR), and the presence of adverse effects before initiation, 4, 8, 12, 24, and 52 weeks retrospectively. <Results>Average age of 45 patients was 66.6 years, 24 were women, and average disease duration was 62 months. At the initiation of sarilumab, mean DAS28 CRP was 4.58 and mean DAS28 ESR was 5.22. Mean DAS28-CRP and DAS28-ESR were gradually decreased after treatment, 2.5 and 2.88 at 4 weeks, 1.33 and 1.35 at 52 weeks, respectively. Stratified analysis with body weight or combination with methotrexate (MTX) revealed no significant differences in effectiveness. Twenty-two patients continued sarilumab without adverse events for more than 3 years. <Conclusions>These results suggested that sarilumab was effective and safe for bio-naïve RA patients.

P1-046

A Study of Sarilumab Efficacy on Patients with Rheumatoid Arthritis at 52 Weeks

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Conflict of interest: None

Purpose: Eight biologics (excluding biosimilars) and five Janus kinase inhibitors (JAKi) are available for rheumatoid arthritis (RA) in Japan. To clarify the clinical position of sarilumab (SAR) among these drugs, a retrospective study was conducted. Subject: Forty-one patients with RA that had been introduced with SAR by October 2022 at Saitama Medical University Hospital and Red Cross Ogawa Hospital and were available for observation after 52 weeks. Results: The mean age of 41 patients at the start of administration was 61.17; the mean duration of disease was 7.90 years; and the mean CDAI was 18.94. Of 41 cases, 30 were still receiving SAR at 52 weeks and 11 discontinued. Four cases were due to adverse events, 6 decreased efficacy and 1 was economic reasons. Of the observed

41 cases, 30 had used biologics and JAKi, and 22 out of 30 that continued for 52 weeks had used them before SAR. The mean CDAI of the 30 cases that continued significantly improved from 19.42 at introduction to 4.49 at 52 weeks, and that of 22 cases who had used other biologics and JAKi prior to SAR also significantly improved from 17.24 at introduction to 5.47 at 52 weeks. Conclusion: Sarilumab remained effective at 52 weeks and showed significant efficacy even when switched from other biologics and JAKi.

P1-047

Comparison of Sarilumab and Golimumab in Bio-naive Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Sarilumab (SAR) was launched in Japan in 2018, but there have been few reports on clinical results. Although TNF and non-TNF inhibitors are equally recommended by the Rheumatoid Arthritis (RA) Guidelines, the data is currently weak. We aimed to examine the effectiveness of SAR by comparing the SAR-introduced group (S group) with the Golimumab (GLM)-introduced group (G group) in bio-naive patients. [Methods] The 19 bio-naive patients who continued SAR for at least 24 weeks from 2019 were included in the S group; those who continued GLM for at least 24 weeks from 2012 were included in the G group. We analyzed MTX and PSL dose (mg/week), DAS28 (ESR), SDAI, and mHAQ from the start to 24 weeks. [Results] The mean age was 70.8/76.1 years in the S/G group. The MTX dose was significantly higher in the S group (S/G: 7.60/4.25), but the PSL dose was not different (S/G: 5.38/4.88). DAS28 (ESR) at the start was not different (S/G: 6.08/5.76), but improved considerably in the S group after 12 weeks (24 weeks; S/G: 2.39/3.49 [$p<0.01$]). SDAI was higher in the S group (S/G: 37.6/27.3 [$p=0.04$]) at the start, but did not vary after that. mHAQ was not different throughout the period (24 weeks; S/G: 0.70/0.62). [Conclusion] In our hospital, SAR had equivalent short-term outcomes to GLM for bio-naive RA patients.

P1-048

The efficacy of Sarilumab to RA patients for three years results

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Conflict of interest: None

Objective: To evaluate Sarilumab (SAR) to RA patients for three years results. Methods: From July 2018 twelve cases treated with SAR were evaluated by recording DAS28 (CRP). Results: DAS28 was 4.3 and decreased to 1.6 at 36 months, CRP was also reduced from 2.5 to 0.15 at 36 momth. CDAI was also reduced from 21.4 to 2.2 at 36 month. Conclusion: the therapy of SAR to RA patients was effective for three years results.

P1-049

Analysis of the efficacy for salirumab in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] The efficacy of salirumab in 36 RA patients out of 300 RA in bDMARD in our clinic. [Methods] Baseline data of salirumab in 36 RA was mean age of 60.6 years, 34 female, 2 male, mean disease duration 7.5 years, mean HAQ 0.77, naïve 47%. DAS28 (CRP) and RF up to 24 weeks was analyzed, in addition to the continuation rate at 3 years was calculated by Kaplan-Meier method. DAS28 (CRP) in switch group was compared with naïve group at 24 weeks statistically. [Results] DAS28 (CRP) was 5.16 at baseline, 2.82 at 4 weeks, 2.5 at 8 weeks, 2.13 at 12 weeks, 2.37 at 24 weeks showing the efficacy from 4 weeks significantly. RF (IU/ml) was 191.2 at baseline, 149.7 at 4 weeks, 126.9 at 8 weeks, 119.7 at 12 weeks, 116.9 at 24 weeks showing the efficacy from 12 weeks significantly. Continuation rate was 74% at 3 years by Kaplan-Meier method. DAS28 (CRP) of switch group was 2.36 showing the efficacy as same as naïve group, 2.37 at 24 weeks. [Conclusions] Salirumab showed rapid efficacy, stable continuation, and especially switch cases was also effective to the same level as to naïve for RA patients.

P1-050

Efficacy of sarilumab according to affected joints (at our institution) with sarilumab

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Conflict of interest: None

[Objective] We will investigate the efficacy of sarilumab, which was launched in Japan in February 2018 as the second IL-6 receptor inhibitor. [Methods] A total of 44 patients (33 females, 11 males) who visited our hospital from February 2018 to November 2021 and started sarilumab. Demographics, disease activity, and laboratory values were retrospectively examined from medical records. In addition, we examined changes in CDAI for each affected joint. [Results] Average age 66.4 years, average weight 57.2 kg, disease duration 6.16 years. Affected joints were 13 shoulders (29.5%), 12 elbows (27.3%), 17 knees (38.6%), 24 wrists (54.5%), and 30 fingers (68.2%). Start of treatment CDAI: 15.91, DAS-CRP: 3.55, DAS-ESR: 4.29, MMP-3: 270.71, white blood cell count: 7.39, RF: 210.58, mHAQ: 0.91, VAS: 52.27, CRP: 2.87, Hb: 11.92, PLT: 290.14. 6 months later CDAI: 7.93, DAS-CRP: 2.20, DAS-ESR: 2.61, MMP-3: 90.37, white blood cell count: 5.16, RF: 166.68, mHAQ: 0.59, VAS: 24.33, CRP: 0.05, Hb: 12.83, PLT: 210.31. CDAI significantly improved in patients with affected joints in the shoulder, elbow, and wrist. [Conclusions] Six months of sarilumab improved disease activity, including CDAI, DAS-CRP, DAS-ESR, and MMP-3. There was also a trend toward improved CDAI in patients with joint symptoms.

P1-051

Tapering of sarilumab for rheumatoid arthritis patients; single-center experience

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Conflict of interest: None

[Objective] The aim of this study was to investigate the effects of tapering of sarilumab (SAR) in patients with rheumatoid arthritis (RA). [Methods] Patents with RA received SAR was tapered was entered. We retrospectively assessed disease activity score (DAS) 28-ESR after tapering of SAR. [Results] A total of 16 RA patients tapered SAR. The mean age was 68.9±13.7 years, 14 women, and the mean disease duration was 5.2±5.4 years. DAS28-ESR was no significantly elevated in baseline 1.36±0.80 to 24 weeks 1.44±1.11 ($p=0.61$). However, 3 patients relapsed disease activity, and were discontinued SAR. Four patients flared disease activity during administration every 4 weeks, however, the patients improved disease activity after returned to 3 weeks administration. [Conclusions] Tapering SAR is realistic strategy for RA patients in clinical practice.

P1-052

Janus Kinase Inhibitors versus Biologic Disease-Modifying Anti-Rheumatic Drugs: Perioperative Complications After Orthopaedic Surgeries in Rheumatoid Arthritis Patients

Hirofumi Bekki[1], Hidetoshi Tsushima[2], Tomomitsu Hashiguchi[3], Seiichi Kawamura[3], Masakazu Kondo[4], Masanari Ota[1], Masamitsu Hara[1], Koji Sakuraba[1], Hisaaki Miyahara[1], Yasuharu Nakashima[2], Junichi Fukushi[1]
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Conflict of interest: None

[Objective] The purpose of current study is to clarify the difference in the postoperative outcome between Janus kinase inhibitors (JAKi) and biologic disease-modifying anti-rheumatic drugs (bDMARDs) treatment. [Methods] This is a retrospective observational study of Japanese RA patients with data analyzed from 2011-2022. A total of 58 cases using JAKi preoperatively who underwent orthopedic surgeries were recruited in the current study. A propensity matched cohort study was conducted, and they were matched to 58 cases using bDMARDs preoperatively to facilitate comparison between two groups. [Results] Comparing bDMARDs group, JAKi group showed higher preoperative DAS28 (3.8 vs 2.7) and more frequency of postoperative inflammation flares (17 vs 5 cases, 29.3% vs 8.3%). For JAki group, the period of perioperative drug holiday wasn't correlated with postoperative complications. [Conclusions] Considering the more frequency of postoperative inflammation flares than bDMARDs, clinicians may restart JAKi early in the postoperative period to prevent postoperative inflammation flares.

P1-053

Therapy for methotrexate (MTX)-induced chronic liver injury---Usefulness of JAK inhibitor on thrombocytopenia

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Conflict of interest: None

[Objective] MTX is used as an anchor drug in the therapy of RA. MTX sometimes induce chronic liver injury, histologically similar to non-alcoholic steatohepatitis. Transaminase fluctuation is minor and platelet reduction is hallmark. It is necessary to discontinue MTX to prevent progression of liver injury. Therapeutic agents are often required to suppress the relapse of RA activity. We previously reported that tocilizumab (Toc) improve liver histological findings in some cases. [Methods] Thrombocytopenia may persist even discontinuation of MTX in some cases. JAK inhibitors (JAKi) (often baricitinib) instead of Toc was administered. [Results] Thrombocytopenia was found to improve markedly. Causes of thrombocytopenia in the chronic liver damage include hypersplenism and thrombopoietin (Tp) reduction. Tp was measured in consideration of possibility that thrombocytopenia was related to Tp, and it was found that Tp decreased and recovered after administration of JAKi. Platelets increased and cholinesterase (Ch-E) elevation were also observed. [Conclusions] Tp and Ch-E are produced in the liver and are reduced ininjury of the liver. Thus, it is thought that JAKi may restore liver function, increased platelet count due to Tp increase, and increased Ch-E.

P1-054

Survey on Anemia of JAK Inhibitors in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] There have been few reports on the effects of JAK inhibitors on anemia in rheumatoid arthritis (RA) treatment. We therefore examined the effect of FIL versus other JAK inhibitors (non-FIL) on anemia in RA patients using JAK inhibitors at our hospital. [Methods] 73 patients who used 4 JAK inhibitors (FIL, TOFA, BARI, UPA) after 2013 were divided into FIL (16 patients) and non-FIL (57 patients) groups, and Hb trends were examined 3 months after initiation. Multivariate analysis was also performed according to age, gender, baseline Hb, CRP, s-Cre, platelet count, presence of anemia-modifying drugs, presence of DOACs, presence of PSL/DMARDs, and history of use of previous bDMARDs/JAK inhibitors. [Results] Hb levels at the start of treatment were 10.5 g/dl in the FIL group and 11.6 g/dl in the non-FIL group, but there was no significant difference between the two groups. Hb levels were significantly higher in the FIL group, while Hb levels were lower in the non-FIL group ($P<0.05$). In addition, there was a significant increase in Hb in the group that switched to FIL as a 2nd JAK inhibitor compared to the FIL group that had no history of JAK inhibitor use ($P<0.05$). [Conclusions] Compared to other JAK inhibitors, FIL did not decrease Hb in many cases.

P1-055

Comparison of anti-angiogenic effect of JAK inhibitor under IL-6 stimulation

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Conflict of interest: None

[Objective] Angiogenesis plays an important role in rheumatoid arthritis (RA) progression. The purpose of this study was to compare the anti-angiogenic effects of JAK inhibitors under IL-6 stimulation in co-cultures of RA patient-derived synovial fibroblasts (RA-FLS) and human umbilical vein endothelial cells (HUVEC). [Methods] RA-FLS were seeded on Type I Collagen gel, and HUVEC were directly added after overnight. Control and estimated blood concentrations of JAK inhibitors TOF 0.3 μM, Baricitinib 0.3 μM, PEF 1 μM, UPA 0.3 μM, FIL 0.1 μM were added to the culture medium, followed by IL-6 (100 ng/ml) and sIL- 6R (100 ng/ml) was added for stimulation. After co-culturing for 6 days, the tube formation abilitywas evaluated by tube formation assay. [Results] Tube formation assay showed that the tube formation ability was significantly suppressed by administration of each JAK inhibitor compared to the control. In addition, the inhibitory effects of BAR, PEF, and UPA on FIL were significantly higher. [Conclusions] JAK inhibitors suppressed IL-6-stimulated angiogenesis in RA-FLS and HUVEC co-cultures. In addition, it was suggested that the inhibitory effect may differ between JAK drugs.

P1-056

Experience with Janus Kinase Inhibitors (JAKi) in Elderly Patients with Rheumatoid Arthritis (RA) at Our Hospital

Yuichi Takahashi
Yu Family Clinic

Conflict of interest: None

[Objective] Patients with elderly-onset RA often experience severe joint symptoms and complications. Monotherapy with JAKi has shown high clinical efficacy, allowing potential dose reduction. We examined the efficacy and safety of JAK inhibitors in elderly patients with RA. [Subjects/Methods] We determined the clinical efficacy of JAK i (tofacitinib (1):, baricitinib (5), peficitinib (1), upadacitinib (4), filgotinib (7) using CRP, DAS28ESR and SDAI in 18 patients with RA over 75 years (mean: 79.7). We also examined adverse events. [Results] Response was observed from Week 4 of JAK i therapy. CRP and DAS28ESR decreased during Week 4, from 2.02 (mg/dL) to 0.28 and from 4.25 to 3.3, respectively. Regarding altered disease activity, approximately 20% of patients achieved remission at Week 4, which increased to 50% on incorporating low disease activity. At Week 12, 50% of subjects achieved remission, increasing to 70% on incorporating low disease activity. Herpes zoster and malignancy were noted during early treatment. [Discussion] JAKi were efficacious in elderly patients with RA prone to frailty, potentially allowing dose reduction. However, the potential development of herpes zoster should be monitored, and a screening test for malignancy before administration was deemed crucial.

P1-057

Incidence for herpes zoster in patients with rheumatoid arthritis treated with JAK Inhibitors may be influenced by disease activity

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Conflict of interest: None

[Background] On Clinical trial, Data show that JAK inhibitors (JAKi) often cause herpes zoster (HZ), especially in Japan. We don't know when it is more likely to occur. [Object] To clarify the correlation between the incidence of HZ in rheumatoid arthritis (RA) patients receiving JAKi and the disease activity of RA [Methods] Using data of NinJa from Apr 1 2015 and Mar 31 2021, We investigate patient's condition of 883 JAKi treated RA patients who responded to the questionnaire of development of HZ. [Results] The total patients was 66 years (SD12.84) We investigate the 83 cases on physician's report, which was thought to be the cause of the onset, JAKi [Baricitinib (20), Tofacitinib (57), Upadacitinib (3), and Peficitinib (3)] Four cases had recurrence of HZ during the same period. Compared with disease activity of the JAKi treated group without HZ, those with HZ were higher. [DAS28-CRP 2.66 (SD1.07) and HAQ-DI 0.95 (SD0.85) on average] DAS28-CRP of both cases with recurrence of HZ were much higher. (average DAS28-CRP was 3.81). Of the 83 patients with HZ, 49were regularly administered concomitant PSL, with an average PSL dose of 3.1 mg (SD 1.90). [Conclusions] In real-world clinical practice, RA patients who developed HZ treated with JAKi had high RA disease activity.

P1-058

Polypharmacy Drug and Dose Reduction for the Treatment of Rheumatoid Arthritis

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Conflict of interest: None

[Objective] This study investigates polypharmacy in patients with RA using JAK inhibitors to achieve a better understanding of the current state of polypharmacy measures. [Methods] Patients with RA who have newly prescribed any JAK inhibitor from April 2020 to March 2022 at the outpatient clinic of the Department of Rheumatology, Showa University Koto Toyosu Hospital were included in this study. All patients had been taking the drug for at least six months at the time of the study. The number of medications at the time of JAK inhibitor prescription, the number of medications after six months of JAK inhibitor use, medications reduced, and medications reduced were measured. [Results] 21 patients (median age: 71 years; range: 61.5-77) were included in the study. The median number of prescriptions at the time of JAK inhibitor initiation was five drugs (3-8.5). 13 patients were prescribed fewer drugs after six months (median: 4.5 drugs; 2.5-6.5). The most commonly-reduced drug was NSAIDs. The median dosages of PSL and MTX were reduced from 3 mg/day (2-5) and 8 mg/week (5.5-8), respectively, to 1 mg/day (0-5) and 7 mg/week (3-8) after six months. [Conclusions] JAK inhibitors may reduce or prevent polypharmacy in patients with RA.

P1-059

Three cases of rheumatoid arthritis who underwent revision to reverse shoulder arthroplasty for rotator cuff tear after total shoulder arthroplasty

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Conflict of interest: None

Rheumatoid arthritis may cause rotator cuff thinning and rotator cuff tears from a relatively early stage. There are few reports of revision to a reverse arthroplasty (RSA) due to rotator cuff tear after TSA for rheumatoid shoulder. We report three cases in our department. Case 1. A 72-year-old female. TSA was performed for rheumatoid shoulder with severe rotator cuff thinning. She underwent revision to RSA 5 years and 7 months after the operation. Pain improved after the operation. Case 2. A 63-year-old female. TSA was performed for rheumatic shoulder with moderate rotator cuff thinning. She underwent revision to RSA at 1 year and 1 month postoperatively. Although the pain improved, an acromion fracture occurred 4 months after the operation. The pain improved with conservative treatment, and the elevation of 110 degrees was acquired. Case 3. A 73-year-old female. She underwent TSA and rotator cuff repair for rheumatic shoulder with repairable rotator cuff tear. 2 years after the operation, loosening and dislocation of the glenoid component were observed. She therefore underwent removal of the glenoid component. Since she did not improve, she underwent revision to RSA 4 years after the initial operation. Postoperatively, her pain improved and she achieved 110 degree elevation.

P1-060

A revision total elbow arthroplasty with a allograft for interprosthetic fracture

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Conflict of interest: None

Case: The patient was a 78-year-old woman with osteoporosis who had longstanding RA. She underwent primary TEA for mutilans deformity of the right elbow 5 years prior to presentation. The patient suffered a periprosthetic humeral fracture after a fall. There was a fracture in the proximal humerus diaphysis and a long spiral fracture in the diaphysis, with the fracture around the stem of a loose prosthesis being associated with bone loss. The patient required early recovery of activities of daily living. We concluded that revision TEA with an allograft was the appropriate procedure for surgical management. The dorsal third of the humerus was opened and the humeral component and remaining cements were removed. A standard humeral component was cemented into the allograft after placement of a proximal cement restrictor. A plate was placed through the deltoid, and the proximal humerus was fixed with locking screws. At 1 year postoperatively, plain radiograph revealed no implant failure and no resorption of the allograft. Discussion: We performed revision TEA using a massive allograft on a patient with periprosthetic humeral fracture around the stem of a loose prosthesis with associated bone loss. Revision TEA using a massive allograft is a reasonable procedure.

P1-061

A case of periprosthetic elbow joint infection with obsolete olecranon fracture that had not been repositioned

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Conflict of interest: None

The patient with rheumatoid arthritis; 68 years old, female, 146.0 cm, 35.5 kg; who had 21 years of disease duration suffered inflammatory arthritis in right elbow joint. This joint had been performed total elbow arthroplasty at 55 years old, furthermore in this joint the olecranon fracture had occurred 62 years old. However, the displaced fragment had not been repositioned. Any bacteria were not detected from this joint, whereas proliferated synovium had kinked ulnar nerve, resulting severe neuralgia and incomplete palsy. To salvage ulnar nerve, synovectomy and neurolysis were performed. Post-operatively, surgical wound was not healed, and S. aureus was detected; diagnosed as pyogenic arthritis, and revised the prostheses in two-stage. 75 days after the revision, pyogenic arthritis had been recalesced. Debridement was performed preserving the prostheses, and the pyogenic lesion was disappeared. However, wound was not healed, and the prostheses were exposed through the skin defect. To cover the prostheses by solid soft tissue, the fascia of triceps brachii muscle which was cut in square based from distal end to proximal site was turned down for anchoring to fracture site of ulnar bone. Moreover, skin was released from

adhered subcutaneous tissue, thereby skin defect was closed.

P1-062

Short-term results of semi-constrained total elbow arthroplasty

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Conflict of interest: None

[Objective] The purpose of this study was to investigate short-term results of semi-constrained total elbow arthroplasty (TEA). [Methods] Eight elbows in 8 patients who underwent Nexel TEA were eligible for inclusion (mean age: 63.3±10.8 years, Steinbrocker class1: 1 elbow, class3: 7 elbows). The mean body mass index was 23.3±4.3. The range of motion before surgery and at the final follow-up was measured and compared by paired t-test. Postoperative loosening in radiographs was investigated. [Results] The average range of motion before surgery was 102.5±18.9 degrees for flexion and -44.4±19.2 degrees for extension. Postoperative flexion and extension was improved to 119.6±11.5 degrees (p=0.01) and -26.0± 15.3 degrees (p=0.04), respectively. One elbow showed loosening of the humeral implant. [Conclusions] Although the reason for the high rate of early failure in Nexel-TEA was unknown, obesity or high activity may be associated with early failure. In this study, many patients were not obese and did not have high activity, however, careful follow-up is needed.

P1-063

An angle between the dorsal tangent of the metacarpal neck and the rotational axis of the metacarpal head

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Conflict of interest: None

[Objective] In silicon joint replacement for the metacarpophalangeal joint using Integra type implant (Integra SJR), the metatarsal neck should be cut in a direction toward rotational axis of the metacarpal head. The aim of this study was to investigate the dorsal tangent angle of the 2nd/3rd metacarpal neck (2DTA/3DTA). [Methods] This study was performed on 29 hands in 29 patients who underwent hand or wrist surgery. The metacarpal three-dimensional model was created using the metacarpal long axis and the rotational axis of the metacarpal head as coordinate axes. The rotational axis of the metacarpal head was defined as the line connecting the distal end of the metacarpal head and the center of the volar surface in the metacarpal head. The dorsal surface shape of the metacarpal neck, and the DTA, comprising the dorsal tangent of the metacarpal neck and the rotational axis of the metacarpal head, was investigated on the horizontal plane at 8 mm proximally from the end of the metacarpal head. [Results] In most cases, a bimodal shape was observed in both the 2nd and 3rd metacarpals. The angles were 77.6° (74.5-81.2) of 2DTA and 81.6° (75.7-85.5) of 3DTA. [Conclusions] In Integra SJR, the neck cutting should be performed at 10° of supination from perpendicular of the dorsal tangent.

P1-064

A knack of Swanson MP joint arthroplasty for the dorsal bone defect at the proximal phalangeal base

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Conflict of interest: None

[Case. Methods] A 51-year-old female with RA that developed with swelling and pain in the MP joint of the left index finger for the past 5 years. She had a severe volar subluxation of the MP joint and a large bone defect of more than 10 mm from the articular surface on the dorsal side of the base of the proximal phalanx. When the osteotomy line was confirmed with a gap spacer, even if the proximal phalanx base was osteotomed by 2 mm, a bone defect of about 9 mm was left on the dorsal side of the proximal phalanx. Bone collected from the 3 cortices of the ilium is formed into a semi-cylindrical shape so that it contains a large amount of cancellous bone. A Swanson implant with a grommet was inserted by intramedullary rasping. Restoration of the dorsal joint capsule and dorsal aponeurosis provided good stability of the implant. [Results] Four months after the operation, bone union of the grafted bone was obtained on X-ray. At 11 months after the operation, the index finger MP joint range of motion is +15°/65° (extension/flexion) and the stability of the implant is good. [Conclusions] Bone grafting from Iliac bone should also be considered when performing Swanson implants in finger MP joints with large bone defects on the dorsal side of the proximal phalanx.

P1-065

Factors associated with walking speed one year after total knee arthroplasty in patients with end-stage knee arthritis

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Conflict of interest: None

[Background and Purpose] The purpose of this study was to measure the walking speed of patients who underwent primary total knee arthroplasty one year after surgery, and to examine the factors most correlated with this. [Subjects and Methods] Among patients with end-stage knee arthritis who underwent initial TKA, walking speed before surgery and 1 year after surgery were measured. We investigated the relationship with basic attributes such as age and gender, pain during walking VAS, Knee Society Score: KSS, skeletal muscle mass of both lower limbs, quadriceps muscle strength, range of motion. [Results and Discussion] Seventy people (54 women) were included in the study. Multivariate analysis was performed with walking speed one year after surgery as the objective variable and age, gender, pain during walking (VAS, KSS), skeletal muscle mass of both lower limbs, quadriceps muscle strength, and range of motion as dependent variables. As a result, skeletal muscle mass, KSS, and range of motion (flexion) of both lower extremities were significantly and independently associated with walking speed (P=0.01, 0.004, 0.02). [Conclusion] A cross-sectional analysis 1 year after surgery showed that decreased leg skeletal muscle mass and poor flexion angle were factors that delayed walking speed.

P1-066

Validation of the Coronal Plane Alignment of the Knee classification (CPAK) in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The coronal plane alignment of the knee (CPAK) classification was recently proposed as an index of coronal plane alignment of the lower limb in knee osteoarthritis (KOA). The purpose of this study was to validate CPAK classification in patients with RA. [Methods] Sixty-three patients with RA and 339 patients with KOA were included in this study. LDFA and MPTA were measured on full-length standing frontal X-ray images of lower extremities, and arithmetic HKA (aHKA=MPTA-LDFA) and Joint Line Obliquity (JLO=MPTA+LDFA) were calculated and classified. [Results] KOA was 51.9% for Type I, 20.6% for Type II, 4.4% for Type III, 16.2% for Type IV, 5.3% for Type V, 1.5% for Type VI, and 0% for Type VII, VIII, and IX. RA was 57.1% for Type I, 27.0% for Type II, 7.9% for Type III, 3.2% for Type IV, 4.8% for Type V, and 0% for Type VIII, IX. [Conclusions] The distribution of CPAK classification in this study was similar to that in previous Japanese studies, with the majority of Type I patients in both KOA and RA. There was no difference in coronal

alignment of the lower extremities between RA and KOA, and CPAK classification is useful for evaluating coronal alignment of the lower extremities in patients with RA.

P1-067

Pain at Pes anserinus burusitis and Gerdy's tubercle burusitis before and after total knee arthroplasty

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Conflict of interest: None

Background: A considerable proportion of the patients feel chronic pain after knee arthroplasty, being the source of the postoperative pain attributed to intra- and extra articular factor. This study focused on the proximal tibia with either Pes anserinus (PA) or around Gerdy's tubercle (GT) as the most common site of the extra articular pain. Methods: The present study investigated the prevalence of PA and GT tenderness over the knee before and after knee arthroplasty procedure and the association between these tenderness and clinical scores. Results: The results of this study demonstrated that 67% of the patients felt tenderness of PA, while 31% of the patients felt tenderness of GT bedore the operation. One year after the operation, 55% of the patients felt tenderness of PA, whereas 23% of the patients felt tenderness of GT. More than half of the tenderness of PA and GT sustain from preoperative days to postoperative days. The postoperative tenderness of PA and GT are associated with a lower clinical score. Conclusion: The symptoms in the extra articular legion (PA or GT) are associated with the postoperative joint pain and function after knee arthroplasty and more than half of the symptoms in extra articular legion sustain from the preoperative to the postoperative days.

P1-068

A successful case of corticosteroid-sparing by belimumab (BLM) for lupus enteritis (LE) recurrence

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Conflict of interest: None

[Object] BLM is not recommended for severe conditions related to SLE. We here report a case of recurrent LE in which disease activity was improved by increasing PSL, which ultimately allowed PSL to be discontinued in combination with BLM. [Case] A 57-year-old woman who had developed LE at the first onset of SLE five years previously experienced cystitis symptoms and gastrointestinal symptoms while continuing treatment with PSL 6 mg, HCQ 300 mg, and MMF 1500 mg. CT showed small intestinal wall thickening and ascites retention, and mild bladder thickening was observed on abdominal echo. Blood tests showed antinuclear antibody 80 titer, anti-ssDNA antibody 37 U/mL, and lupus anticoagulant test positive. A diagnosis of recurrence of LE was made, and PSL was increased to 30 mg after steroid pulse treatment. After two weeks, the patient's LE improved and PSL was then reduced by 5 mg every two weeks. Although there was no worsening of LE at PSL 10 mg, BLM 10 mg/kg was initiated. After BLM combination, the dose of PSL was slowly reduced, until it was finally discontinued after 21 months, and no relapse of LE has been observed in 18 months of follow-up. [Discussion] Although BLM is effective in LE, the timing of administration should be considered according to the individual case.

P1-069

Efficacy of belimumab for refractory cytopenia associated with systemic lupus erythematosus: three case series

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Conflict of interest: None

[Background] Belimumab (BEL) is applied for systemic lupus erythematosus (SLE), but little evidence is available with regards to its efficacy for cytopenia. Here we report three cases of refractory cytopenia associated with SLE that were successfully treated with BEL. [Case 1] 73-year-old female with SLE presented with high fever. She had been on betamethasone 1 mg. Her blood test showed a severe neutropenia (neutrophils 0.43×10^9/L). Neither prednisolone (PSL) nor intravenous immunoglobulin (IVIg) was effective. We administered BEL, cyclosporine and hydroxychloroquine. The neutrophil count gradually improved to 1.5×10^9 /L. [Case 2] 70-year-old female with SLE had been treated with PSL 5 mg and myzoribine 50 mg. Her blood test showed thrombopenia (platelets 10×10^9/L), but increased dose of PSL was ineffective. We administered BEL and the platelet count increased to 150×10^9/L. We tapered PSL to zero. [Case 3] 39-year-old female diagnosed as ITP had been treated with PSL 4 mg. The platelet count decreased to 10×10^9/L, and showed low complement and high levels of anti-dsDNA antibody, so she was diagnosed as SLE. We initiated BEL and increased PSL to 10 mg. The platelet count increased to 100×10^9 /L. [Conclusion] BEL can be effective for refractory cytopenia associated with SLE.

P1-070

A Clinical Study of Six Patients with Active Lupus Nephritis Treated with Concomitant use of Belimumab forInduction of Remission

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Conflict of interest: None

Background: Belimumab (BELI) for active lupus nephritis (LN) has not yet been fully reported. Methods: We evaluated 6 patients who were treated with BELI for the induction of remission of LN. Cases: The 6 patients ranged in age from 20 to 43 years, and all were female. The renal pathology of LN was 1 of LN class IV (A)+V, 2 of class IV (A), 1 of class V, 1 of class II, and 1 of unattached. The cases of class II and class V were referred to our department because of insufficient response to initial treatment at other department. Four patients were positive for anti-ds-DNA antibodies, three for anti-Sm antibodies, and six for anti-SS-A antibodies. All patients received PSL (0.8-1.0 mg/kg/day) and MMF (one patient later switched to IVCY), and five patients received HCQ. All patients achieved remission induction relatively early, with improvement in anti-ds-DNA antibody from 212±81.5 to 21.3±16.0 IU/mL and C3 from 51±25.1 to 76.2±21.1 mg/dL at 3 months. All 4 patients treated for 6 months achieved a reduction of PSL to 10 mg/day or less. No relapse or adverse events were observed. Discussion: BELI has been shown to be safe and effective in inducing early remission, preventing relapse of organ damage, and reducing steroid, and its use may be considered for many more patients in the future.

P1-071

Examination for continuation rate of Belimumab in patients with systemic lupus erythematosus

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Conflict of interest: None

Examination for continuation rate of Belimumab in patients with systemic lupus erythematosus. Objective: To examine for continuation rate of Belimumab in patients with systemic lupus erythematosus (SLE) Methods: Thirty-four patients with SLE who were treated with Belimumab at Tokai University Hospital between 2018 and 2022 were screened. Reasons of Belimumab initiation and factors of the differences in continuation period of Belimumab were examined retrospectively. Results: Of 34 SLE patients, 31 were female with an average age of 44.2 years. Average disease duration was 5.6 years. Main purpose to initiate Belimumab were to reduce prednisolone (PSL) dosage or to improve joint symptoms. In 8 pa-

tients, Belimumab was discontinued within 1 year since the start of Belimumab because of pain, depression, and general fatigue. Belimumab was effective and reduction of PSL dosage wad achieved in patients who were able to continue Belimumab more than 1 year Conclusions: SLE patients who are taking Belimumab r continuously achieved the reduction of PSL dosage.

P1-072

Analysis of efficacy one year after treatment with belimumab in systemic lupus erythematosus

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Conflict of interest: None

[Objective] To investigate the treatment response after 1 year of treatment with belimumab (BEL) for systemic lupus erythematosus (SLE). [Methods] 34 patients with SLE who received BEL from 2018 to September 2021 and are on maintenance therapy with PSL 10 mg or less will be included. [Results] Patient background: Age at BEL administration: 50 years, disease duration: 221 months, 29 patients with positive anti-DNAAb, 11 patients with a history of lupus nephritis. Treatment for SLE: average daily PSL 5.8 mg, 15 patients with HCQ, 29 with immunosuppressant. Three patients discontinued by 1 year (91.2% continuation rate), no flares. Anti-dsDNA antibodies (24.6 to 16.2), C3 (79.1 to 87.3), and C4 (15.6 to 19.2) improved significantly, and the PSL dose was significantly reduced from 5.8 to 4.3 mg. The factors associated with the response rate of C3 and C4 were examined. A history of anti-DNA positivity, antibody titer, and C3 and C4 values were significantly correlated. [Conclusions] The safety and efficacy of BEL for SLE treated with less than 10 mg of PSL were confirmed, and a gradual tapering about PSL can be expected. Serological improvement can be expected in patients with positive anti-DNA antibodies and those with residual hypocomplementemia.

P1-073

Therapeutic effect and safety of subcutaneous belimumab for systemic lupus erythematosus

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Conflict of interest: None

[Objective] To investigate the maintenance therapeutic effect of subcutaneous belimumab (BLM) in patients with systemic lupus erythematosus (SLE). [Methods] Twenty-two patients (47±15 years of age, four males, 18 females) were recruited. The clinical features were examined at 0, 12, 24, and 48 weeks after the administration of BLM. [Results] The patients included 12 cases of lupus nephritis. Remission induction started PSL 46±11 mg/day (0.9±0.2 mg/kg/day), and steroid pulse therapy was administered in nine patients, and IVCY in two. At the introduction of BLM, PSL was 16±11 mg/day, MMF in five cases, HCQ in 10, TAC in 12, and MZR in five. 10±11 years before the introduction of BLM, 0.5 (0-2) relapses occurred. There was no significant difference in median WBC, Hb, PLT, CRP, HbA1c, eGFR, anti-DNA antibodies, C3, and C4 at 0, 12, 24, and 48 weeks, but CH50 increased at weeks 0-12 and 0-24 ($p=0.017$, $p=0.035$), and PSL decreased at weeks 0-24 and 0-48 ($p=0.007$, $p=0.032$). Three cases discontinued BLM before 48 weeks (each one case of pulmonary aspergillosis, abdominal pain, and exacerbation of interstitial pneumonia). One patient (5%) relapsed SLE within 48 weeks of starting BLM. [Conclusion] BLM may be useful to reduce PSL dosage safely without recurrence of disease activity of SLE.

P1-074

High-dimensional analysis of T-cell profiling changes induced by belimumab treatment in systemic lupus erythematosus

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Conflict of interest: None

[Objective] The purpose of this study is to explore changes in T-cell immune profiling by Belimumab (BEL) in SLE, where various immune cells are involved in the pathogenesis. [Methods] We employed mass cytometry with 25 marker panels for immune profiling in peripheral blood T cells (CD3+) from 22 BEL-treated SLE patients (0 M, 3 M, 12 M) and 20 BEL non-treated SLE as control (at enrollment, 12 M). Unsupervised machine learning clustering, Flow-SOM (Self-Organizing Maps), was used to identify 39 T cell clusters (TCL, No. 01-39). For comparing groups of time series data, TCLs (% of CD3+) significantly ($p<0.05$) affected by BEL (BEL-TCL) were selected by a liner mixed effects model (LMEM). [Results] Clinically, the use of BEL significantly reduced serum CH50 ($p=0.003$, by LMEM), C3 ($p=0.00001$) and daily prednisolone use ($p=0.0007$) in this cohort. Four unique BEL-TCLs (TCL 04, 07,11,27) were selected in this study. Notably, Treg-like cluster TCL11 ($CD28^+CXCR3^+Fas^+$Treg) was significantly increased by BEL ($p=0.037$). In contrast, TCL27 ($CXCR3^+CCR4^+CD28^+Fas^+$ICOS+activated central memory $CD4^+$T), which correlated negatively with C3 values, was increased by BEL ($p=0.037$). [Conclusions] These results provide a basis for the exploration of methods to achieve immunological remission in SLE.

P1-075

A case of successful treatment with anifrolumab and cyclosporine for bullous lupus with anti-type VII collagen antibodies

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Conflict of interest: None

A 24-year-old female presented to a previous physician with monthly recurring fever in the 38's, enlarged lymph nodes, stomatitis, lip blisters, facial erythema, and alopecia. Blood tests showed antinuclear antibody positive, anti-Sm antibody positive, and hypocomplementemia, and a diagnosis of systemic lupus erythematosus was made. After administration of hydroxychloroquine (HCQ) 200 mg/day, the bullous lesions worsened, so HCQ was discontinued, and a skin biopsy was performed. Prednisolone (PSL) 20 mg/day was started, but there was no improvement, and she was referred to our hospital. Skin biopsy results showed a consistent finding of bullous lupus erythematosus, and later examination detected anti-type VII collagen antibodies. HCQ 200 mg/day was resumed and PSL was increased to 45 mg/day, but the rash worsened. HCQ was discontinued and tacrolimus (TAC) 3 mg/day was started, but the effect was insufficient. After starting anifrolumab 300 mg/month and changing TAC to cyclosporine (CSA) 150 mg/day, the skin rash showed a tendency to improve. We experienced a case of bullous lupus associated with anti-type VII collagen antibodies that responded to anifrolumab and CSA. We report this case with literature review.

P1-076

Anifrolmab were effective in a patient with refractory Systemic Lupus Erytematosus (SLE)

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Conflict of interest: None

[Background] SLE is a highly heterogeneous disease, and we sometimes encounter refractory cases. We report a case of SLE markedly improved by anifrolumab. [Case] A 48-year-old woman presented with ede-

ma, purpura, hematuria and proteinuria 2 years ago. She was rushed to our hospital due to abdominal pain, and CT demonstrated intestinal wall thickening. Because of the accompanying symptoms of alopecia, ulcers on both legs, and psychiatric symptoms, we suspected SLE and administered mPSL pulse immediately. After mPSL pulse, her abdominal pain abated, but psychiatric symptoms continued. In addition, she developed nephrosis and was treated with IVCY. However, she couldn't continue IVCY due to side effects, so we switched her immunosuppressant from IVCY to MMF and Tac. We then added belimumab and three mPSL pulses with little effect. However, when we switched from belimumab to anifrolumab she went into remission immediately. Although her autoantibodies were all negative, we diagnosed her with SLE based on skin biopsy findings of leukocytoclastic vasculitis, fluorescent antibody staining showing IgA, IgM, C1q, C3, and C4 deposits, and her concomitant APS. [Result] Anifrolumab may be significantly effective in SLE that doesn't respond to conventional therapy.

P1-077

Efficacy of Anifrolumab for NPSLE

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Conflict of interest: None

[Objective] Type I interferon (IFN) plays a central role in the pathogenesis of systemic lupus erythematosus (SLE), and anifrolumab is expected to be effective. While IFN involvement has been reported for cutaneous mucosa and joint symptoms, the importance of IFN for central nervous system lupus (NPSLE) has not been clearly determined. [Methods] We retrospectively evaluated the efficacy of treatment in patients with NPSLE in whom anifrolumab was initiated after prednisolone (PSL) dose reduction and exacerbation of cutaneous and mucocutaneous disorders. [Results] The patients were four female patients aged 20-32 years. The symptoms of NPSLE varied from acute confusion state, regression, aseptic meningitis, and cerebrovascular disease. In all cases after initiation, improvement of cutaneous symptoms and gradual reduction of PSL were possible. There were no exacerbations or relapses of CNS symptoms, and a decrease in the number of hospitalizations. [Conclusions] The CNS symptoms improved along with other manifestations of SLE, suggesting that anifrolumab may be a potential treatment option for patients with NPSLE.

P1-078

Optimal treatment targets for lupus nephritis using per-protocol repeat kidney biopsy at 2 years and clinical data up to 5 years

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Conflict of interest: None

[Objective] To determine the optimal timing of reevaluation and targets to be achieved using per-protocol repeated kidney biopsy findings 2 years after the induction therapy and clinical data up to 5 years. [Methods] Twenty-three lupus patients who underwent repeat kidney biopsies at 2 years were included. First, two ideal clinical outcomes at 5 years were defined: "A. SLEDAI remission and PSL≦5 mg/day" and "B. Proteinuria ≦0.2 g/day with normal Cr level and PSL ≦5 mg/day". [Results] The optimal timing for reevaluation was at 2 years after starting induction therapy; items with AUCs ≧0.8 that predicted optimal outcomes of A and B were as follows: for A, A (0.91), DORIS remission (0.87), B (0.83), electron microscopic remission and/or fluorescent remission (0.83), and SLEDAI remission (0.82); for B, A (0.87), B (0.87), DORIS remission (0.83), and electron microscopic remission (0.82). Two patient groups meeting outcomes of A and B, set from different perspectives, were almost identical. [Conclusions] The best target was "Criteria A at 2 years"; the importance of serologic indices, overall indices including PSL dosage, as well as the importance of electron microscopy and fluorescence staining findings in repeat kidney biopsy were demonstrated.

P1-079

Evaluation of the correlation between renal pathology and clinical course of lupus nephritis

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Conflict of interest: None

[Objective] Lupus nephritis (LN) is one of important prognostic factors in systemic lupus erythematosus (SLE). Our goal is to assess the correlation between renal pathology and clinical course of LN. [Methods] 87 patients with LN proven by renal biopsy from 2001 to 2022 were enrolled. We assess the correlation among clinical characteristics, laboratory data, and pathohistological findings. [Results] Female were 69. Mean age was 48.9 years old. According to ISN/RPS classification, I, II, III, IV, III/IV+V, and V were 6, 6, 18, 18, 31 and 8 cases, respectively. Intensive therapies included mPSL pulse therapy (50%), IVCY (20%%) and oral immunosuppressants (48.3%). In all cases, oral PSL was administrated and the average of initial PSL dosage was 30.4±2.1 mg daily. After 1 year, 54 patients had remission, but 6 had poor prognosis. In LN III/IV+V and LN V, proteinuria levels were higher (3.7 g/gCr vs 1.6 g/gCr: $p < 0.01$) and ds DNA antibodies levels were lower (69.6 IU/mL vs 116.5 IU/mL) than those in LN III/IV only. In LN III/IV+V, renal dysfunction tend to be severe and resistant to treatment. [Conclusions] In LN exhibiting LN V, severe proteinuria was observed. In LN III/IV+V, renal function and prognosis tended to be poor.

P1-080

A study of clinical manifestations and pathological findings in patients who underwent multiple renal biopsies for lupus nephritis at our hospital

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Conflict of interest: None

[Objective] The significance of performing renal biopsy has been discussed. This study aims to review the renal pathology and clinical findings in lupus nephritis at our hospital. [Methods] We reviewed the medical records of patients who underwent multiple renal biopsies for lupus nephritis at our hospital. [Results] Clinical data were available for 30 patients. The mean age was 40.2 years (1st session) and 46.6 years (2nd session). Gender was male in 6 patients (20%). The mean clinical data for the first and second sessions were creatinine of 1.02 mg/dL (95% CI: 0.72-1.33) and 1.03 mg/dL (95% CI: 0.66-1.41), anti-ds-DNA antibodies of 69.6 IU/mL (95% CI: 29.1-110.1) and 69.3 IU/mL (95% CI: 20.0-118.5), C3 was 54.7 mg/dL (95% CI: 46.7-62.7), 64.6 mg/dL (95% CI: 53.2-76.1), C4 was 9.4 mg/dL (95% CI: 7.0-11.7), 11.0 mg/dL (95% CI: 8.0- 13.9). 24 hours urinary protein was 2.96 g/day (95% CI: 2.05-3.87) and 1.61 g/day (95% CI: 1.00-2.21), showing a decreasing trend. The renal pathological findings were proliferative lesions 60.0% (1st session), 60.0% (2nd session), and membrane lesions 50.0% (1st session), 56.7% (2nd session). [Conclusions] Our data also showed that proteinuria improved clinically, but this did not necessarily correspond to changes in pathological findings.

P1-081

A case of suspected overlap syndrome due to ANCA-associated vasculitis and lupus nephritis

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Conflict of interest: None

[Case] A 70-year-old man. He had pain in both lower limbs for the past 6 months. He was admitted to our hospital with numbness in the extremities and hematuria 2 months ago. He was positive for MPO-ANCA 36.0 IU/ml and anti-ds-DNA antibody 13.3 IU/ml. We suspected microscopic polyangiitis (MPA). A renal biopsy was performed on the ninth day,

and the diagnosis of lupus nephritis class II was made based on the mesangial proliferation and deposition of a full house pattern on immunofluorescence staining. We considered that he had ANCA-positive systemic lupus erythematosus (SLE) or an overlap syndrome of MPA and lupus nephritis. He was started on PSL 45 mg (0.8 mg/kg), cyclophosphamide 500 mg/month, and hydroxychloroquine 400 mg. Hematuria and numbness were relieved, ANCA and anti-ds-DNA antibody levels improved, and the patient was discharged from the hospital on the 34th day. [Discussion] SLE is often associated with ANCA positivity, but there is an overlap syndrome between SLE and ANCA-associated vasculitis, which has been reported in several cases. Even in cases where ANCA-associated vasculitis is suspected, renal biopsy should be considered in cases with urinary findings, considering the possibility of SLE.

P1-082

A case of lupus nephritis after SARS-CoV-2 mRNA vaccination

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Conflict of interest: None

[Objective] To report a case of lupus nephritis (LN) after SARS-CoV-2 mRNA vaccination. [Case] A 51-year-old man with rheumatoid arthritis and Sjögren's syndrome had been treated with 8 mg/week of methotrexate and 2 mg/day of prednisolone. In mid-March X, he was administered the third SARS-CoV mRNA vaccine. On the next day, headache, malaise, and leg edema appeared and they increased gradually. He was referred to our hospital in early April because of an abnormal urinalysis. Blood tests revealed decreased renal function, pancytopenia and hypocomplementemia, while antinuclear antibody and anti-ds-DNA antibody were negative. Urinalysis revealed proteinuria and multiple abnormal casts. A renal biopsy revealed mesangial proliferation for the most part of glomeruli, which LN type 4 suggested. Although he was not classified as systemic lupus erythematosus (SLE) by the 2019 EULAR/ACR classification criteria, he satisfied the 2012 SLICC classification criteria. We treated high-dose prednisolone for SLE at first, but it was refractory. Therefore, we added immunosuppressive agents. [Clinical Significance] Recently, a number of cases of SLE and/or glomerulonephritis after COVID-19 vaccination have been reported. We reported an atypical case of LN which was negative for antinuclear antibodies.

P1-083

A case of Lupus nephritis (ClassV) with lupus-related tubulointerstitial nephritis and onset at age 55 years

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Conflict of interest: None

A 55-year-old woman was admitted to our hospital with hypertension and proteinuria in addition to erythema butterfly and polyarticular pain that had appeared a year earlier. Renal biopsy was performed with eGFR 46.4, Anti-ds-DNA antibody 80.9 U/mL, CH50 13 U/mL, urine protein 1.4 g/gCre, glomerular hematuria. Light microscopy showed 2/24 sclerotic glomeruli. The glomerular lesions were mainly spike formation and stippling, but tubulointerstitial fibrosis and inflammatory cell infiltration were seen in about 50%. Immunofluorescence staining showed granular IgG deposits along the glomerular wall, Bowman's cyst and tubular wall, IgG subclasses IgG1, G2, G3, G4 and C1q were also positive. Electron microscopy showed deposits mainly in the glomerular epithelium, but also in the mesangium and endothelium, as well as in Bowman's sac and tubular wall. The diagnosis of lupus nephritis class V with tubulointerstitial nephritis was made. The patient was treated with high-dose corticosteroid therapy followed by PSL40 mg, MMF, and HCQ. Tacrolimus was then added, and remission was achieved and maintained. Lupus nephritis is usually reported as a glomerular disease. We report here an atypical case of lupus nephritis class V with tubulointerstitial nephritis with a later onset than usual for SLE.

P1-084

A case of acute postrenal failure caused by bilateral ureteral stenosis due to lupus cystitis

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Conflict of interest: None

A 67-year-old woman with 50-year history of SLE and localized scleroderma systemic sclerosis visited a hospital and was stable on prednisolone 5 mg/day. In late April, X, she was rushed to the emergency room due to headache and vomiting, and was hospitalized as an emergency. At the time of her visit, her blood pressure was elevated, serum BUN, Cre, and K levels were elevated, and abdominal CT revealed bilateral hydronephrosis, suggesting postrenal failure. She was started on CHDF, she had her right renal fistula indwelled on the second hospital day, her renal function improved, and she was weaned from CHDF on the fourth hospital day. Contrast-enhanced CT and retrograde pyelography performed on the 15th day of illness showed stenosis of the bilateral ureters continuous from the bladder wall, and a bladder biopsy led to the diagnosis of lupus cystitis. Her ureteral stenosis extended to the upper part of the ureter, and she thought that therapeutic intervention would be difficult. [Discussion] Lupus cystitis is often found with abdominal symptoms or bladder symptoms, but in this case there were no notable symptoms until acute renal failure. Based on past literature reports and cases, we will review this case.

P1-085

A Case of Systemic lupus erythematosus with Cyclic thrombocytopenia (CTP)

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Conflict of interest: None

[Case] A 34-year-old female was diagnosed with SLE based on thrombocytopenia, malar rash, and positive ANA and anti-Sm antibody at the age of 23. She has been treated with prednisolone (PSL), but the thrombocytopenia recurred when the dose of PSL was tapered. In June X, her platelet count decreased to $15\times10^3/\mu l$ with purpura on her lower leg. We increased the dose of PSL from 5 to 30 mg/day and the platelet count increased rapidly. However, when the PSL tapered to 10 mg/day, the platelet count decreased to $9\times10^3/\mu l$ again. She complained recurrent purpura on her lower leg before menstruation, so we suspected CTP. While maintaining PSL10 mg/day, we measured the platelet count once a week for three months. Three cycles of periodic platelet fluctuation, ranging $<50\times10^3/\mu l$ to $>150\times10^3/\mu l$, were observed. We diagnosed CTP with SLE. [Discussion] CTP is a rare disease in which the platelet count fluctuates from $<50\times10^3/\mu l$ to normal levels over 3-5 weeks, and the pathogenesis remains unclear. Although patients with CTP are almost misdiagnosed with idiopathic thrombocytopenic purpura, CTP can be diagnosed by frequent platelet count monitoring, and unnecessary administration of corticosteroids can be avoided. CTP should be suspected in SLE patients with refractory thrombocytopenia.

P1-086

Autopsy case of catastrophic antiphospholipid antibody syndrome with acute respiratory distress syndrome

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Conflict of interest: None

[Case] A 80 year-old woman presented with acute respiratory failure. She had episode with two months history of leg edema, two weeks history of ulcer on the dorsum of fingers and five days history of purple digits of toes. A chest CT revealed pulmonary embolism and bilateral widespread ground-glass attenuation with dense consolidation, which indicated acute respiratory distress syndrome. She was treated with methylprednisolone,

heparin, furosemide, and antibiotics on the first day of hospitalization. On the second day, disturbance of consciousness appeared, and subsequent head MRI revealed cerebral infarction. Along with skin pathology of purple digits of toe which showed thrombotic microangiopathy in small vessels and positive anti-β2 glycoprotein I IgG antibodies, diagnosis of catastrophic antiphospholipid antibody syndrome (CAPS) was made. She was treated with plasma exchange twice and intravenous immunoglobulin, which was responsive, but she died of a gastrointestinal bleeding on day 41. [Discussion] Wide spread ground glass opacity is relatively rare imaging presentation of CAPS. In addition, detailed pathological study is scarce. We reported the pathological findings of CAPS with ARDS-like pulmonary shadows obtained from our autopsy case with a review of the literatures.

P1-087

Two cases of subarachnoid hemorrhage during induction remission therapy for systemic lupus erythematosus

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Conflict of interest: None

[Case 1] A 62-year-old woman was diagnosed with systemic lupus erythematosus (SLE) 16 years before, and was treated with prednisolone (PSL) 10-20 mg monotherapy. She was urgently hospitalized due to urinary tract infection and macrophage activation syndrome (MAS). The head MRI scan on admission showed no cerebral aneurysm. Despite the combination therapy with PSL, cyclosporine and cyclophosphamide for 2 months, her MAS was not completely controlled. She developed subarachnoid hemorrhage (SAH), and died. [Case 2] A 51-year-old woman was diagnosed with SLE 13 years before, but she had self-interrupted from her hospital visits since 10 years before. She came to our hospital with abdominal pain and diarrhea lasting for 3 weeks. The diagnosis of lupus enteritis and lupus nephritis was made. She was treated with tacrolimus, mycophenolate mofetil and PSL. She showed temporary improvement of gastrointestinal symptoms, but had repeated flare of lupus enteritis. She developed SAH, and died. [Clinical Significance] It was reported that the incidence of SAH is higher in SLE patients than general population. The two cases were refractory to SLE treatment and under high SLE disease activity, and developed SAH. The possibility of vasculopathy related to the SLE disease status were considered.

P1-088

A case of SLE with thrombotic microangiopathy in Lupus vasculopathy

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Conflict of interest: None

[Case] 30-year-old female. Slight fever and extremity edema occurred. She had pancytopenia, nephrotic syndrome, low complement, positive anti-dsDNA antibodies (2300 IU/l), and was diagnosed with SLE. Renal failure, decreased haptoglobin, appearance of fragmented red blood cells, and increased LDH were observed, suggesting TMA as a complication. She underwent a renal biopsy on hospital day 23. Light microscopic findings showed intraductal proliferative lesions in almost all glomeruli, cellular crescents and subepithelial deposits in some areas, and lupus nephritis IV-G (A)+V was diagnosed. Her arterioles were constricted or occluded with PAS-positive deposits. Immunofluorescence findings were positive for IgG, IgA, IgM, C1q, C3, and C4 in glomerular loops, mesangial regions, and arteriolar walls. [Discussion] Lupus vasculopathy is a non-inflammatory necrotic vascular lesion, mainly in arterioles, with deposition of immune complexes that correspond to the site of injury. If a TMA lesion is found in a renal biopsy of an SLE patient, it should be differentiated by the presence or absence of immunoglobulin and complement deposition, with Lupus vasculopathy and APS in mind.

P1-089

A case of Hemophagocytic Syndrome Associated with SLE presenting with hyperferritinemia

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Conflict of interest: None

A woman in her 60s was diagnosed with SLE 20 years ago based on the 1997 American College of Rheumatology (ACR) classification criteria, had been followed up by our hospital. In September, she presented to our hospital with fatigue, drowsiness, and fever. Prednisolone (PSL)30 mg/day started within a few weeks. However, febrile thrombocytopenia and liver damage worsened. On the 4th day, intravenous methylpredonisolone (mPSL) at 1000 mg/day for was given for 3 days, but no improvement was observed. On the day 6, further deterioration was observed with ferritin 3030 ng/mL, LDH 504 IU/L, and platelets 28,000/μL, and the patient was diagnosed as having hemophagocytic syndrome. On the day 14, her general condition deteriorated, and she was managed in ICU and was conducted plasma exchanges. After this, the data improved temporarily, but her ferritin level increased 44636 ng/mL on the day 18. To remove excess fluid, hemofiltration (CHDF) and dehydration were performed. She was in a state of multiple organ failure and her general condition continued to deteriorate and died on the day 27. [Clinical Significiance] Every immunosuppressive therapy was invalid. It is characteristic of very high ferritin level and rapid progressive hemophagocytosis. We report this case with some literature review.

P1-090

Patient with neuropsychiatric systemic lupus erythematosus presenting with severe weightloss and disturbance of consciousness: a case report

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Conflict of interest: None

A 35-year-old female presented with polyarthralgia, malaise, anorexia, erythema, and personality changes. A weight loss of 10 kg was observed in one month. The patient was referred to our hospital due to altered consciousness and dysarthria. No body image distortion was observed, and anorexia nervosa was ruled out. Hepatic and renal disorders, pancytopenia, and extremely high LDH and ferritin levels were observed, and the patient was suspected of having hemophagocytic syndrome and was admitted to our division. Chest computed tomography (CT) showed diffuse granular shadows in both lung fields, suspected to indicate bronchiolitis. The patient had an oral ulcer, low complement, positive anti-ds-DNA antibody, proteinuria, and elevated CSF IL-6 levels and was diagnosed with neuropsychiatric systemic lupus erythematosus (NPSLE). Following steroid pulse therapy, her consciousness gradually improved. Intravenous cyclophosphamide was administered, her food intake increased, and the lung lesions disappeared. Only a few reports of the association between NPSLE and significant weight loss exist. Therefore, we report a case of immunosuppressive therapy and nutritional management in a patient with SLE who presented with weight loss and organ dysfunction, including a literature review.

P1-091

A case of systemic lupus erythematosus (SLE) with positive anti-AQP4 antibody

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Conflict of interest: None

[Background] NPSLE, which presents with a variety of syndromes, is sometimes difficult to differentiate from many other diseases, including NMOSD. We report a case of NPSLE with positive anti-AQP4 antibody. [Case] A 59-year-old woman who had been maintained in remission with HCQ+TAC for SLE for 20 years. She presented to our hospital because of disturbance of consciousness, cysto-rectal disturbance, and lower limb muscle weakness and sensory disturbance. CSF examination revealed an elevated white blood cell count with mononuclear cell predominance and elevated protein, but infectious disease tests were negative. MRI showed L2-L3 high-signal area on STIR image, high-signal area in the right frontal lobe on FLAIR image, and contrast effect on the dura mater. We diagnosed NPSLE with aseptic meningitis complicated by myelitis with positive anti-AQP4 antibody, which could not be explained by NMOSD alone. Steroid pulse therapy and IVCY were started, and the neurological symptoms tended to improve. [Discussion] Anti-AQP4 antibody is considered to be specific for NMOSD and is widely used as a diagnostic aid. However, it should be noted that even 3% of NPSLEs are known to be positive, and there are cases that are positive for anti-AQP4 antibody but do not meet the characteristics of NMOSD.

P1-092

A case of NPSLE in a patient who was being treated for Alzheimer's disease

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Conflict of interest: None

A 77-year-old woman was diagnosed with Alzheimer's disease (AD) based on an amyloid PET scan and was followed by a neurologist. She was referred to our hospital because of generalized edema and positive antinuclear antibody. At the time of her first visit, she had a chilblain-like skin rash, positive antinuclear antibody, low complement level, positive anti-dsDNA antibody, positive anti-sm antibody, and positive urinary protein. She was diagnosed with SLE, and treated with prednisolone 1 mg/kg/day. Although a renal biopsy was not performed due to cognitive impairment, lupus nephritis was suspected based on laboratory findings, and mycophenolate mofetil was added. Subsequently, since the patient was found to be positive for anti-ribosomal p antibody, CSF IgG-index 0.88, and IL-6 8.0 pg/mL, she was also diagnosed with neuropsychiatric-SLE (NPSLE), and treatment was switched to cyclophosphamide. NPSLE is a factor that determines the cause of death and prognosis in SLE, so early diagnosis and treatment are important. Cognitive decline is a common symptom of aging. Although amyloid PET has become more accessible in recent years, it lacks specificity for diagnosis of AD, so physician should consider the possibility of underlying treatable cause of cognitive decline.

P1-093

A case of systemic lupus erythematosus diagnosed by longitudinally extensive transverse myelitis

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Conflict of interest: None

With the improvement of MRI image quality, the number of reports of longitudinally extensive transverse myelitis (LETM) associated with SLE has been increasing. We report a case of LETM that led to the diagnosis of SLE. [Case] A woman in her 40s was referred to our department because of fever, posterior neck pain, and dysuria. She had meningeal irritation signs, urinary retention, muscle weakness in both lower legs, and weakened tendon reflexes. CSF examination revealed pleocytosis. Blood tests showed leukopenia, hypocomplementemia, antinuclear antibodies at a titer of 1: 80, positive of anti-DNA antibodies, and negative of Anti-AQP4 antibody. MRI showed a high-signal area on T2WI mainly in the gray matter at the Th8-12 level and contrast-enhanced T1WI at the L1/2 level. She was treated with intravenous immunoglobulin, steroid pulse, intravenous cyclophosphamide, and hydroxychloroquine as myelitis due to SLE. And her symptoms have almost improved. [Clinical Significance] Gray matter lesions have a hyperacute onset and are extremely serious immediately, suggesting that early diagnosis and early initiation of treatment are important. Evaluation of gray matter and white matter lesions is important but difficult to distinguish, and multifaceted evaluation is crucial.

P1-094

Effects of dersimelagon (MT-7117), a novel oral melanocortin 1 receptor agonist, in preclinical models of systemic sclerosis

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Conflict of interest: Yes

[Objective] To investigate the potential of dersimelagon (MT-7117) as a therapeutic agent for SSc in preclinical models. [Methods] The effects of MT-7117 on skin fibrosis and lung inflammation were evaluated in bleomycin (BLM)-induced SSc murine models. The effect of MT-7117 on TGF-β-induced activation of human dermal fibroblasts (FBs) was evaluated in vitro. Immunohistochemical analyses of MC1R expression in SSc skin were performed. [Results] Skin fibrosis and lung inflammation were inhibited by prophylactic treatment with MT-7117 (≧0.3 mg/kg) and anti-fibrosis effect was also confirmed by therapeutic treatment (≧3 mg/kg) in BLM models. DNA array analysis demonstrated that MT-7117 exerts an anti-inflammatory effect via suppression of inflammatory cells (e.g. monocytes/macrophage) and signals (e.g. IL-6), additionally, vascular dysfunction was extracted as the pathology targeted by MT-7117. MT-7117 inhibited the activation of human dermal FBs. MC1R immunoreactivity was observed in monocytes/macrophages, neutrophils, FBs, blood vessels, and epidermis in skin of SSc patients. [Conclusions] MT-7117 is a potential therapeutic agent for SSc showing disease-modifying effects on three cardinal features, inflammation, vascular dysfunction, and fibrosis. A phase2 clinical trial is in progress.

P1-095

Clinical characteristics of anti-RNA polymerase III antibody positive systemic sclerosis with interstitial lung disease in our department

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Conflict of interest: None

Objective: To report the clinical characteristics of anti-RNA polymerase III (RNAPIII) antibody positive systemic sclerosis with interstitial lung disease (SSc-ILD). Methods: Thirty anti-RNAPIII antibody positive SSc patients. Results: Of the 30 anti-RNAPIII antibody positive SSc patients who visited our department, 20 had ILD and 10 had no ILD during the observation period. Median (interquartile range) below. Twenty SSc-ILD, 70 (55.3-72.8) years old, 16 female, 8 diffuse type, mRSS 9 (0-20), ILD duration 5 (0-33) months. KL-6 548 (377.3-947.3) U/ml, LDH 231 (205-273) U/l, Cre 0.7 (0.6-0.9) mg/dl, CRP 0.3 (0.1-1.1) mg/dl, anti-RNAPIII antibody 111 (81-143) index. Of these, age, KL-6, LDH, and anti-RNAPIII antibody titer were all significantly higher than those of the 10 patients without ILD. A/S-ILD was found in 8 cases (40%), and the mMRC at diagnosis of SSc was 1.5 (1-2), which was significantly higher than C-ILD. A/S-ILD had more PSL, MMF and IVCY use than C-ILD, and significantly more deaths due to ILD. Conclusions: Anti-RNAPIII antibody titer may be a risk factor for developing anti-RNAPIII antibody positive SSc-ILD, and mMRC may be a risk factor for progression of ILD. A/S-ILD was 40% of SSc-ILD, ILD-related deaths were significantly

higher with A/S-ILD compared with C-ILD.

P1-096

Relationship between anti-U1-RNP antibody titer and clinical features in patients with mixed connective tissue disease

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Conflict of interest: None

[Objective] This study aimed to clarify the relationship between anti-U1-RNP antibody titer and clinical features in patients with mixed connective tissue disease (MCTD). [Methods] A total of 372 MCTD patients were enrolled. We measured the anti-U1-RNP antibody by double immunodiffusion and divided the patients into low-titer (≦1:16), medium-titer (1:32-1:62), and high-titer (≧1:128) groups accordingly. Clinical features and treatment options in each group were retrospectively examined. [Results] Based on the titer measurement, 159, 125, and 88 patients were classified into the low-, medium-, and high-titer groups, respectively. Patients in the high-titer group had a higher prevalence of pulmonary arterial hypertension ($p = 0.011$), serositis ($p < 0.001$), interstitial lung disease ($p < 0.001$), and elevated serum creatin kinase ($p = 0.001$) than those in the lower titer groups. There was no significant difference in the administration rates of glucocorticoid and immunosuppressive agents among the groups. [Conclusions] We found a specific association between high anti-U1-RNP antibody titers and clinical manifestations in patients with MCTD. The risk of developing severe organ involvement can be predicted by the presence of a high anti-U1-RNP antibody titer.

P1-097

Clinical analysis of systemic sclerosis complicated by interstitial pneumonia

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Conflict of interest: None

[Objective] SSc cases with interstitial pneumonia have a poor prognosis. Therefore, some indices that can be easily used are needed for early detection. [Methods] Patients with SSc who visited our center from 2012 to 2022 were recruited. A retrospective analysis was performed by using the clinical data in interstitial pneumonia patients at the time of onset, and in other patients at the time of SSc diagnosis. [Results] Excluding those with smoking history, 81 cases were included only in women. The mean age was 62.7±11.9 and 31 cases had interstitial pneumonia. The number of peripheral blood monocyte increased significantly in the group with interstitial pneumonia (278±86.5 vs 445±176, $p<0.0001$), and the cutoff value of 300/ul allowed the two groups to be assigned with a sensitivity of 84% and specificity of 62%. Multivariate analysis showed that only the increase in peripheral blood monocyte was significantly correlated with the group with interstitial pneumonia. (OR 1.02, $p=0.004$) [Conclusions] SSc with interstitial pneumonia had an elevated number of peripheral blood monocyte. It might reflect the increased monocyte differentiation associated with the scleroderma progression and be involved in interstitial pneumonia by promoting fibroblast proliferation.

P1-098

Factors associated with poor renal prognosis in patients with scleroderma renal crisis using sparse estimation

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Conflict of interest: None

[Objective] To explore factors associated with end-stage renal disease (ESRD) in patients with scleroderma renal crisis (SRC). [Methods] Consecutive patients with SRC diagnosed in our department between 1996 and 2022 were enrolled and classified according to the presence or absence of ESRD at the final observation. Clinical factors at SRC diagnosis associated with ESRD were explored by sparse estimation. The discriminative ability of individual factors and their combination to identify ESRD was examined. [Results] We identified 12 SRC patients; 11 had diffuse scleroderma; 6 were positive for anti-Scl-70 and 1 for anti-RNA polymerase III; the mean disease duration at SRC diagnosis was 3.2 years; 4 were on immunosuppressives before SRC diagnosis. The mean creatinine, hemoglobin, and platelet count were 2.1 mg/dL, 10.3 g/dL, and 150,000/μL, respectively. Six finally had ESRD. Sparse estimation detected elevated LDH, schistocyte, low hemoglobin, urinary protein, and hemolytic anemia as factors associated with ESRD. Elevated LDH, schistocyte, and low hemoglobin remained valid candidates for prognostic models. Moreover, the combination of them tended to improve discrimination. [Conclusions] Elevated LDH, anemia, and schistocytes may be key poor renal prognostic factors in SRC patients.

P1-099

A case of simultaneous onset of systemic sclerosis and rheumatoid arthritis in which pulmonary function was improved by the combination of tocilizumab and an immunosuppressant

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Conflict of interest: None

[Case] A 59-year-old man manifested shortness of breath, swelling of limbs, and arthralgia in August. In December, physical findings included Raynaud's phenomenon, skin sclerosis in fingers, forearms and chest, arthralgia in wrist, elbow, shoulder, knee and ankle, and joint swelling. Lab findings included CRP 1.5 mg/dl, IgG 2883 mg/dl, RF 33 U/ml, ANA x80, negativity for anti-CCP, anti-Scl70, anti-Centromere, anti-RNA polymerase III antibodies, and interstitial lung disease (ILD) on radiographic exam. He was diagnosed with systemic sclerosis (SSc) and rheumatoid arthritis. Considering that the period from the onset was short and the effect of aggressive treatment could be expected, tocilizumab and mycophenolate mofetil were administered. The joint symptoms improved rapidly. After 10 months, the modified Rodnan skin score worsened from 16 to 26, shortness of breath improved, interstitial lung shadows tended to improve, and FVC increased from 69% to 75%. [Clinical Significance] Both drugs have been reported to be effective for ILD of SSc (Phase III clinical trial, Lancet Respir Med. 2020; SLS study, Arthritis Rheumatol. 2017), but they are not yet approved. Although the additive effect of both drugs was not evident, the clinical course advocated early agressive intervention.

P1-100

1st interim report of post marketing surveillance (long-term use) for ofev capsule in patients with systemic sclerosis associated with interstitial lung disease (SSc-ILD)

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Conflict of interest: Yes

[Objective] Nintedanib was approved for SSc-ILD in Japan in Dec 2019. This PMS has been conducted since 1 Apr 2020 to investigate the safety and the effectiveness of nintedanib in actual clinical settings of long-term use (104 weeks). [Methods] We analyzed the patient characteristics and frequency of adverse drug reactions in 135 cases in the safety analysis set who were enrolled in this survey by 15 Apr 2022 whose 12-week case reports had been fixed. [Results] Of the 135 cases in the safety analysis set, 76.30% was female. The mean age, BMI and SSc disease duration at baseline were 63.2 years, 21.87 kg/m^2 and 6.43 years, respectively. The adverse drug reactions were reported in 65 cases (48.15%). The most common adverse drug reactions were diarrhoea in 39 cases (28.89%), nausea in 13 cases (9.63%), and hepatic function abnormal in 12 cases (8.89%). Serious adverse events were reported in 14 cases (10.37%), and for which a causal relationship to nintedanib could not be ruled out were

hepatic function abnormal in 2 cases, drug-induced liver injury in 1 case, and liver enzyme elevation in 1 case each. In all cases, the outcome was recovered. [Conclusions] No new safety concern was observed in nintedanib within the survey period. The data collected by 15 Oct 2022 will be presented at JCR2023.

P1-101

Clinicopathological features of scleroderma renal crisis (SRC)

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Conflict of interest: None

[Objective] We report the study of clinicopathological features in scleroderma renal crisis (SRC). [Methods] Backgoroud, laboratory data, histopathological findings, treatment, and prognosis were retrospectively analyzed in 7 cases of SRC. [Results] Onset of SSc 53.7±12.1 y/o, onset of SRC 62.7±11.0 y/o, duration 9.0±13.0 y, male to female ratio 2:5. Hypertensive was 28.6%, normotensive was 28.6%, and 42.9% were unclear. In 4 cases had no sclerema, however, scleroderma was rapidly worsened just before onset of SRC. Skin ulcer (57.1%), arthralgia (42.9%), myalgia (71.4%), pericarditis (85.5%) were noted. Glucocorticoid was used in 71.4% (28.3±7.5 mg, -496.6±1120.4 days). Cr 1.36±0.8 mg/dL, CK 848± 1347 U/L. The autoantibody were as follows: Scl-70 1 case, RP3 1 case, ACA 4 cases, SS-A 4 case, Ro-52 2 cases. 3 cases received renal biopsy, autopsy was performed in 1 case. Five cases used ACE inhibitors (24.2± 28.7 days). Five cases started hemodialysis (31.6±30.4 days). Five cases patients died (130.2±119.5 days). [Conclusions] SRC patients seemed to have some features such as skin ulcers or pericardial effusion, and anti-SS-A antibodies. Further studies are needed in order to clarify the clinicopathological features of SRC.

P1-102

Evaluation of Potential Poor Prognostic in Patients with Anti-MDA5 Antibody-Positive Dermatomyositis-Associated Rapidly Progressive-Interstitial Lung Disease: A Retrospective Observational Cohort Study

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Conflict of interest: None

[Objective] The purpose of our study is to elucidate the potential poor prognostic factors in patients with anti-MDA5 antibody-positive (Ab^+) dermatomyositis-associated rapidly progressive-interstitial lung disease (DM RP-ILD). [Methods] Sixteen patients with anti-MDA5 Ab^+ DM RP-ILD were divided into survival and non-survial groups (each n=8), who were admitted to our hospital between 2014 and 2022. The differences in clinical characteristics were analyzed. [Results] The non-survial group had significantly higher age at the disease onset, serum levels of AST, LD, CK, CRP, ferritin, and percentage of hypoxia on admission or pulmonary lesions before treatment compared to those of the survival group. The potential poor prognosis factors with higher risk ratios for death were identified as age >60 years, and high levels of serum CRP or CK. Of these poor prognostic factors, all 8 patients who satisfied ≧2 factors died. On the other hand, all 8 cases with <1 factor survived. [Conclusions] Our results indicated that anti-MDA5 Ab^+ DM RP-ILD patients had age >60 years, elevated serum levels of CRP or CK with a very poor prognosis. In the cases with these multiple potential poor prognostic factors, it may be necessary to administer more early intensive intervention for lifesaving.

P1-103

Effectiveness of switching to tofacitinib in two cases of anti-MDA5-antibody positive dermatomyositis that unable to continue triple-combination therapy

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Conflict of interest: None

Background: Anti-MDA5-antibody positive dermatomyositis (anti-MDA5+-DM) is associated with rapidly progressive interstitial lung disease. Triple-combination therapy including high-dose corticosteroids, a calcineurin inhibitor, and intravenous cyclophosphamide (IVCY) is reportedly effective in anti-MDA5+-DM, but some cases have difficulty continuing this therapy due to side effects. Case 1: A man in his 30s with anti-MDA5+-DM developed liver dysfunction (AST 43 U/L, ALT 138 U/L) while receiving triple-combination therapy. Tacrolimus and IVCY were switched to tofacitinib (TOF) on day 42 of treatment. The patient remained in remission until 8 months after switching. Case 2: A woman in her 60s with anti-MDA5+-DM complained of painful muscle spasm of lower extremities during 4th IVCY. The possibility of side effect of IVCY could't be ruled out. IVCY was switched to TOF on day 69 of treatment. The patient remained in remission until 6 months after switching. Discussion: There have been some reports that adding to TOF to triple-combination therapy is effective in the treatment of anti-MDA5ab+-DM. The utility of switching some of the three drugs to TOF is unknown. Our experience suggests usefulness of switching to TOF in cases with anti-MDA5+-DM with triple-combination therapy intolelance.

P1-104

A case of anti-MDA5 antibody positive DM failed to a conventional treatment and responded to JAK inhibitor tofacitinib and plasma exchange

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Conflict of interest: None

59-year-old man presented fever, muscle pain and weakness in limb and skin rash such as Gottron papules. He was also pointed out elevated-CK, positive anti-melanoma differentiation-associated gene5 (anti-MDA5) antibody and interstitial lung disease. He was diagnosed with anti-MDA5 antibody positive dermatomyositis (DM) with rapidly progressive interstitial lung disease (RP-ILD). Combined immunosuppressive therapy including high dose glucocorticoids (GCs), tacrolimus (Tac) and intravenous cyclophosphamide (IVCY) is effective in DM with RP-ILD, but he was resistant to this therapy. ILD progressed worse and new shadows appeared after 4 weeks of the immunosuppressive therapy. Plasma exchange (PE) was carried out in addition to the conventional therapy. PE showed a significant decrease of anti-MDA5 antibody level and inhibited the progression of ILD. But new lung shadows appeared after 4 weeks of PE, and Janus kinase (JAK) inhibitor tofacitinib (TOF) is added to this patient, because JAK inhibitor TOF is reportedly effective in the management of anti-MDA5-related ILD. New lung shadows disappeared by combination therapy of JAK inhibitor TOF and PE. Here we reported a case of anti-MDA5 antibody positive DM failed to a conventional treatment and responded to JAK inhibitor tofacitinib.

P1-105

A case of Anti-MDA5 Dermatomyositis that achieved remission with concomitant use of Tofacitinib, complicated by pneumatosis cystoides intestinalis

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Conflict of interest: None

A 50-year-old woman with anorexia nervosa (AN) was admitted to our hospital with leg weakness, presenting with Gottron's sign. Creatinine Kinase (CK) was elevated. An MRI showed T2W1 high and an enhancement effect in the quadriceps, and the muscle biopsy showed probable dermatomyositis (DM). Meanwhile, a lung CT showed reticular shadows.

KL-6 was elevated and anti-MDA5-antibody was positive. With a diagnosis of anti-MDA5 DM, following steroid pulse, prednisolone (PSL) 40 mg/day and tofacitinib (TOF) was started. After 7 weeks, CK was normalized and muscle strength was improved, but she had dysphagia and the feeding tube was started. We performed a whole CT. There was an improvement in the reticular shadows, but it revealed emphysema in the transverse to ascending colon without symptoms. With a pneumatosis intestinalis (PI) diagnosis, fasting and O2 therapy were performed for one week and laxatives for constipation were intensified. After 13 weeks, the emphysema resolved, and her swallowing function improved. She was discharged with PSL 13.5 mg/day. In existing reports, PI is a rare complication of anti-MDA5 DM. Although AN, PSL, and constipation have been implicated as causes, we report a case in which DM was induced in remission with TOF and was complicated by PI.

P1-106

Two cases of recurrences of anti-MDA5 antibody positive dermatomyositis with interstitial lung disease

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Conflict of interest: None

[Case 1] A 48-year-old woman presented with a dry cough, rash, and arthralgia. Further examination revealed a positive anti-MDA-5 antibody and ground-glass appearance in the lung on CT. She was diagnosed with dermatomyositis (DM) with interstitial lung disease (ILD) and treated with high-dose prednisolone (PSL), tacrolimus (TAC), and intravenous cyclophosphamide (IVCY), and PSL was tapered. One year after the treatment initiation, she developed a dry cough following the COVID-19 infection. CT revealed the exacerbation of ILD. PSL was increased followed by additional IVCY, then the lung lesions were improved. [Case 2] A 55-year-old woman presented with a rash, arthralgia, and fever. Further examination revealed a positive anti-MDA-5 antibody and irregularly shaped pulmonary nodules on CT. She was diagnosed with DM with ILD and treated with high-dose PSL, TAC, and IVCY. Chest CT of one-year follow-up revealed the emergence of novel irregularly shaped nodules. IVCY was added and her lung lesion remains stable without exacerbation. [Discussion] The cases of anti-MDA-5 positive DM with ILD often associated with high mortality, but the cases of relapse are less after long-term remission. Although IVCY was effective in our cases, treatment for relapse should be established.

P1-107

A case of anti-MDA5-positive dermatomyositis with interstitial lung disease that developed after a long prodrome and achieved GC-free

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Conflict of interest: None

A 48-year-old woman. Four months before admission, she presented with arthralgia, fever, pruritic skin rash, and sore throat. Adult-onset Still's disease was suspected due to elevated ferritin, but she did not meet Yamaguchi criteria. Thereafter ferritin and βD-glucan increased as well as the appearance of frosted shadows on CT scan of the chest. Then anti-MDA5 antibody titer of 6490 index, a diagnosis of anti-MDA5-positive dermatomyositis with interstitial lung disease was made. She was started on a three-drug combination therapy of PSL, cyclosporine, and cyclophosphamide, but She was not improved. So she was treated with plasma exchange and rituximab, but there was little improvement. Her treatment was switched to tofacitinib, which resulted in a decrease in both anti-MDA5 antibody and ferritin levels, and improvement in lung shadows. After two and a half years of treatment, PSL was completed and She has remained negative for anti-MDA5 titer. We have experienced a case of anti-MDA5-positive dermatomyositis, and achieved GC-free treatment. She was successfully induced into remission with JAK inhibitors, which have recently been shown to be effective in the treatment of dermatomyositis. We report the results of this study with a review of the literature.

P1-108

A case of dermatomyositis with the high titer of anti-MDA5 antibody without obvious interstitial lung disease

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Conflict of interest: None

A 17 year-old male first noticed fever and muscle weakness of lower extremity, polyarthralgia, erythema since March 2022. Because of his Gottron's sign, periungual erythema, mechanic's hand as well as mild proximal muscle weakness and polyarthritis, he was suspected of having dermatomyositis (DM). Blood examination showed mild elevation of serum CRP and KL-6 and ferritin and high titer of anti-MDA5 antibody. Chest CT revealed a few tiny nodules on lower lungs without obvious interstitial changes. Together with these observations, the diagnosis of anti-MDA5 positive DM was made and treatment with 60 mg prednisolone (PSL) with 6 mg tacrolimus daily was initiated, skin manifestation and joint involvement, KL-6, ferritin, titer of anti-MDA5 antibody were improved. However, when PSL was tapered to 45 mg/day, anti-MDA5 titer increased again with the elevation of KL-6 and CRP levels. Although the chest CT findings had no obvious change without respiratory symptoms, considering the poor control of the disease, we decided to add methyl-prednisolone pulse therapy followed by intermittent intravenous cyclophosphamide. With these additional treatment, anti-MDA5 titer with serum KL-6 and CRP levels decreased with no worsening of physical symptoms and he was discharged when PSL wea reduced to 30 mg daily.

P1-109

A case of MDA-5 antibody positive dermatomyositis complicated with rheumatoid arthritis showed the atypical time course; chronic progressive interstitial pneumonia

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Conflict of interest: None

MDA-5 antibody-positive dermatomyositis (Dmy) is associated with rapidly progressive interstitial pneumonia (IP) that is refractory to treatment and has a poor prognosis. We report a case of MDA-5 antibody-positive Dmy with an atypical time course. A 67-year-old woman with skin rash of hands and muscle weakness was diagnosed with Dmy and IP in X. Steroid pulse therapy and prednisolone (PSL) 50 mg with cyclosporine (CyA) 150 mg were initiated and PSL dose was reduced. Anti-ARS and Jo-1 antibodies were negative. On March X+13, IP and skin rash were worse. Her reexamination of MDA5 antibody showed high titer; 1400 and she had polyarthritis with RF 81 and CCP antibody 89.4. Therefore, she was diagnosed with MDA-5 antibody positive Dmy with rheumatoid arthritis (RA). In spite of the additional treatment with mycophenolate mofetil (MMF), IP was worse with the mediastinal and subcutaneous emphysema. The MDA-5 antibody was also still high titer: 1550. We considered treatment resistant IP, and plasma exchange and cyclophosphamide intravenous therapy (IVCY) 750 mg were performed. IP was gradually improved. MMF1500 mg+PSL10 mg+IVCY600 mg/4 w has been continued. In X+15, the MDA-5 antibody titer has been decreasing, and both symptoms, blood data and imaging findings have been gradually improving.

P1-110

A case of positive anti-MDA5 antibody after diagnosis of eosinophilic pneumonia

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Conflict of interest: None

A 71-year-old man had sputum and became aware of dyspnea in March of X year. In August, he visited previous physician, who pointed out frosted shadows on chest x-ray, and referred him to our respiratory medicine department. CT image showed extensive frosted and reticular shadows predominantly below the pleura in the lower lobes of both lungs, and he was admitted to the hospital. And bronchoscopy was performed: eosinophils 41%, lymphocytes 24%, macrophages 34% (collection rate 61%), with no malignant findings, and cultures were negative. And he had smoked 20 cigarettes/day x 50 years and had quit in January of X year, but started smoking again in July. They diagnosed acute eosinophilic pneumonia, and started treatment with prednisolone (PSL)30 mg/kg/day (PSL0.5 mg/kg/day), but after 2 weeks of treatment, there was no improvement. They performed steroid pulse therapy (mPSL 1000 mg/day x 3 days) two times, but he showed poor response. After that, they founded positive for anti-MDA5 antibodies. He was then treated intermittent intravenous cyclophosphamide, and tacrolimus in addition to high-dose PSL for the diagnosis of anti-MDA5 antibody-positive dermatomyositis. We report a case of anti-MDA5 antibody-positive interstitial pneumonia with an atypical course.

P1-111

A case of anti-MDA5 antibody-positive dermatomyositis associated lung cancer

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Conflict of interest: None

[Case Presentation] A 35-year-old man visited the hospital with the chief complaint of dyspnea in May X. A chest CT scan revealed a 44-mm mass lesion in his right upper lobe and an interstitial pneumonia in both. A needle biopsy of a lymph node ipsilateral to the mass led to the diagnosis of pulmonary adenocarcinoma. Over the same period, he developed proximal myalgia and muscle weakness in the upper and lower extremities, elevated myogenic enzymes, heliotrope rash, Gottron's sign, generalized joint pain, and rapidly progressive interstitial pneumonia. Anti-MDA5 antibody was elevated to 4250 index. We diagnosed lung cancer associated anti-MDA5 antibody-positive dermatomyositis and rapidly progressive interstitial pneumonia. Resection of right upper lobe lung cancer was performed. On the 7th day after the operation, a combination of three drugs (steroid, IVCY, and TAC) was started, and the symptoms of dermatomyositis and interstitial pneumonia were improved. [Consideration] We encountered a case of dermatomyositis with anti-MDA5 antibody-positive rapidly progressive interstitial pneumonia associated with lung cancer. Reports of anti-MDA5 antibody-positive dermatomyositis with malignant tumors are increasing. We report based on our own experience.

P1-112

A case of intravascular disseminated aspergillosis in a patient with anti-MDA5 antibody-positive dermatomyositis, which was difficult to differentiate from exacerbation of the underlying disease

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Conflict of interest: None

A 65-year-old male was admitted because of skin rash, muscle weakness and painful erythema on both hands two months ago. On admission, palmar papules and Gottron's sign were observed, anti-MDA5 Ab was positive, and a CT scan revealed GGO in the multiple lung fields. He was diagnosed with rapidly progressive ILD with anti-MDA positive amyopathic dermatomyositis (MDA5-ADM). High-dose glucocorticoid (GC), cyclosporin, and IVCY were started; however, the lung infiltration was worsened, and serum ferritin levels were increased. We added tofacitinib which improved his condition, and he was discharged. After the discharge, his skin rash worsened, disorientation appeared, liver dysfunction revealed and he was readmitted to the hospital the same month. Under the diagnosis of exacerbation of MDA5-ADM, he was treated with GC pulse and IVCY, which transiently improved his condition. However, he developed consciousness disturbance, pancytopenia with schistocytes, and worsening pulmonary infiltration and passed away despite the administration of anti-bacterial and fungal agents. An autopsy was performed, which showed intravascular invasive aspergillosis. Physicians must be aware of lethal aspergillosis when using intensive immunosuppressive therapy, including JAK inhibitors.

P1-113

A case of anti-melanoma differentiation-associated gene 5 antibody positive dermatomyositis after COVID-19 infection

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Conflict of interest: None

A 66-year-old male after COVID-19 infection admitted to our hospital because of persistent fever with dyspnea, skin lesions, diffuse myalgias. He had a limited role in the treatment of broad-spectrum antibiotic and aitiviral agent, and got hypoxemic. The chest computed tomography (CT) findings showed ground-glass opacity and mass suspected to interstitial lung disease and cancer. The blood tests revealed the significant elevation of anti-melanoma differentiation-associated gene 5 (MDA5) antibody value, but no change of creatine kinase. He was finally diagnosed with anti-MAD5 antibodies positive dermatomyositis. After the administration of pulse methylprednisolone therapy for 3-day, He was treated with oral prednisolone 60 mg/body/day with tacrolimus 3 mg/body and cyclophosphamide 750 mg/body/2-week. Additionally, the plasma exchange therapy was performed. The symptoms and CT findings were improved, and anti-MAD5 antibody level was normalized after the treatment. Here, we experienced a case of anti-MAD5 antibody positive dermatomyositis after COVID-19 infection. In the case with skin rash, acute respiratory failure, and myalgias after COVID-19 infection, the screening including anti-MDA5 antibody may be useful for considering alternative diagnoses.

P1-114

A case of giant cell arteritis mainly affected bilateral vertebral arteries diagnosed by [(18)F] FDG-PET-CT

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Conflict of interest: None

[Case] A 80-year-old woman was admitted to our hospital for general malaise and persistent high CRP levels in September. She began having bilateral upper arm pain and headache seven months ago. Those symptoms spontaneously remitted. However, the pain in the extremities recurred two months ago. She was seen by a general practitioner, who found high CRP level of 12.6 mg/dl and pyuria. With diagnosis of urinary tract infection, adminstration of LVFX resulted in disappearance of pyuria. However, as the CRP level remained high, she was referred to our department. PET-CT showed prominent FDG uptake in the bilateral vertebral artery, and moderate uptake in the left temporal artery, cervical spine, lumbar spine, ischium, pubic bone, shoulder joints, knee joints, and ankle joints. She was diagnosed with giant cell arteritis (GCA) according to 1990 ACR criteria. Remission was achieved by 30 mg of prednisone. [Discussion] PET-CT showed residual inflammation in the vertebral and temporal arteries after spontaneous improvement of polymyalgia rheumatica. GCA mainly affected vertebral arteries like our case is rare. We could treat it before the onset of blood flow disturbance. Our case shows the usefulness of FDG-PET for early diagnosis of GCA, especially of rare site lesions.

P1-115

Clinical outcome of patients with giant cell arteritis in our hospital: A single-center study

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Conflict of interest: None

[Objective] The study evaluated the clinical outcomes of patients with giant cell arteritis (GCA) in our hospital. [Methods] We extracted and retrospectively analyzed the health records of patients with GCA who visited our hospital from April 2020 to October 2022 and were diagnosed and treated at our hospital. [Results] A total of 11 GCA patients, comprising six men and five women, were included. The average age at onset was 71.2 ± 9.7 years and it took 40 days from the onset of symptoms to diagnosis. Of the 11 patients, 10 had headache, six had fever, and three had temporomandibular joint pain or trismus. Biopsies were performed in nine cases, of which six were consistent with the diagnosis. In many cases, biopsy findings were consistent with GCA when temporal artery ultrasonography showed findings such as wall thickening. Seven of the 11 patients had polymyalgia rheumatica (PMR); of them, three had concurrent PMR, three had prior PMR, and one developed PMR during GCA treatment. [Conclusions] GCA may occur simultaneously with PMR, and it may be overlooked when PMR symptoms stand out and lack characteristic symptoms such as temporal headache. In some patients, the first symptom was trismus, which underscores the importance of recognizing GCA as a differential diagnosis of trismus.

P1-116

Gut Dysbiosis is Associated with Aortic Aneurysm Formation and Progression in Takayasu Arteritis

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Conflict of interest: Yes

[Objective] Novel biomarkers are needed for predicting high-risk groups of vascular complications such as aortic aneurysms in Takayasu arteritis (TAK). The objective of this study was to investigate the relationship between the gut microbiota and clinical features in patients with TAK. [Methods] Fecal microbiota of 76 patients with TAK were examined by 16S ribosomal RNA sequencing for comparison with that of 56 age-sex matched healthy controls. The relationship between clinical features and the gut microbiota composition was investigated. [Results] The patients with TAK showed gut dysbiosis with an increased abundance of oral-derived bacteria, such as Streptococcus. The patients with surgery or endovascular treatment for aneurysm had significantly higher rates of certain oral-derived bacteria than those without. In a prospective analysis, patients with these bacteria were significantly more likely to require interventions for aortic aneurysm than those without. These bacteria were also detectable by PCR, and the patients positive for these bacteria tended to have severe aortic aneurysms even under adequate immunosuppressive therapy. [Conclusions] A specific increase in the oral-derived bacteria in the gut may be a novel predictor of aortic aneurysm in patients with TAK.

P1-117

Relapse of ANCA-associated vasculitis after termination of rituximab maintenance therapy

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Conflict of interest: None

[Background] Rituximab (RTX) maintenance therapy is useful in ANCA-associated vasculitis (AAV) to keep remission, though there are problems of immunosuppression and cost associated with long-term therapy. On the other hand, relapse is concern after maintenance therapy is discontinued. [Methods] We reviewed 4 AAV patients who relapsed after RTX maintenance therapy in our department. [Results] All had granulomatous polyangiitis, 3 MPO-ANCA (+), 1 MPO-ANCA/PR3-ANCA (+). Median age was 77 years (range; 74-80), 2 males and 2 females. RTX was administered 4~6 months after remission induction for 2 courses, and thereafter, 1 course/6~8 months for 3~4 times. Median time from remission induction to relapse was 1579 days (1476-1890), and from last RTX dose to relapse was 852.5 days (457-938). MPO-ANCA was elevated in all patients at relapse. Median prednisolone dose at relapse was 2 mg (0-3); one patient took methotrexate, and one took tacrolimus. The median BVAS at first was 10.5 (3-23), whereas at the time of relapse was 7 (4-11). All had pulmonary involvement at relapse. No one developed severe organ damages. [Conclusion] After RTX maintenance therapy is terminated, it is necessary to be careful about relapse. MPO-ANCA elevation could be helpful in predicting and avoiding relapse.

P1-118

Effects of Rituximab in Maintenance Therapy of ANCA-Associated Vasculitis

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Conflict of interest: None

[Objective] The purpose of this study was to clarify the efficacy of rituximab (RTX), an anti-CD20 antibody, in maintaining remission in patients with ANCA-associated vasculitis (AAV) [Methods] AAV at onset treated with RTX for remission induction and maintenance (every 6 months) at our department after 2020 were included, requiring at least 12 months of observation or confirmation of events (death, relapse). The control group consisted of AAV at disease onset treated with intravenous cyclophosphamide (IVCY) and azathioprine for induction and maintenance therapy. The remission maintenance rate, BVAS change, and PSL volume change after 12 months were compared between the groups. [Results] Twenty-seven patients in the RTX group were included in the study. Age and BVAS at the baseline did not differ between the 2 groups, PSL higher dose reduction was achieved in the RTX group (52 ± 19 mg/day vs. 40 ± 10 mg/day; $p = 0.01$), PSL doses were similar in both groups at 12 months. There was no difference in the incidence of drug-related complications in the two groups. [Conclusion] RTX had a remission maintenance rate at 12 months comparable to IVCY; the RTX group received a higher dose of PSL at remission induction, but the dose was reduced to a level comparable to the IVCY group at 12 months.

P1-119

Two cases of ANCA-associated vasculitis otitis media (OMAAV) with recurrent otitis media but negative for ANCA

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Conflict of interest: None

[Case 1] A 55-year-old man, with bronchial asthma since 20 years old, had undergone otolaryngological operations for recurrent pansinusitis and otitis media. Glucocorticoid therapy, antibiotic therapy, and removal of granulation was done for otitis media, however right facial palsy was developed. Although ANCA was negative, meeting the criteria made the diagnosis of OMAAV. Prednisolone (PSL) started, but two years later right sensorineural hearing loss got worsen. We started pulse cyclophosphamide (IVCY), and transferred to azathioprine (AZA) after 6 courses of IVCY. Another year later, rituximab was begun for aggravation of nasal congestion and hearing loss. [Case 2] A 74-year-old man had recurrent otitis media despite antibiotic therapy and insertion of ventilation tube. Although ANCA was negative and no vasculitis found in other organs, hearing loss improved by PSL 30 mg/day (≒ 0.5 mg/kg/day) and exacerbated after cessation, which met the criteria for OMAAV. We resumed PSL and added AZA, and OMAAV didn't flared up despite tapering PSL. [Discussion] Among OMAAV, MPO-ANCA positive is relatively common, however 17% cases are ANCA negative. Duration of untreated tend to be longer in these cases, thus we should recall OMAAV at treating recurrent otitis media, even if ANCA is negative.

P1-120

Granulomatosis with Polyangiitis exhibiting Central Nervous System Symptoms, Successfully Treated with Aggressive Immunosuppressive Therapy

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Conflict of interest: None

[Abstract] A 67-year-old woman was admitted to our hospital for diplopia, dysphagia, and otitis media. One month prior to admission, she was diagnosed with bilateral exudative otitis media and right vocal cord median fixation at a local hospital. On admission, the patient had diplopia, right external rotation disorder, ptosis, and dysphagia. Laboratory findings were negative for inflammatory markers, MPO-ANCA and PR3-ANCA. MRI scan of the head showed a mass around the crista galli and in the right cerebellar pontine angle. In addition, PET-CT scan showed an accumulation in the same area and nasal sputum. Pathology revealed necrotizing granulitis with giant cells and necrotizing granulomatous vasculitis of the small arteries in the tissue of the nasal septum. Based on these findings, the patient was diagnosed with Granulomatosis with Polyangiitis (Yoshida M, et al. 1999: 239-246). The patient was treated with glucocorticoids and rituximab (RTX). The tumor lesions in the head shrank and neurological symptoms improved. Corticosteroid and RTX treatment are useful for multiple vasculitis granulomatosis, but can also be useful in cases of central lesions.

P1-121

A case of ANCA-associated vasculitis using rituximab effectively and safely in remission maintenance

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Conflict of interest: None

Case: A 77-year-old woman complained of fever and pain in her extremities. The laboratory studies showed CRP 7.92 mg/dL and MPO-ANCA 710 U/mL. The right quadriceps muscle biopsy was performed, making the diagnosis of ANCA-associated vasculitis (AAV). 50 mg of prednisolone (PSL) and 50 mg of azathioprine (AZP) are administered. But after 1.5 months, AZP was discontinued due to elevated liver enzyme. Thereafter, 500 mg of cyclophosphamide was administered every 2 weeks for 6 courses. As remission maintenance (RM), 500 mg of RTX was administered twice every 2 weeks, followed by 500 mg of RTX every 6 months. There has been no relapse or side effects, and the PSL has been reduced to 1 mg 14 months later. Discussion: Recently the effectiveness of RTX as RM for AAV has been attracting attention. In the IMPROVE trial, AZP had significantly fewer relapses than MMF, while the MAINRITSAN trial reported that RTX had significantly fewer relapses than AZP. Because of the results and side effects of AZP, we used RTX as RM. Based on the MAINRITSAN3 trial, 500 mg of RTX every 6 months will continue to be administered. Almost all RCTs of RM with RTX for AAV have included relatively young patients. Although the patient in this case was elderly, RTX can be used effectively and safely for RM of AAV.

P1-122

Multiple pulmonary nodules developed at her relapse of microscopic polyangiitis which was successfully treated with rituximab

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Conflict of interest: None

[Case] A 57-year-old woman who had been followed up for scleroderma for 11 years developed microscopic polyangiitis (MPA) with arthritis and renal disorder 8 years before. She was started with prednisolone (PSL) monotherapy. Two years before, MPA relapsed accompanying with cerebral hemorrhage and she was treated with PSL, azathioprine, mycophenolate mofetil, and followed by rituximab (RTX). Those treatment induced her MPA into remission. She did not willing to receive subsequent maintenance treatment with RTX. While she was taking 12 mg/day of PSL, she presented with fatigue, elevated MPO-ANCA and multiple pulmonary nodules. Based on bronchoscopic examination, flare of MPA was confirmed. Treatment with RTX 500 mg four times and subsequently every 6 months successfully improved her symptoms and pulmonary lesions. [Discussion] It has been reported that in ANCA-associated vasculitis, granulomatous lesions such as multiple nodules are less responsive to RTX and relapse more frequently than vasculitis lesions. In this case, remission re-induction and maintenance treatment with RTX was effective for the pulmonary lesions. [Significance] Reporting this case is valuable in that MPA rarely present with multiple pulmonary nodules which can be successfully treated with RTX.

P1-123

A case of PR3-ANCA-positive interstitial pneumonia responding to rituximab

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Conflict of interest: None

An 80-y/o man was referred to our hospital because of dry cough and dyspnea on exertion. One year ago chest X-ray revealed no abnormality. One month prior to the visit, dyspnea on stair climbing appeared and chest X-ray abnormality showing diffuse shadows in the bilateral lung fields, There was no fever, but anorexia and weight loss were observed. SpO2 was 95% at rest and 90% on exertion, and no physical abnormalities were observed except for fine crackles heard in the bilateral middle and lower lung fields. Urinalysis was normal, serum creatine 0.9 mg/dL, CRP 0.27 mg/dL, KL-6 964 U/mL, and PR3-ANCA 19.7 U/mL. CT scan showed interstitial pneumonia. Since there were no vasculitis symptoms, we made a diagnosis of having ANCA-positive interstitial pneumonia. He was treated with a moderate dose of steroids and rituximab, and the pulmonary lesions, including imaging findings, improved. It is not clear whether ANCA-positive interstitial pneumonia represents an early stage of ANCA-associated vasculitis or is a separate disease concept. There is no established treatment for this disease. In this case, the patient responded well to steroids and rituximab, suggesting that the disease shares the etiology and pathogenesis with ANCA-associated vasculitis.

P1-124

Is that glucocorticoid really necessary? A Case of Microscopic Polyangitis Treated with Rituximab Monotherapy

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Conflict of interest: None

Case: a 76-year-old female was presented to our hospital with polyarthralgia and cough for a month. She was diagnosed as interstitial pneumonia with CT scan and under follow-up for 5 years. Physical examination revealed tender joints with mild swelling, and bibasilar fine crackles on lung auscultation. Blood/urine tests showed CRP 6.7 mg/dl, KL-6 574 IU/L, RF 128 U/L, ACPA (-), MPO-ANCA 370 IU/mL, HbA1c 8.5%, urine protein (-), urine blood 2+. Chest CT showed honeycomb and ground glass opacity lesions, which had gradually worsened over the past 5 years; respiratory function tests showed a gradual decrease in %FVC from 125 to 102 over 5 years. Joint ultrasound showed mild synovial thickening without PD signals. This patient, diagnosed with microscopic polyangiitis (MPA), was considered a high-risk case for glucocorticoid treatment due to diabetes mellitus. Considering organ damage relatively mild, the patient was treated with rituximab without glucocorticoids, and her symptoms improved markedly within a month. Her diabetes mellitus was controlled with HbA1c of 6.8% with the addition of oral medication. **Clinical Significance**: In patients with mild to moderate MPA, rituximab monotherapy may be an hopeful option for high risk patients with glucocorticoid treatment.

P1-125

A case of microscopic polyangiitis with lethal diffuse alveolar hemorrhage with normal CRP levels

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Conflict of interest: None

A 73-year-old man was found to have fibrotic interstitial lung disease with elevation of CRP 6 weeks before admission. Thereafter, he was noted to develop decreased renal function (Cr 1.8 mg/dl), proteinuria (1.53 g/gCr) and microscopic hematuria. MPO-ANCA was positive at 649 U/ml. He was diagnosed with microscopic polyangiitis (MPA) and intravenous pulsed methylprednisolone (mPSL) at 125 mg/day for 5 days was initiated, followed by oral prednisolone (PSL) at 60 mg/day (1 mg/kg/day) combined with rituximab (RTX). On the 9th day of the treatment, the CRP levels returned to normal. The dose of PSL was reduced to 40 mg/day on the 15th day and 35 mg/day on the 22th day. Hematuria was improved and MPO-ANCA levels were decreased, while continuous proteinuria and renal dysfunction were not improved. On the 26th day, he developed bloody sputum and chest CT showed extensive consolidation without CRP elevation. Administration of antibiotics was ineffective, suggesting the possibility of diffuse alveolar hemorrhage due to MPA. Although intravenous pulsed mPSL at 1 g/day and cyclophosphamide were administrated, he died of worsening respiratory failure on the 30th day. Severe diffuse alveolar hemorrhage could occur in patients without CRP elevation during glucocorticoids tapering.

P1-126

Rituximab treatment in a patient with microscopic polyangiitis associated with hypertrophic pachymenigitis

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Conflict of interest: None

A 75-year-old male was diagnosed with microscopic polyangiitis (MPA) due to respiratory distress, myalgia in both lower limbs and positivity for MPO-ANCA in august X-2, and was treated with prednisolone (PSL). He was admitted to our hospital because of fever, headache, diplopia, purpura and weakness in both lower limbs. Head MRI showed acute multiple cerebral infarctions and hypertrophic pachymeningitis. He received four courses of rituximab (RTX) at a dose of 375 mg/m2/week in addition to PSL 1 mg/kg/day. His symptoms improved promptly and CRP became negative, then the PSL dose was tapered. After a month, contrast-enhanced head MRI showed improvement of hypertrophic pachymenigitis. Remission induction therapy for MPA with high disease activity often consists of cyclophosphamide (CY) or RTX as well as high-dose glucocorticoid. RTX is recommended over IVCY in terms of adverse events. Several cases of ANCA-associated vasculitis complicated with hypertrophic pachymenigitis have been reported, suggesting that RTX may be effective in the treatment of elderly patients with MPA associated with central nervous system disease.

P1-127

IVCY dose and the occurrence of severe infections in remission induction therapy for ANCA-associated vasculitis

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Conflict of interest: None

[Objective] To investigate optimal doses of IVCY in remission induction therapy for ANCA-associated vasculitis from using the data from J-CANVAS. [Methods] AAV patients with first onset or severe relapse between January 2017 and June 2020 were retrospectively enrolled at 25 centres. Eighty patients were eligible who received IVCY every 2 to 3 weeks during the induction phase. We examined the association between doses of IVCY and infection-free survival until 48 weeks by Cox regression analysis. Secondary outcome was defined as relapse-free survival. We divided the patients into three groups according to the restric cubic spline plot, with the very low dose group (VL: <7.5 mg/kg), the low dose group (LD: 7.5-12.5 mg/kg) and the conventional dose group (CD: >12.5 mg/kg). [Results] Compared with the LD group, the Hazard ratio for infection-free survival until 48 weeks was 4.30 (95% CI, 0.69-26.9) in the VL group, and 5.33 (95%CI, 1.26-22.5) in the CD group. There was no apparent difference in relapse free survival. [Conclusions] IVCY 7.5-12.5 mg/kg is likely to be associated with fewer infections in remission induction therapy.

P1-128

Time to normalization of CRP and incidence of relapse in microscopic polyangiitis: A medical records review study in Japan

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Conflict of interest: None

Objectives: Despite the identification of risk factors for relapses in anti-neutrophil cytoplasmic antibody-associated vasculitis, the relationship between the changes in C-reactive protein levels after initial treatment and relapse incidences remains unknown. **Methods:** This study included 85 consecutive patients with newly diagnosed microscopic polyangiitis who achieved remission after six months of immunosuppressive treatment at Aichi Medical University Hospital, between 2009 and 2017. The relationship between the time to normalization of C-reactive protein after initial immunosuppressive treatment and relapse incidences was evaluated using multivariable Cox proportional hazard models. **Results:** During the

follow-up period, 13 (30.2%), 7 (41.2%), and 16 (64.0%) patients relapsed (P=0.025) within 1-14, 15-28, and ≧29 days of normalization, respectively. Hazard ratios (95% confidence intervals) of the time to normalization of C-reactive protein of 1-14, 15-28, and ≧29 days were 1.00 (reference), 2.42 (0.92-6.39), and 3.48 (1.56-7.76), respectively. **Conclusions:** A significant association between the time to normalization of C-reactive protein and relapse incidence in Japanese patients with microscopic polyangiitis was observed.

P1-129

Clinical features and outcome of elderly-onset granulomatosis with polyangiitis (75 years old or older) in daily clinical practice: a two-center study in Fukushima, Japan

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Conflict of interest: None

[Objective] This study was conducted to investigate the clinical features, therapy and outcome in patients with elderly-onset (75 years old or older) granulomatosis with polyangiitis (GPA) in Fukushima region, Japan. [Methods] We collected newly diagnosed GPA patients treated in Fukushima Medical University hospital or Ohta-Nishinouchi hospital between 2004 and 2019. We retrospectively reviewed the clinical features, immunosuppressive therapy including rituximab (RTX), and outcome using Kaplan-Meier analysis between elderly and younger GPA group. [Results] Among 26 GPA patients, 14 patients were female and the mean age was 65.4 years old (range: 20-81). The mean BVAS scores at initial hospitalization were 15.4. Elderly-onset GPA patients showed significant elevation of CRP levels and ESR (1 hour). Three-year survival rates were high (96.2%) and no significant difference between elderly and younger GPA patents was observed (100% vs 94.4%, respectively). RTX was administered in 11 patients and were effective. Elderly-onset Microscopic polyangiitis (MPA) patients had relatively worse three-year survival compared to GPA patients (100% vs 57.8%, respectively). [Conclusions] Elderly-onset GPA may show stronger inflammation, whereas survival rates seem to be good compared to MPA patients.

P1-130

Clinical characteristics of 6 cases of microscopic polyangiitis

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Conflict of interest: None

[Objectives] ANCA-associated vasculitis (AAV) usually occurs in elderly population, and onset at over 75-year-old is considered elderly onset. We analyzed to clarify the clinical characteristics of elderly-onset and younger microscopic polyangiitis (MPA) patients. [Methods] We investigated the clinical characteristics of 6 patients diagnosed as MPA, based on MPO-ANCA positivity and clinical features, during the five years from 2018 to 2022. [Results] In 4 elderly-onset patients, the mean age was 80.5 (76-85) years, and 3 (75%) were female. BVAS was not significantly different between the two groups (15±9 vs 17.5±3.5, p=0.77). In the elderly group, the time from onset to diagnosis was 1.5±0.5 months, and all patients lost weight, and pulmonary, kidney involvement were frequently observed, while fever were less frequent. The initial dose of steroids was 38.8±5.4 mg/day in the elderly patients and 50.0 mg/day in the younger ones. In the elderly, only one patient who was refractory disease treated with IVCY. [Conclusion] The prognosis for patients with elderly-onset vasculitis is considered to be poor, and immunosuppressive therapy is required immediately in case of severe organ damage. Early diagnosis based on complaints may prevent progression to severe disease and improve prognosis.

P1-131

Clinical features of eosinophilic granulomatosis with polyangiitis (EGPA)

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Conflict of interest: None

[Purpose] The clinical features of EGPA in our department were analyzed. [Patients and Methods] Background, laboratory data, histopathological findings, treatment, and prognosis were retrospectively analyzed in 10 cases of EGPA (5 males, 5 females). [Result] The age of onset was 57.9±20.4 y/o. Four ANCA-positive cases and 6 negative cases were identified. Compared to the ANCA- group ($ANCA^-G$), the ANCA+ group ($ANCA^+G$) had higher white blood cell counts (21690±3315 vs. 12120±4009/μL, P<0.01) and eosinophil counts (13490±2875 vs. 4075±2310/μL, P<0.01), and lower Five Factor Scores (FFS: 0.25±0.50 vs 1.33 ± 0.52, P<0.05). In $ANCA^+G$, duration from onset of EGPA to diagnosis (1.5±0.6 vs 7.4±6.3 months, P<0.05) was shorter than in $ANCA^-G$. IN $ANCA^-G$, one case had myocardial lesion, and another had gastrointestinal lesion. There was no significant difference between $ANCA^+G$ and $ANCA^-G$ in IgE (975±979 vs 983±848 U/L) and CRP (4.28±5.70 vs 2.99±3.47 mg/dL), Birmingham Vasculitis Activity Score (BVAS: 16.0±9.49 vs 17.3±6.3), treatment intensity, Vasculitis damage index (VDI: 2.33±1.75 vs 2.25±2.22), and number of relapses. No deaths were observed. [Conclusion] Early diagnosis of EGPA is important because some patients have serious complications. Further study is warranted.

P1-132

Retrospective analysis of factors affecting duration for diagnostic procedure for ANCA associated vasculitis

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Conflict of interest: None

[Objective] To determine the relevant factors affecting length of time to diagnosis for ANCA-associated vasculitis (AAV). [Methods] We analyzed medical records date in 33 cases who were admitted to our department in 2017-2021 and diagnosed with AAV for the first time. [Results] Patients were diagnosed with MPA n 25 patients, EGPA in 7, and GPA in 1. As initial symptoms, 14 patients had fever, 12 had respiratory symptoms, 10 had constitutional symptoms other than fever, 7 had musculoskeletal symptoms, 4 had neurological symptoms, 3 had cutaneous symptoms, and 3 had otological symptoms, respectively. The median duration for diagnostic procedure was 2 months. All patients were divided into “early diagnosed group” (13 cases; diagnosed within 2 months) and “late diagnosed group” (20 cases, diagnosed after 2 months). The former tended have fever and cutaneous symptoms than latter have. Three patients required long time (> 17 months) for diagnosis. Two, of them first visited respiratory medicine. [Conclusions] We considered that fever and skin symptoms are distressing and often specific, leading to prompt consultation, referral to a specialized institution, and early diagnosis. Respiratory symptoms as the initial symptom may result in delayed diagnosis for AAV.

P1-133

A case of Familial Mediterranean Fever that relapsed with gastrointestinal lesion recurrence after withdrawal of canakinumab

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Conflict of interest: None

[Case Presentation] A 37-year-old man was diagnosed with Familial Mediterranean Fever several years ago. He had been in remission with colchicine and canakinumab, but due to personal reasons, he did not see a doctor for about half a year and was in a drug-free state. He presented to our outpatient clinic complaining of light-headedness and malaise, and was admitted to our hospital for severe anemia. We performed endoscopy and found mucosal damage and bleeding in the lower gastrointestinal tract resembling inflammatory bowel disease. We resumed colchicine, and the abdominal symptoms and melena disappeared on the day after administration. Since then, he has been in remission with colchicine monotherapy. [Discussion] Molecular-targeted drugs such as CAN and TNFα inhibitors are also used in intractable cases, but one of the problems is the high drug cost. Although this patient had gastrointestinal mucosal disorder, remission was achieved by fasting, symptomatic treatment, and administration of colchicine alone. Even for refractory cases that have used CAN in the past, starting treatment with classical therapy can be evaluated from the viewpoint of medical economics.

P1-134

Effectiveness and safety of tocilizumab and TNF inhibitors in refractory systemic adult-onset Still's disease. Single center, retrospective study of 18 patients

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Conflict of interest: None

[Objective] To evaluate the safety and effectiveness of tocilizumab (TCZ) and TNF inhibitors (TNFi) in patients with refractory systemic AOSD (rsAOSD). [Methods] The rates of remission, treatment failure, and adverse events, including macrophage activation syndrome (MAS) in rsAOSD patients treated with TCZ and TNFi were retrospectively assessed. Remission was defined as no disease activity with a prednisolone equivalent of ≦5 mg/day. [Results] Among 18 patients (89% female; median age, 47 years) included, TCZ was initiated in 16 and TNFi in 2. Overall, 26 treatments were identified, 21 of which were with a calcineurin inhibitor (CNI). Among 18 TCZ treatments, including the second treatment at 2 relapses, 10 achieved remission within 6 months, 2 continued on TCZ, and 4 and 2 switched to a TNFi due to MAS and arthritis, respectively. Among 8 TNFi treatments, including 6 switched from TCZ, were combined with a CNI, and all switched cases achieved remission within 6 months. MAS developed in 7 cases (6 on TCZ and 1 on TNFi). No deaths were observed. Finally, 15 patients were in sustained remission without glucocorticoids and biologics. [Conclusions] TCZ and TNFi showed effectiveness for refractory sAOSD, especially TNFi with CNI as salvage therapy after TCZ treatment failure.

P1-135

Clinical study of adult-onset Still's disease in our hospital

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Conflict of interest: None

[Objective] To clarify the treatment results of adult-onset Still's disease (AOSD) in our hospital. [Methods] Characteristics of the patient, percentage and characteristics of rash, recurrence rate, rate of macrophage activation syndrome (MAS), mortality rate. We investigated the characteristics of cases in which steroids could be discontinued. [Results] 28 cases were extracted. The median age was 61. Observation period was 49 months. Elderly onset was 39.2%. Rash was observed in 85.1%, and pruritus was present in 63.6%. The relapse rate was 28.5%, MAS rate was 21.4%, the mortality rate was 10.7%, and the steroid discontinuation rate was 48.1%. CRP, ferritin, and D-dimer at the time of diagnosis were significantly higher in the elderly onset than in the younger onset. There were no significant differences in parameters at diagnosis in patients with MAS compared with those without MAS, and in relapsed patients compared with non-relapsed patients. All of the 3 cases that died were of elderly onset. MAS, Ferritin, sIL-2R, LDH, and D-dimer were significantly lower in patients who were able to discontinue steroids than in patients who were unable to discontinue steroids. [Conclusion] There are few reports about AOSD, and we report here as valuable data.

P1-136

A case of adult onset Still's disease with lobular histolysis due to hypercytokinemia refractory to steroid therapy

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Conflict of interest: None

[Background] Several cases of sJIA have been reported in which liver injury develops after systemic inflammation remitted. Although these cases do not meet the diagnostic criteria for MAS, the intrahepatic macrophage activation is proven pathologically. In our case, steroid-resistant liver injury was observed during the course of AOSD, and the pathological findings demonstrated autoimmune liver injury. [Case] A-24-year-old man presented to his previous physician with complaints of fever, sore throat, polyarthralgia, and skin rash. He was diagnosed as AOSD. He was transferred to our hospital after one course of steroid pulse therapy and three courses of half steroid pulse therapy, which did not work. Liver biopsy showed that the Glisson's capsule was preserved and that there was severe central cytolysis, vesicular degeneration, and pinocytotic siderosis, suggesting lobular histolysis due to hypercytokinemia. He was treated with steroid pulse therapy followed by cyclosporine and tocilizumab, and his liver function got normalized. [Conclusion] When liver injury persists despite the resolution of systemic inflammation during treatment of AOSD, lobular histolytic autoimmune hepatitis-like disease should be considered.

P1-137

A 71-year-old man with symptoms consistent with VEXAS syndrome but was negative for peripheral blood UBA1 variant

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Conflict of interest: None

We here report a 71-year-old man exhibited multi-organ inflammatory symptoms refractory to various anti-inflammatory treatments. The patient is a 71-year-old man who was diagnosed with MDS in year X-15, his IPSS-R score was in the low-risk group. In July year X-1, the patient noticed myalgia of extremities. PET-CT showed FDG accumulation in multiple intramuscular nodules and ascending aorta. Myositis was confirmed by muscle biopsy. In the same year, polyarticular arthralgia appeared, and psoriatic arthritis was suspected based on accompanying symptoms such as head rash and Achilles tendonitis. Immunosuppressants including MTX and MMF were initiated, but his symptoms relapsed when PSL was tapered off. At the time of referral to our hospital, VEXAS syndrome was suspected based on a diverse clinical picture similar to previous cases of VEXAS syndrome. However, his bone marrow smear showed only mild vacuole formation within myelocytes. MCV was within normal range, inconsistent with VEXAS syndrome. The *UBA1* gene variant in the peripheral blood was negative. We report on the characteristics of this case, comparing them to the PET-CT findings of cutaneous and intramuscular accumulation seen in a genetically confirmed case of VEXAS syndrome.

P1-138

A case of intestinal Behçet's disease and extensive cutaneous mucosal lesions complicated with plasminogen deficiency

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Conflict of interest: None

[Case] A 22-year-old woman was under treatment for ligneous periodontitis caused by plasminogen deficiency (PD). She was admitted with a persistent fever of 39 degrees, sore throat, abdominal pain, diarrhea, and bloody stool. [Clinical Course] On admission, her CRP level was 15.94 mg/dL. The colonoscopy revealed mesalazine-ineffective erosions of the mucosa from the rectum to the cecum. On day 13, erythema 1 cm in size on the extremities and positive needle reaction were observed. On day 19, painful erythema rapidly expanded to the extremities, which turned into bloody blisters and deep ulceration. Skin biopsy showed leukocytoclastic vasculitis in the subcutaneous fatty tissue. In addition, positive HLA-B51 and thickening of the ileocecal region by contrast-enhanced CT led to the diagnosis of intestinal Behçet's disease with severe mucocutaneous findings. Steroid pulse therapy and adalimumab was effective both for the intestinal and the mucocutaneous lesions. [Discussion] PD is characterized by pseudomembrane adhesion due to fibrin precipitation on the mucosa, but does not cause ulceration or vasculitis. Interestingly, neutrophil activation is triggered by fibrin deposition in a mouse model of PD, which may have contributed to the development of Behcet's disease in this case.

P1-139

Correlation between clinical phenotype and drug-free remission in adult-onset Still's disease

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Conflict of interest: Yes

[Objective] To classify the clinical phenotype of adult-onset Still's disease (AOSD) and investigate a correlation between phenotype and prognosis. [Methods] One hundred and fifty-three AOSD patients (43 men and 110 women) were included. We classified these patients by hierarchical cluster analysis using 12 items including age, sex, skin lesion, arthralgia, serositis, and serum ferritin. We then investigated the correlation between groups and drug-free remission. [Results] AOSD patients were classified into four groups, 1. Younger-onset typical group (59 cases), 2. Younger-onset severe group (27 cases), 3. Atypical group (14 cases), 4. Elderly-onset group (53 cases). Sixty years-old or higher was frequent in group 4 ($P<0.001$), skin lesion and lymphadenopathy was less frequent in group 3 ($P=0.005$ and $P<0.001$), typical skin lesion was less frequent in group 3 and 4 ($P<0.001$), serositis and DIC was frequent in group 4 ($P<0.001$). Cyclosporine and methylprednisolone pulse therapy was used less frequently in group 3 ($P=0.0287$ and $P=0.0403$). Overall survival tended to be poor in group 4 ($P=0.054$), and drug-free remission rates were lower in group 4 and higher in groups 2 and 3 ($P=0.004$ and $P=0.007$). [Conclusions] AOSD patients were classified into four groups. Group 4 had a poor prognosis.

P1-140

A case of refractory adult Still's disease complicated with macrophage activation syndrome successfully treated with baricitinib

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Conflict of interest: None

(Case) A 49-year-old woman started to suffer from fever and pain in neck, shoulders and knees in February. She visited our department because of her sustained arthralgia and fever in April. Her symptoms once improved after starting low-dose glucocorticoids (GCs) and methotrexate based on the diagnosis of seronegative rheumatoid arthritis. But in October, she developed a fever, sore throat, and pain in shoulders, lumbar, thighs and chest. She was diagnosed as adult Still's disease (ASD) because of liver dysfunction, elevated serum ferritin level and pleural effusion. She was treated with high-dose GCs (maximum 120 mg/d of prednisolone), tacrolimus and tocilizumab (TCZ). Although her fever and inflammatory markers were improved, arthralgia, pancytopenia, elevated serum liver enzymes and ferritin were not well controlled. Bone marrow aspiration/biopsy showed hemophagocytosis and she was diagnosed as a complication of macrophage activating syndrome (MAS). Administration of baricitinib instead of TCZ improved her symptoms and laboratory abnormalities. (Discussion) Baricitinib, a JAK1/2 inhibitor, can be effective for refractory adult Still's disease with MAS which is resistant to high-dose GCs and other immunosuppressants.

P1-141

Behcet's disease complicated with myelodysplastic syndrome with 5q-. A case report

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Conflict of interest: None

[Case] A 78-year-old woman with incomplete Behcet's disease for 21 years, was diagnosed on the basis of oral and genital ulcers, erythema nodosum, folliculitis-like rash and arthritis. She had visited to our hospital regularly, and her symptom had been in remission or low disease activity by taking 7 mg/d of oral prednisolone for 6 years. Since last May, her blood tests had showed progressive anemia that was rapidly worsened (Hb 5.3 g/dL) in this March. Gastroscopy revealed active bleeding from gastric ulcer, and endoscopic hemostasis was successfully applied. There were no findings in colonoscopy. A month later, her blood tests still showed severe anemia (Hb 4.5 g/dL). Gastro- and colonoscopy showed no bleeding region. Laboratory tests showed macrocytic anemia (MCV 111.7 fL) and reticulocyte was not elevated (0.7‰) despite the severe anemia. Bone marrow aspiration demonstrated markedly reduced erythroid lineage, normal granulopoiesis/megakaryopoiesis without dysplasia. Chromosomal analysis of bone marrow cells revealed 46, XX, del (5q). Based on these findings, she was diagnosed as myelodysplastic syndrome (MDS) and was treated with lenalidomide. [Clinical Significance] We report a rare case of Behcet's disease complicated with MDS with 5q-.

P1-142

Investigation of the usefulness of intra-articular glucocorticoids for new-onset oligoarticular juvenile idiopathic arthritis

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Conflict of interest: None

[Background] Intra-articular glucocorticoids (IAGCs) for new-onset

oligoarticular juvenile idiopathic arthritis are “strongly recommended as an initial treatment” in other countries, but in Japan, IAGCs are mainly treated with systemic medications. [Objective] To evaluate the usefulness of IAGCs for new-onset oJIA. [Methods] New onset oJIA with IAGCs from August 2018 to May 2022 were retrospectively reviewed using medical records. [Results] Twelve patients (2 boys, 10 girls), 1-4 years old (median 3 years), 26 joints (23 knee joints, 2 elbow joints, 1 ankle joint) were treated with IAGCs. Arthritis remitted rapidly in 10 patients (85%), but not in 2 (15%). Five patients (40%) remained in remission for more than 16 weeks without systemic medication, and two remained in remission for more than 3 years with a single IAGCs. Seven patients (60%) subsequently required systemic medications and methotrexate was often effective, while biologic agents were required in 2 cases of non-remission. No statistical predictors of response to IAGCs were found. Transient desaturation and vomiting due to sedation were observed in a few cases, but no long-term complications were observed. [Conclusion] IAGCs can avoid systemic medications in 40% of oJIA.

P1-143

A case of other iatrogenic immunodeficiency-associated lymphoproliferative disorders with juvenile idiopathic arthritis

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Conflict of interest: None

In adult patients with RA, other iatrogenic immunodeficiency-associated lymphoproliferative disorders (OIlA-LPD) are recognized as adverse events that should not be overlooked. Meanwhile, there have been a few reports of children with Juvenile idiopathic Arthritis (JIA) developing LPD, and no unified view has been obtained. We report a case of JIA complicated with OIIA-LPD. **Case**. A 13-year-old girl was diagnosed with polyarticular JIA in X. She was initially treated with oral MTX, but she had only a partial response. Adalimumab was added one year after the diagnosis. At age 12 years 10 months (X+1), her right cervical lymphadenopathy was noted. She had no associated fever, weight loss, and nocturnal sweating. After the symptom, she stopped taking medicine. Because of the persistence of the node, an excisional biopsy was performed that revealed Hodgkin lymphoma. **Discussion.** In RA patients, elderly age, duration of disease, and long-term MTX administration have been reported as risk factors in LPD. In addition, a 40% spontaneous resolution rate after MTX discontinuation has been reported in RA, but in children, as far as can be determined, there is only one case reported in 2017, which might be severe. Therefore, we think LPD should be considered when treating patients with JIA.

P1-144

13 cases of psoriatic arthritis (PsA) subtype of Juvenile Idiopathic Arthritis (JIA)

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Conflict of interest: None

[Objective] Juvenile Idiopathic Arthritis (JIA) is rare disease and patients of psoriatic arthritis (PsA) subtype are uncommon in Japan. We aimed to clarify the clinical picture of patients with PsA. [Methods] We diagnosed patients as PsA of JIA who met the classification criteria of the International League of Associations for Rheumatology (ILAR) or the Vancouver classification criteria for pediatric psoriatic arthritis. We examined clinical information using electronic medical charts. [Results] Of 13 PsA cases, the age of onset ware 1 to 15 year of age (median 6), 3 boys (23%) and 10 girls (77%). Six cases (46%) had a family history of psoriasis (PsO) and 12 cases (92%) had skin manifestations of psoriasis. Nine patients (69%) had chronic pain syndrome and autonomic insufficiency which suggest the possibility of small fiber neuropathy (SFN). Methotrexate (MTX) was used in 11 patients (85%), biologics (Adalimumab or Secukinumab) in 9 patients (69%) and corticosteroids in 2 patients (15%). Eight of the 11 patients (73%) met inactive disease (ID) and 3 patients (27%) met clinical remission off medication (CR) at the last visit. [Conclusions] PsA patients were treated with medicine such as MTX, biologics and they worked well.

P1-145

A case of localized scleroderma associated with juvenile idiopathic arthritis

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Conflict of interest: None

Localized scleroderma is one of the autoimmune diseases whose main symptoms are limited sclerotic lesions of the skin. This disease occurs at any age, from children to the elderly. Enthesitis-related arthritis is a JIA category of ILAR. Here we report a case of localized scleroderma that occurred during the course of enthesitis-related arthritis. Case; 6-year-old girl. It was difficult for her to move both hands about a year ago. The joint findings showed limited range of motion at the left and right finger DIP, PIP, wrist, and knee joints. The patient was diagnosed with enthesitis-related arthritis. Treatment started with NSAIDs and MTX, but adalimumab was introduced because arthritis remained. Later, the joint findings tended to improve, but skin rashes appeared on the insteps and buttocks. A skin biopsy was performed for diagnosis, and localized scleroderma was diagnosed together with clinical symptoms. Conclusion: We experienced a case of localized scleroderma associated with enthesitis-related arthritis. Overseas, childhood-onset localized scleroderma has been reported to be 1-2 in 100,000. About 20% of localized scleroderma is associated with arthritis. On the other hand, the frequency of localized scleroderma associated with JIA is reported to be 0.9%.

P1-146

Clinical features of multicentric Castleman disease in our hospital

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Conflict of interest: None

[Objective] Idiopathic multicentric Castleman disease (iMCD) is a polyclonal lymphoproliferative disease with a chronic course and multiple lymphadenopathy. TAFRO syndrome, which presents with marked fluid retention, acute renal dysfunction, thrombocytopenia, and rapidly deteriorates general condition, is interpreted as a subtype/severe type of iMCD. We examined the clinical features of 22 patients with iMCD and TAFRO syndrome at our hospital. [Methods] We investigated the clinical features of 17 idiopathic multicentric Castleman’s disease (iMCD-NOS) and 5 TAFRO syndrome (iMCD-TAFRO) diagnosed at our hospital from 1997 to March 2022. We reviewed the clinical characteristics, CHAP score, initial treatment and treatment course of all 22 patients. [Results] There were 13 males and 9 females, lymph node histology was plasma cell type in 18 cases, mixed type in 3 cases, and hypervasclar type in 1 case. Steroids and tocilizumab were administered in almost all cases, and cyclosporin A was used in 3 cases of TAFRO syndrome. [Conclusions] iMCD-NOS has a relatively good prognosis if treated appropriately. On the other hand, patients with iMCD-TAFRO are often severely ill and have a high mortality rate, so it is important to promptly diagnose and initiate treatment before the disease becomes severe.

P1-147

A case of rheumatoid arthritis complicated by idiopathic Castleman disease

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Conflict of interest: None

<Case>A 69-year-old Japanese woman was admitted to our hospital for fever and lower leg edema. Blood test showed anemia, CRP and IL-6 elevation, thrombocytosis and hyper gammaglobulinemia. Computed tomography showed hepatomegaly and swollen lymph nodes in both inguinal areas. An inguinal lymph node biopsy revealed marked plasmacytosis and hemosiderin deposition in the interfollicular area. HHV-8 stain were negative, so she was diagnosed with idiopathic Castleman disease (iMCD). She also suffered from swelling and tenderness of bilateral shoulder, wrist, knee and ankle joints. Ultrasound revealed marked synovitis and X-ray test showed deformity or destruction of these joints. A synovium biopsy revealed plasmacytosis and detritic synovitis. Serum anti-CCP antibody was negative, but serum RF was positive. These findings were aggressively activated rheumatoid arthritis (RA). She was treated with intravenous injection of tocilizumab (8 mg/kg/2 week). She achieved remission of the iMCD and RA. <Discussion>The case of RA complicated by iMCD is very rare. Hypercytokinemia through IL-6 is observed in iMCD patients. IL-6 plays an important pathologic role in both iMCD and RA progression. IL-6 over production, which has spiraled out of control, could have involved aggressively activated RA.

P1-148

A case of Evans syndrome associated with Castleman's disease successfuly treated with rituximab

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Conflict of interest: None

A case is 77 years-old female. She had history of surgery for esophageal caner in X-1. Hyper IgG4emia was observed during the follow-up, and she was referred to our hospital for suspicion of an IgG4-related disease in the same year. There was subjective symptom of Raynaud's phenomenon, and antinuclear antibody, anticardiolipin antibody, and direct Coombs test positive, and hypocomplementemia were observed. CT scan showed mediastinal lymphadenopathy and abnormal lung shadows, and lung biopsy suggested Castleman's disease. From around August X, she became aware of malaise, severe anemia and thrombocytopenia were observed at another hospital. Gastrointestinal bleeding was negative, but direct Coombs test positive, indirect type hyperbilirubinemia, hyperLDH, decrease in haptoglobin, and reticulocytosis were considered to be autoimmune hemolytic anemia (AIHA). We started steroid therapy. Bone marrow examination revealed AIHA and idiopathic thrombocytopenic purpura. Hemolysis and thrombocytopenia were improved by the addition of a thrombopoietin receptor agonist and rituximab. Castleman's disease is rarely associated with Evans syndrome, and treatment is difficult. We report this including some literature considerations.

P1-149

A case report of Multicentric Casthleman Disease (MCD) requiring differentiation from IgG4 related disease with bilateral periureteral mass lesions

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Conflict of interest: None

[Case] A 71 years-old man was pointed out of hypoalbuminemia and inflammation incidentally. CT scan revealed bilateral periureteral mass lesions and systemic lymphadenopathy, suggesting lymphoma or IgG4RD. Inguinal lymph node biopsy was performed, which showed germinal center atrophy and interfollicular plasma cell (PC) infilteration. He visited us to search for possibility of MCD. Physical examination showed neither swealling of lacrimal nor salival glands. Urine analysis showed no abnormity. Blood analysis: C3 107 mg/dL, C4 27.1 mg/dL, IgG 4027 mg/dL, IgA 218 mg/dL, IgM 433 mg/dL, IgG4 696 mg/dL, ANA x40 (speckle), anti-SS-A Ab <1.0 IU/mL, IL-6 18 pg/mL. We re-evaluated the lymph node specimen and performed CT-guided needle biopsy of the periureteral mass. The former showed 20% of IgG4/IgG ratio and IL-6 positive PCs. The latter showed PC infiltration and 20% of IgG4/IgG ratio. From these new findings and the known, we diagnosed as MCD, PC type. Considering progressive exaution, we started to treat by Tocilizumab. [Discussion] Both patients of IgG4RD and MCD can have lymphadenopathy. Periureteral mass lesion was reported in many cases of IgG4RD. However, it could be lesion of MCD. Comprehensive evaluation including pathological data to differentiate both diseases is important.

P1-150

A fetal case of TAFRO syndrome complicated by hemophagocytic lymphohistiocytosis and invasive candidiasis after the treatment of biologics

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Conflict of interest: None

A 65-year-old man was referred to our hospital with subcutaneous bleeding. He was diagnosed with TAFRO syndrome based on thrombocytopenia, renal failure, elevated CRP, anasarca, reticulin fibrosis and lymphadenopathy. The effect of prednisolone and cyclosporine was not enough, so tocilizumab (TCZ) was initiated. Platelet count was increased, but kidney function did not improve and ascites remained. TCZ was switched to rituximab (RTX), and ascites decreased. After fourth RTX infusion, amnesia and respiratory failure appeared and he went into shock. He was diagnosed with septic shock and received antibiotics. High dose catecholamine and massive rehydration were needed to maintain blood pressure and anasarca increased, suggesting increased vascular permeability. Based on the elevated serum ferritin level and pancytopenia, he was considered to have hemophagocytic lymphohistiocytosis. Steroid pulse therapy and plasma exchange therapy were added, but he died of circulatory failure. Pathological autopsy revealed invasive Candidiasis. On the other hand, serum IL-6 and VEGF levels significantly increased, suggesting the involvement of TAFRO syndrome. It needs further evidence of the treatment of TAFRO syndrome, and treatment related increased susceptibility to infection should be noted.

P1-151

A case of refractory TAFRO syndrome successfully treated with mycophenolate mofetil

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Conflict of interest: None

[Case] A 52-year-old woman presented edema, renal dysfunction and thrombocytopenia 1.3 years ago. She was diagnosed as TAFRO syndrome from the symptoms and the biopsy results and was treated with steroid pulse therapy followed by high dose prednisolone (PSL), tocilizumab (TCZ) which was switched to rituximab (RTX) later and calcineurin inhibitor (CNI). Two months ago, she developed epistaxis and subcutaneous bleeding after COVID-19 vaccination, and blood tests showed thrombocytopenia and elevated inflammatory markers. Although increased PSL (20 mg/day) temporally improved thrombocytopenia, her symptoms flared up with PSL reduction. She was admitted to our hospital because of exacerbation of the symptoms (elevated inflammation, thrombocytopenia, anasarca and renal dysfunction). Steroid pulse therapy followed by high dose PSL and CNI improved renal function and inflammation, but anasarca and thrombocytopenia were prolonged. Alternation to mycophenolate mofetil (MMF) from CNI improved the refractory syndromes. She was discharged and maintained with low dose PSL and MMF. [Conclusions] TAFRO syndrome is often resistant to immunosuppressive therapy like steroid with CNI, TCZ or RTX. To our knowledge, this is the first report to show the efficacy of MMF on refractory TAFRO syndrome.

P1-152

Relationship between ego state, disease activity, and ADL in rheumatoid arthritis patients: using egograms

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Conflict of interest: Yes

[Objective] Although there have been several reports on the personality patterns of RA patients and their habits and tendencies in thinking, feeling, and acting when interacting with others (ego state). In this study, we investigated the relationship between ego state and disease activity, and ADL in RA patients. [Methods] A total of 133 RA outpatients of Showa University Hospital and Showa University Northern Yokohama Hospital who agreed to participate in this study were included. Patient background included age, gender, DMARDs and PSL use, the SDAI, and the HAQ. The TEG-II was used to assess ego status; the TEG-II consists of pattern categories and types, and the associations with SDAI, HAQ, and gender were examined. [Results] The Egogram of the entire subject population showed that the adapted Child (AC) was the highest, and Critical Parent and Adult was the lowest. Pattern classification showed that the AC-dominant type was the most common (45 patients); no significant difference was found between HAQ remission or not; low and high disease activity; by gender. [Conclusions] The present study showed that AC was predominant, while NP was predominant in the egogram of RA patients. This may be due to the improvement of rheumatoid arthritis results and the decrease in disease activity.

P1-153

Comparison of 3-year progression free survival rate with and without adjuvant chemotherapy in cancer-bearing rheumatoid arthritis

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Conflict of interest: None

[Objective] To compare the 3-year progression free survival (PFS) rate with and without adjuvant chemotherapy in cancer-bearing rheumatoid arthritis (RA). [Methods] We retrospectively investigated the presence or absence of adjuvant chemotherapy and PFS in cancer-bearing RA patients who were outpatients at the rheumatology department of Tsugaru General Hospital. Indications for adjuvant chemotherapy were in accordance with the guidelines for the onset of each malignant tumors. [Results] Adjuvant chemotherapy was indicated for 26 patients out of 1179 RA, 27% male, age 71.5, HAQ 0.15, CDAI 4.2, breast cancer in 8, colon cancer in 7, gastric cancer in 5, rectal cancer in 3, lung cancer in 2 and ovarian cancer in 1. Eight patients (30.8%) did not undergo adjuvant chemotherapy, and the reasons were old age in 3 patients, unknown in 3 patients, poor PS in 1 patient, and pulmonary fibrosis in 1 patient. With or without adjuvant chemotherapy, 3-year PFS rate, 3-year overall survival rate, male, age, HAQ, CDAI were 92.3 vs 80.1% p=0.49, 100 vs 100%, 50 vs 17% p=0.1490, 68.5 vs 76.5 p=0.046, 0.1 vs 0.2 p=0.5259, 4.1 vs 6.3 p=0.5259 there were. [Conclusions] The 3-year progression-free survival rate after adjuvant chemotherapy in cancer-bearing RA patients was favorable.

P1-154

13 cases of other iatrogenic immunodeficiency-associated lymphoproliferative disorders (0IIA-LPD) in patients with rheumatic diseases: a retrospective single institutional study

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Conflict of interest: None

[Objective] To clarify the clinical characteristics and disease activity in rheumatoid arthritis (RA) patients with iatrogenic immunodeficiency-associated lymphoproliferative disorder (LPD) at our hospital [Methods] We retrospectively reviewed medical records of patients with biopsy-proven LPD >16 years old at our hospital from 2013 to 2021. Data were collected on clinical features, medications and disease activity of RA. [Results] 13 cases of LPD were identified. The median age at the onset of LPD was 68 years and 61.5% were women. All cases were treated with methotrexate (MTX) and 2 were with biologics. The most predominant pathological subtype was DLBCL (61%). After withdrawal of MTX and biologics, 4 cases were spontaneously regressed within a month. 7 cases (54%) received chemotherapy. One died with LPD and others achieved clinical remission (CR) of LPD. 3 cases (50%) were achieved steroid-free remission and 3 patients (50%) sustained CR or low disease activity with low dose glucocorticoid (GC) and immunomodulators. [Conclusion] The spontaneous regression rate of LPD at our hospital was similar to previous studies. Although prognosis of LPD may be not good, chemotherapy often declines disease activity of RA. In that case, we should try to taper or stop GC in order to adverse effect of GC.

P1-155

Pursuing suppression of methotrexate (MTX)-associated lymphoproliferative disease (LPD) by reducing the dose of MTX every other week in Japanese rheumatoid arthritis (RA) patients

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Conflict of interest: None

[Objective] MTX-LPD occurs frequently in elderly RA patients, and spontaneous regression is observed 2 weeks after stoppage of MTX. Thus, the biweekly use of MTX could reduce the probability of developing LPD. This study is to examine whether biweekly MTX can be effective for RA. [Methods] Of the RA patients being treated at our hospital, we investigated changes in RA activity in 12 patients who were taking biweekly MTX. [Results] 5 males, 7 females, mean age 76.8±3.3 years, mean disease duration 20.3±11.4 years. The biweekly dose of MTX was 4 mg in 11 patients and 6 mg in 1 patient. All patients changed from weekly use of the same dose or resumed administration of the same dose every other week after discontinuing every week MTX. The dose was later reduced to 2 mg in 1 case and increased to 6 mg in 1 case. Changes in RA disease activity flared in one case and was changed to weekly dosing, but there was no worsening in seven evaluable cases. One patient was stable on 4 mg of biweekly MTX, and relapsed when MTX was stopped. Two patients relapsed after completing weekly MTX of 4 mg, and achieved low disease activity after resuming administration of biweekly administration. [Conclusions] Elderly patients may have decreased metabolism, suggesting that biweekly use of MTX may be effective.

P1-156

Clinical features and treatment results of the rheumatoid arthritis patients with MTX-associated lymphoproliferative disease in Ehime university hospital

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA) patients, MTX-LPD is a rare disease, but it has recently increased. We aim to analyze the clinical features of MTX-LPD in our hospital. [Methods] We analyzed 21 patients with MTX-LPD from December 2009 to January 2022, and they are patients currently undergoing treatment for RA at our department. [Result] 21 patients (8 males, 13 females) were between 36- and 79-year-old (mean 66). The median time to onset of LPD from RA diagnosis was 123 months, the average MTX dose was 9.5 mg/week, and biologic agents were used in 5 cases. Hodgkin's lymphoma and diffuse large B-cell lymphoma were pathologically diagnosed in 8 cases each. About half of the cases resolved after discontinuing MTX, but the other cases required rituximab-containing chemotherapy. Treatment of RA after diagnosis of MTX-LPD required steroids, csDMARDs, and biologics alone or in combination in most cases. There were no cases of LPD recurrence, and RA was also maintained

with low disease activity in half of the cases, but there were cases in which treatment of RA was difficult due to other complications. [Discussion] MTX-LPD is a disease that affects prognosis, and early diagnosis and appropriate treatment are required. We report clinical features and treatment results in our hospital.

P1-157

Two cases of elderly rheumatoid arthritis combined with steroid resistant rheumatic pleurisy treated with tocilizumab

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Conflict of interest: None

Case 1 75-year-old male. Clinical course: In X-17 diagnosed with rheumatoid arthritis (RA) at another hospital. Salazosulfapyridine (SASP) was administered and the controls were good. In January of X year, pleural effusion retention appeared and was hospitalized. Rheumatic pleurisy was diagnosed, and large-scale steroids treatment was performed, but the effect was insufficient. When tocilizumab (TCZ) administration was started in October, it was noticeably pleural effusion and steroid weight loss was possible and discharge from the hospital. Currently continuing treatment with PSL5 mg and TCZ there is no relapse of pleural effusion. Case 2 87-year-old female Clinical course: X-50 years RA was diagnosed and treated. X-5 bilateral pleural effusion retention appearance. PSL treatment was started for the rheumatic pleurisy. In January X-1 she developed a gastrostomy. I was gradually decreasing steroids and controlled at 5 ~ 10 mg, but in March X the fever and the high inflammatory response were prolonged and pleural effusion increased. Balicitinib administration ineffective. When TCZ subcutaneous injection was started, pleural effusion gradually decreased. : Two rare cases of TCZ significantly effective in steroid-resistant rheumatic pleurisy patients were experienced.

P1-158

Effect of the magnetic medical plasters for leg cramps in the patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] I research into leg cramps in the patients with rheumatoid arthritis and the effect of the magnetic medical plasters for their leg cramps. [Methods] 266 patients with rheumatoid arthritis (mean age 67.1 y.o. male 65 female 201) were examined about their leg cramps, from June through August in 2022. When their leg clamps happened, the magnetic medical plasters were recommended to the patients. [Results] 48 patients (18.0%) have experienced leg cramps frequently. The frequency of leg cramps did not have a difference between men and women, and the use or nonuse of glucocorticoid. 18 patients applied the magnet medical plasters in times of leg cramps. Of those who tried the magnetic medical plasters, eleven patients were very effective, six patients were effective and one patient was ineffective. About the adverse effect, one patient appealed for itching. [Conclusions] 18% of the patients with rheumatoid arthritis have frequent leg cramps. The magnetic medical plasters were effective for their leg cramps.

P1-159

Sarilumab for the treatment of rheumatoid arthritis associated with lymphoproliferative disorder

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Conflict of interest: Yes

Although lymphoproliferative disorders (LPD) associated with rheumatoid arthritis (RA) sometimes shows spontaneous regression after the discontinuation of methotrexate (MTX), the treatment of RA after LPD is a matter of concern. We present a case of successful treatment of RA flares in a patient after LPD using tocilizumab and sarilumab. A senior male patient with RA, who had been treated with MTX for 5 years, was referred to our hospital for a pharyngeal mass. He was diagnosed with diffuse large B-cell lymphoma (DLBCL) by a histological examination. The lymphoma regressed in a month after the discontinuation of MTX, but at the same time, RA rapidly worsened (DAS28CRP 7.02). Treatment with tocilizumab and iguratimod induced remission in 6 months, but RA flared after a respiratory infection 2 years later. He showed severe arthritis of the knees and a ruptured Baker's cyst in his left knee (CDAI 18.7). We started sarilumab 150 mg sc every 2 weeks, and his RA gradually subsided. CDAI was 7.7 after 1 year and 2.5 after 2 years. His RA and LPD remained in remission, thereafter, suggesting a beneficial role of sarilumab in patients with RA after LPD.

P1-160

A case of Intravascular Large B-cell Limphoma in a Patient during administration of MTX and bDMARDs

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Conflict of interest: None

[Case Report] A 73-year-old man who was diagnosed with rheumatoid arthritis 14 years ago had been treated with MTX, MZR, SASP, BUC and PSL. Low disease activity had been achieved after he started to be treated with ADA and discontinued taking drugs without MTX. He was admitted to our hospital due to complaining of fever and loss of appetite for a week. We stopped administration of MTX and ADA, because pancytopenia as a complication of MTX and infection were suspected based on anemia, thrombocytopenia and elevated levels of serum CRP. Although obvious lymphadenopathy was not detected by whole-body CT, intravascular lymphoma was suspected due to high levels of sIL-2R. Bone marrow biopsy and random skin biopsy were performed, which detected CD20 positive atypical lymphoid cells within both the bone marrow and the small blood vessels in the subcutaneous tissue, so that we diagnosed MTX-associated intravascular large B-cell lymphoma. The symptoms were disappeared spontaneously on or about the 28th hospital day after complicated by DIC and HLH, and so the lymphoma went into remission. [Conclusion] We think that tissue biopsy including random skin biopsy should be performed, in the case of a patient during administration of MTX has high levels of sIL-2R without lymphadenopathy.

P1-161

Change in locomotive degree, frailty, and sarcopenia by total knee arthroplasty

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Conflict of interest: None

Knee osteoarthritis is associated with locomotive syndrome. The purpose of this study is to investigate changes in locomotive syndrome, frailty, and sarcopenia after total knee arthroplasty (TKA). [Method] TKA was performed from July 2020 to May 2021, and patients who were tested for locomotive syndrome, frailty, and sarcopenia. [Results] Subjects were 70 patients (16 males, 54 females, average age 74.9±8.5 years). Preoperative locomo degree was 0: 0 cases, 1: 3 cases, 2: 8 cases, 3: 59 cases, 17 in grade3 improved to grade2, and 5 improved to grade 1 postoperatively. Locomo degree changes significant improvement of 2.46±0.66 ($p=0.018$). Preoperative frailty: no-frailty: 8, pre-frailty: 36, frailty: 24. two pre-frailty improved postoperatively in the no-frailty. Preoperative Sarcopenia: no-sarcopenia: 65, sarcopenia: 3, severe: 1. Sarcopenia and frailty did not change significantly. [Discussion] TKA patients had a preoperative locomotive index of 3 (83%), and the incidence of pre-frailty and frailty was high at 88%, but sarcopenia patients were few (5%). Significant improvement was only in locomotive syndrome, which most reflected post-TKA. [Conclusion] The degree of locomotive syndrome is considered to be useful for estimating the situation after TKA.

P1-162

A case of yellow nail syndrome associated with elderly onset rheumatoid arthritis

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Conflict of interest: None

An 83-year-old female visited our hospital for polyarthritis persisted 2 months. She also had asthma, chronic sinusitis, bronchiectasis, and chronic bronchitis. She was diagnosed with organizing pneumonia five years before visitation, and was treated with prednisolone (PSL) 30 mg/day. PSL was tapered and maintained with 5 mg/day for asthma. Two years before the visitation, benralizumab was initiated to reduce PSL since bilateral pitting edema appeared and bronchitis repeatedly occurred. PSL was tapered off 4 months before the visitation, but bilateral edema remained. On physical examination, multiple thickened and yellowish nails were observed with polyarthritis. Chest CT revealed bilateral pleural effusions, and MRI showed synovial effusions in the wrist joints with erosions of the carpal bones. The diagnosis of rheumatoid arthritis (RA) was made based on polyarthritis and MRI findings, and yellow nail syndrome (YNS) based on nail findings, lung involvements, edema in bilateral legs. Salazosulfapyridine 1 g/day was initiated, which ameliorated her arthritis. Her yellow nails also improved, while the edema and pleural effusion did not. If edema and pleural effusion are observed in RA, the nail findings should be confirmed considering the possibility of YNS.

P1-163

A summary of six cases with invasive pulmonary aspergillosis (IPA) that occurred during immunosuppressive treatment in rheumatic diseases

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Conflict of interest: None

[Objective] To review our cases with invasive pulmonary aspergillosis (IPA) that occurred during treatment of rheumatic diseases and to clarify clinical picture of IPA in patients with rheumatic diseases by adding to literature references. [Methods] We conducted a review of our six cases with IPA that occurred during treatment of rheumatic diseases. [Results] Five cases of them were coincident with probable IPA, and one with possible IPA according to EORTC/MSG criteria. Nodular lesions in chest CT findings were observed in five cases of them, while a pulmonary consolidation was in only one case. Cases were consisted of two patients with dermatomyositis, two with ANCA-associated vasculitis, one with polyarteritis nodosa and one with rheumatoid arthritis-associated interstitial lung disease. All cases had some pulmonary complications and had received high dose of glucocorticoids until IPA developed in them. Tapering glucocorticoids as well as administration of VRCZ leaded to clinically significant improvements in all cases. [Conclusions] In the diagnosis of IPA, host factors, chest CT findings, mycological examinations, and ruling out other diseases play very important roles. After the diagnosis, prompt administration of VRCZ and tapering glucocorticoids would be effective.

P1-164

Actual clinical practice of cytomegalovirus infection in our department and verification of its detection method

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Conflict of interest: None

[Objective] To evaluate the clinical usefulness of cytomegalovirus (CMV) antigenemia assay (HRP-C7) and blood CMV DNA polymerase chain reaction (PCR) in patients with collagen tissue disease (CTD), and to assess the incidence of cytomegalovirus infection in our patients. [Methods] Medical records of the hospitalized patients who were treated in our department from February 2021 to July 2022 were reviewed retrospectively. Among the patients, those who received the blood tests of HRP-C7 and CMV DNA PCR were enrolled. The results and the related clinical data were analyzed. [Results] A total of 416 patients are enrolled in this study. The median age was 65 years, and the male-female ratio was 1: 2.5. While the results of the HRP-C7 were highly correlated with that of the PCR, the results of PCR relatively deviated from those of the HRP-C7 when the number of positive cells in the HRP-C7 was small. In cases requiring treatment, the PCR showed positive followed by the HRP-C7. After the treatment, when the HRP-C7 was confirmed negative twice, the result of the PCR also tended to turn negative. [Conclusions] In clinical practice of CTD, the PCR may be useful for early detection, and the HRP-C7 may be useful for assessing therapeutic effects in CMV infection.

P1-165

A case of rheumatoid arthritis (RA) with acute respiratory distress syndrome (ARDS) secondary to non-HIV pneumocystis pneumonia (PCP) successfully treated with tocilizumab (TCZ)

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Conflict of interest: None

[Background] Non-HIV PCP is severe due to ARDS pathology in relation to cytokine storm and known with a high mortality rate. We have experienced the benefit of TCZ treatment for ARDS associated with COVID-19. [Case] A 73-year-old woman was diagnosed with RA and methotrexate (MTX) 8 mg/week with prednisolone (PSL) 5 mg/day was initiated. Two months later she became aware of dyspnea. Chest-CT revealed bilateral diffuse ground-glass attenuation, β-D glucan was elevated, and positive *P. jirovecii* DNA lead to PCP diagnosis. Sulfamethoxazole trimethoprim12 tablets/day and methylprednisolone pulse therapy (IVMP) were initiated. However, hypoxia progressed and noninvasive positive pressure ventilation in supine position therapy was started on day 8, and a total of 3 IVMP cycles were performed, but oxygenation improvement and negativity of CRP was not observed. After confirming negative β-D glucan and increased serum IL-6, TCZ 400 mg was additionally administered. Oxygenation improved rapidly, and the patient was weaned off high-flow nasal cannula oxygen therapy on day 33. [Conclusion] This is a case of RA with ARDS associated with non-HIV PCP refractory to IVMP, and the patient was successfully treated with TCZ, suggesting the potential of TCZ in lung injury associated with non-HIV PCP.

P1-166

Evaluation of factors affecting SARS-CoV-2 antibody titers after BNT162b mRNA vaccination in patients with rheumatoid arthritis: A single-center, observational study in Japan

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Conflict of interest: None

***Objective*:** To investigate the factors affecting SARS-CoV-2 antibody titers after BNT162b mRNA vaccination. ***Methods*:** In this study, using the ADVIA Centaur SARS-CoV-2 immunoglobulin G (IgG) assay, SARS-CoV-2 antibody titers were measured at least 2 weeks after the administration of two doses of the BNT162b mRNA vaccine. ***Patients*:** We enrolled 593 patients with RA between April and October 2021. ***Results*:** Among patients with RA, compared with the antibody-positive group (n=511), the antibody-negative group (n=82) was older; had longer disease duration; shorter height; and higher Steinbrocker stage and class, patient visual analog scale score, disease activity, and use rate of prednisolone (PSL), Biologics/Janus kinase (JAK) inhibitors, and non-steroidal anti-inflammatory drugs ($p<0.05$). In the multivariate analysis, age over 65 years and use of Biologics/JAK inhibitors and PSL were factors that suppressed antibody elevation. ***Conclusion*:** SARS-CoV-2 IgG titers may be low in patients

with RA aged over 65 years and in those treated with Biologics/JAK inhibitors or PSL.

P1-167

A case of miliary tuberculosis that developed during treatment for rheumatoid arthritis and for which liver MRI imaging was useful for diagnosis

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Conflict of interest: None

A 74-year-old man with rheumatoid arthritis who was in remission with methotorexate (MTX) and addalimumab (ADA) was admitted to the hospital for fever. We considered the possibility of MTX-LPD or infection as the cause of the fever, and discontinued MTX and ADA, and treated him with antibacterial medication, but he did not improve. He had a positive T-SPOT, which had been negative before treatment for rheumatoid arthritis. Cultures of sputum, urine, gastric juice, blood, and bone marrow were performed, but no bacteria were detected in any of them. CT showed slight granular findings in hepatic portal region. Because of these imaging findings, he had an MRI of the liver. MRI showed numerous ill-defined nodular signal elevations on DWI and T2WI in the liver and spleen. Liver biopsy revealed the formation of small epithelial granuloma and the diagnosis of miliary tuberculosis was made. He started taking antitubercular drugs and fever quickly resolved. Discussion. Although tuberculosis was strongly suspected by the positive T-SPOT result, it often takes time to obtain the results of antimicrobial cultures. But tests other than cultures, such as MRI of the liver imaging in this case, may be effective in determining the initiation of treatment.

P1-168

Primary cytomegalovirus infection in adult patients mimicking relapse of adult-onset Still's disease

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Conflict of interest: None

[Background] Relapse occurred in approximately 40% of adult-onset Still's disease (AOSD). In Japan, primary acute cytomegalovirus (CMV) infection has recently been increasing. Here, we reported a case of primary CMV in an adult patient with a history of AOSD. [Case] 50-year-old man. 8 years before the admission, he was diagnosed with AOSD and was treated with prednisolone. 2 years later, prednisolone was discontinued. He had been in good condition with no therapy for 4 years. 2 weeks before the admission, he had a sore throat and fever. Laboratory tests revealed liver dysfunction and increased serum ferritin levels. He was admitted to our hospital under the suspicion of a flare of AOSD. In the hematological examination, lymphocytosis with an increase in atypical lymphocytes (mainly CD8 + cells) was found. Additionally, anti-CMV IgM was positive, anti-CMV IgG was negative, and CMV antigen was detected in WBC. He was diagnosed with primary CMV infection. He was given acetaminophen alone, his symptom improved, and he is in good condition without any medications. [Conclusions] In Japan, most primary CMV infections occur in infancy without symptoms. However, primary CMV infection should be considered even in middle-aged patients with fever and liver dysfunction.

P1-169

Case Report: 4 cases of COVID-19 with rheumatoid arthritis showing various prognosis

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Conflict of interest: None

Case 1: A 75-year-old female treated by SASP, diagnoses as COVID-19 in screening test, while she had no symptoms. She was commenced sotrovimab, but kept asymptomatic and discharged. Case 2: A 67-year-old male treated by SASP, MTX and PSL. He was admitted for dyspnea. CT scan showed the appearance of COVID-19 pneumonia and was commenced remdesivir (RDV) and dexamethasone (DEX). He improved and was discharged. Case 3: A 87-year-old male treated by abatacept, SASP, iguratimod and PSL. While he was hospitalized due to head trauma and bacterial pneumonia, was infected with COVID-19. He was commenced molnupiravir but the pneumonia deteriorated, and he was initiated on RDV. His symptoms got improved and discharged. Case 4: A 87-year-old female treated by PSL and SASP. While she was hospitalized due to bacterial pneumonia, was infected with COVID-19. She was commenced sotrovimab, but her pneumonia deteriorated, and she was initiated on RDV and DEX. Initially her symptoms got improved and started tapering steroids. But her pneumonia relapsed afterwards. She succumbed after 27 days from admission. Clinical significance: The number of case series about COVID-19 patients with RA is still small, and their clinical course remain unclear. We will report 4 cases that followed various courses.

P1-170

A case of clostridium difficile colitis-associated reactive arthritis after total knee arthroplasty

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Conflict of interest: None

A 77 -year-old woman who was performed total knee arthroplasty one month ago elevated inflammation data (CRP 2.47 mg/dL). She was diagnosed to surgical site infection of total knee arthroplasty (TKA) joint and treated with cefalexin. A few days later, she had watery diarrhea and the antibiotics treated for 34 days were withdrawn. Clostridium difficile (CD) stool antigen assay and stool culture were positive, but toxin was not detected. She was not diagnosed CD colitis and was not treated with antibiotics against CD. One week later, she suffered from both lower extremities and ankle joints swelling and her inflammation data become exacerbated (CRP 15.5 mg/dL). She was diagnosed with CD colitis-associated reactive arthritis (ReA). After treatment with metronidazole for 10 days, her symptoms improved immediately. ReA is an inflammatory syndrome that can result from certain gastrointestinal or genitourinary infections. CD is a "possible cause" of ReA, with approximately 40 cases (Infect Dis Clin North Am 20: 827-847, 2006. Clin Rheumatol 27: 253-355, 2008.). Here we report a interesting case of CD colitis-associated ReA after TKA.

P1-171

A case of HTLV-1-associated arthropathy (HAAP) with treatment-resistant PMR-like symptoms

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Conflict of interest: None

[Case] 75-year-old woman with positive anti-HTLV-1 antibody. She had been suffering from recurrent fever and polyarthralgia since January. She was admitted to our hematology department in July due to drug-induced pancytopenia. On admission, there was no atypical cell in the peripheral blood. However, after her blood cell counts recovered, flower cells began to appear in peripheral blood, and the patient was diagnosed with adult T-cell leukemia-lymphoma (ATL) smoldering type. In September, fever and polyarthralgia emerged again. PET-CT scan showed FDG concentrations in polyarticular, lumbar spinous process, sciatic tuberosity, and greater trochanter. RF and anti-CCP antibody were negative. Ultrasonography revealed long heads of biceps brachii tendonitis bilaterally. 15 mg of prednisolone (PSL) was started for her polymyalgia rheumatica (PMR)-like symptom, but it did not improve. PSL was increased to 25 mg/day, but the pain and inflammation remained. A diagnosis of HTLV-1-associated arthropathy (HAAP) was made. Tocilizumab would be the treatment option with careful follow-up for ATL. [Discussion] HAAP is char-

acterized by poor response to glucocorticoids, as in this case, and is often refractory to treatment. We report this case with a literature review.

P1-172

Non-bacterial vertebral osteitis as the first manifestation of pustulotic arthro-osteitis

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Conflict of interest: None

Pustulotic arthro-osteitis (PAO) is an osteoarticular comorbidity of palmoplantar pustulosis (PPP), a chronic, recurrent, inflammatory skin disease presenting with erythema, scales, and pustules on the palms and soles. PPP is one of the most common skin diseases in Japan and is accompanied by PAO in 10-30% of patients. PAO often involves anterior chest wall lesions, and vertebral involvement is uncommon. The present report describes a case of PAO in which the initial manifestation was only non-bacterial vertebral osteitis, with palmoplantar pustulosis developing eight months after its onset. To the best of our knowledge, there is no previously reported case of PAO in which the patient presented with only vertebral osteitis. A patient with vertebral osteitis of unknown etiology should be followed up and examined periodically for skin problems which may provide a clue to the presence of PAO.

P1-173

Efficacy of rupatadine for eosinophilia in 12 patients

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Conflict of interest: None

[Objective] Rupatadine is a second-generation antihistamine with anti-PAF (platelet activating factor) effect. It has been reported that rupatadine with anti-PAF effect significantly reduces eosinophils. We investigated the eosinophilic effect of rupatadine in patients treated in our department. [Methods] We compared the eosinophil counts before and after the administration of rupatadine in 12 patients with eosinophilia (>500/μl) before rupatadine administration and who received rupatadine for allergic rhinitis or other reasons. [Results] Patients in this study consist of 8 female patients and 4 male patient, and the main target diseases during treatment in our department were 4 cases of EGPA, 2 cases of eosinophilic angioedema, 1 case of eosinophilic fasciitis, 1 case of Kimura's disease, 1 case of Hypereosinophilic syndromes, 1 case of SLE, 1 case of scleroderma, 1 case of IgG4 related disease in 1 case. The median eosinophil count before rupatadine administration was 891.15 [676-1766], and the median eosinophil count after administration was 869.55 [530-1459], the median eosinophil count decreased significantly (p=0.01). [Conclusions] We confirmed that additional rupatadine administration decreased eosinophils.

P1-174

A case of rheumatoid arthritis with repeated cellulitis and left shoulder pain considered associated with infection

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Conflict of interest: None

A 69-year-old man with rheumatoid arthritis and diabetes mellitus got an episode of left shoulder pain. One week later, he visited to our hospital because of right foot pain, resulting in disturbance of walking. He was diagnosed with cellulitis on foot. Staphylococcus aureus was also detected in blood culture. The treatment with antibiotics brought into recovery from his cellulitis and sepsis. Two months later, he was again admitted to our hospital due to right foot pain and difficulty in walking. He also got exacerbation of left shoulder pain. MRI of left shoulder revealed lesions of head of left humerus and glenoid cavity with low signal in T1 weighted image and high signal in T2 weighted image. Cellulitis and left shoulder pain were getting better after administration with antibiotics. Since his left shoulder pain might be associated with infection, needle biopsy of shoulder was done. Although bacterial culture of the biopsy sample showed negative result, the sample contained no synovial tissue, but showed infiltration of neutrophils. These results indicated an association with infection on his shoulder. We, therefore, decided the administration with antibiotics for longer time. He had no episode of exacervation of shoulder pain since then.

P1-175

Three cases of SLE after COVID19 vaccination

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Conflict of interest: None

We report three cases of systemic lupus erythematosus (SLE) after vaccination with SARS-CoV-2 vaccine. Case 1: A 15-year-old woman developed fever, malaise, arthralgia, malar rash 4 weeks after receiving 3 doses of vaccine. Lymphocytopenia, hyper IgGemia, hypocomplementemia, positive anti-nuclear antibody 1:2560 (Speckled type), positive anti-DNA antibody, positive anti-SSA antibody, positive anti-Sm antibody, positive anti-U1RNP antibody, and multiple enlarged lymph nodes on CT imaging were observed, and a diagnosis of SLE was made. Prednisolone (PSL) 40 mg/day was started for fever and arthritis, and her symptoms improved. Case 2: A 19-year-old woman had arthritis, malar rash, cervical lymphadenitis, lymphopenia, hyper IgGemia, positive antinuclear antibody 1: 5120 (Speckled type), and positive anti-DNA antibody, and a diagnosis of SLE was made. She was started on PSL 30 mg/day and her symptoms improved. Case 3: 27-year-old woman developed low-grade fever, malaise, arthralgia 6 weeks after with 3 doses of vaccine. She was diagnosed with SLE based on malar rash, hyper IgGemia, anti-nuclear antibody 1: 640 (Speckled, Nucleolar type), positive anti-DNA antibody. She was started on Mizoribine 100 mg/day and NSAIDs, but the treatment was not effective.

P1-176

Idiopathic multicentric Castleman disease complicated by diffuse panbronchiolitis and that required differentiation from IgG4-related diseases

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Conflict of interest: None

The patient was an 81-year-old man who had been diagnosed with diffuse panbronchiolitis around X-22. In October X-12, his IgG level increased to 4921 mg/dl, which was thought to be associated with diffuse panbronchiolitis. In July X-3, a blood sample showed increase levels of IgG (7988 mg/dl) and IgG4 (1050 mg/dl), increased CRP, deterioration of the kidney function, and progression of anemia. Furthermore, CT showed multiple enlarged lymph nodes in the mediastinum and enlarged bilateral axillary lymph nodes. In December X-3, mediastinal lymph node biopsy was performed by EUS-FNA, however, although increased plasma cells were observed, IgG4-related diseases could not be diagnosed, and samples were considered insufficient for the diagnosis of Castleman disease. In May X, Multicentric Castleman disease (plasma cell type) was diagnosed based on a biopsy of the right axillary lymph node. Prednisolone was started in July X. Thereafter, the patient's IgG and CRP levels decreased and his renal function and anemia improved. Multicentric Castleman disease is sometimes difficult to distinguish from IgG4-related diseases. Furthermore, this patient had diffuse panbronchiolitis, and multicentric Castleman

disease took more than 10 years to diagnose.

P1-177

The reality of the medical cooperation of Collagenosis care in the Eastern Hokkaido areaThrough a case of the dermatomyositis, scleroderma overlap syndrome having various complications

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Conflict of interest: None

[Clinical Significance] We examine the establishment of the regional medicine cooperation system for collagenosis that often has various organ lesions. [A case] 59 years old women. In X-2 year, she was found for skin hardening of dorsum manus, Gottron sign, the heliotrope eruption, but no rise of CPK in labo data. At this chance we detected the polycystic kidney disease by CT scan and became the follow start with kidney medicine. In X year, she detected acute aggravation of the interstitial pneumonia and became this hospital internal medicine hospitalization. For interstitial pneumonia, she received steroid-pulse therapy, IVCY. Acute aggravation of heart failure, renal failure was detected and it was hospital transfer in K hospital heart blood vessel medicine and was under the medical treatment with a diuretic and she was improved and have been changed hospitals again. The condition of interstitial pneumonia, heart failure, renal failure preserved a lull, but plural refractory disease were complicated with her, and multidisciplinary medical care was in a necessary condition, and it was hospital transfer to H University hospital in S City which was a cooperation institution. We examined regional medicine cooperation of multicenter and multiarea in East Hokkaido area through this case.

P1-178

A case of chronic thyroiditis requiring differentiation from polymyositis/dermatomyositis

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Conflict of interest: None

A 52-year-old man had coarse and ichy skin. In March X, he was diagnosed as atopic dermatitis and treated with topical steroids, but his condition got worse. In October X, he was admitted to the orthopedic surgery for a right ankle fracture. Even after the fracture was healed, his generalized muscle weakness and high levels of myogenic enzymes went on. So he was suspected of having polymyositis/dermatomyositis, and visited our hospital. Desquamation with hyperpigmentation was found on the eyelids and trunk, MP, PIP of the hands. Blood tests showed markedly increased CK 5261 U/L, elevated AST 121 U/L, ALT 113 U/L, LDH 633 U/L, but CRP was 0.24 mg/dL, FT3 <0.67 pg/ml, FT4 0.05 ng/μL, TSH 107.59 μIU, namely thyroid function decreased. Thighs MR showed diffuse T2 STIR high-signal areas in the bilateral hamstrings, consistent with myositis, but negative for ANA and myositis-specific antibodies. The skin biopsy revealed spongiform dermatitis with mucinosis. So we diagnosed him Hoffmann syndrome due to chronic thyroiditis. We treated him with Levothyroxine, his symptoms gradually improved and myogenic enzymes were normalized. Hypothyroidism is also one of the causes of muscle weakness with high CK, but the differential diagnosis was very difficult because of his abnormally high CK and skin symptom.

P1-179

Polypharmacy-induced cytopenia in a scleroderma patient triggered by mild infection or heart failure

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Conflict of interest: None

A 77-year-old woman was diagnosed with scleroderma at another hospital at the age of 75 years due to swelling of her fingers and Raynaud's symptoms, and was referred to our hospital after starting treatment. She was also positive for anti RNA polymerase III antibody and interstitial pneumonia, and was treated with multiple medicines mainly for skin hardening and finger ulcer. Sildenafil was started due to fatigue and elevated TRPG. 3 days later, she was admitted to the hospital for fever. Blood tests showed WBC 800/μL, Plt 125,000/μL, and slightly elevated CRP levels. CT showed atelectasis, pleural effusion, and increased cardiac enlargement. Although exacerbation of heart failure and mild infection were present, leukopenia was suspected to be a side effect of the medicine. The newly initiated sildenafil did not list this side effect. Blood counts improved with symptomatic treatment by reducing or discontinuing most drugs. In this case, we focused on CYP3A4 and actively reduced the dosage of the drug that is the substrate of CYP3A4, and the patient showed improvement. We report this case with some discussion, as it is considered important to be aware of the increasing use of multiple medicines in combination with the development of various therapeutic agents.

P1-180

Challenges of collaboration between specialists and non-specialists in the transition of treatment to home care and the role of medical social worker (MSW)

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Conflict of interest: None

[Objective] Elderly RA patients may have difficulty attending the hospital. When transitioning to home care, it is often difficult for non-specialists to continue Bio/JAKs treatment. We discuss the challenges of collaboration between specialists and non-specialists and the significance of MSW intervention. [Methods] They were asked about their experience with RA treatment, medication use, concerns at the time of acceptance, information needed at the time of collaboration, and expectations for referral after the establishment of a collaborative system. [Results] 90% of the patients had experience with RA treatment. Regarding drug therapy, 100% painkiller, 88.9% steroids, 77.8% DMARDs, 55.6% Bio, and 22.2% JAKs. 70% were concerned about side effects of Bio/JAKs. The information needed by 90% was "precautions for Bio, examination, and consultation with a specialist" (of the respondents), with an expected value of 7.4 points after the establishment of a collaborative system. [Conclusions] Information sharing about medications and tests is inadequate. Collaboration is based on clarifying roles and accurately communicating and sharing necessary information. This requires smooth communication, and MSWs can contribute to building a foundation for collaboration from a professional standpoint.

P1-181

Survey on nurses' opinions on rehabilitation-related education practiced by nurses for patients with rheumatoid arthritis - Differences of nurses' experiences depending on engage years in rheumatic care

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Conflict of interest: None

[Purpose] This study aimed to investigate the differences of patient education practiced by nurses depending on engage years in rheumatic care. [Method] Nurses engaged in rheumatic care were enrolled at nationwide. The survey contents were nurses' experiences on being asked by patients and educating patients regarding rehabilitation, necessity and feasibility regarding educating precautions in daily life. In accordance with the qualification requirements for The Certified Nurse by Japan Rheumatism Foundation, nurses below it were categorized non-fulfilled group. Nurses with more than 3 years of nursing career were classified into groups of over 1 year, over 6 years, over 11 years, and over 21 years, depending on engage years in rheumatic care. [Result] 274 nurses completed the questionnaire. The percentages of experiences being asked and educating were: [non] 62.5%/40.6%, [over 1] 57.1%/50.0%, [over 6] 75.4%/66.7%, [over 11] 90.7%/74.7%, [over 21] 96.2%/88.5%. The degree of necessity and feasibility were: [non] 9.06/6.42, [over 1] 8.80/5.99, [over 6] 9.21/6.64, [over 11] 9.53/8.18, [over 21] 9.60/7.69. [Conclusions] It was shown that nurses with less than 6 years of engage years in care had little experience of education, and they felt it more difficult to educate precautions in daily life.

P1-182

Rheumatic disease patients that bring what they want to say to the doctor in writing

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Conflict of interest: None

[Objective] It is not uncommon to hear complaints from patients in outpatient clinics, such as, "I remembered what I asked before I came to the hospital, but I forgot what I asked", or "I cannot explain well in front of the doctor". [Results] [Case 1] A 25-year-old woman who had worked at a convenience store since she was 18 years old. She was diagnosed with bipolar disorder and fibromyalgia (FM). At each outpatient visit, she brought a written report with illustrations of her progress up to that point and information about FM that she had researched on her own and handed it to the doctor. [Case 2] A 72-year-old woman with rheumatoid arthritis (RA). She was introduced to biologic agent, although her disease activity was well controlled, she complained of heat and pain in the skin after administration of the agent. She was concerned about how much she should tell her doctor about the side effects. She wrote down what she wanted to say and showed them to the nurse before the examination. [Conclusions] It is not easy to convey exactly what patients want to say in the special environment of being in front of a doctor and in the short time available for the examination. Therefore, writing down the main points in advance will enable communication among the doctor, the nurse and the patient.

P1-183

Survey on makeup use in RA patients

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Conflict of interest: None

[Objective] RA patients seem to be different from ordinary people because of deformities in fingers. Therefore, we conducted a questionnaire to investigate the makeup situation of RA patients. [Methods] A questionnaire survey was conducted on 102 RA patients (20's to 70's) and 102 women as a comparison group. The target group was classified according to [deformation and precision], group A [no deformation and fine work possible] 37 people, group B [deformation but not inconvenient for fine work] 31 people, group C [They were classified into 29 people with deformed fingers and wrists, and some difficulty in fine work], and 6 people in group D [severe deformation of fingers and wrists, considerable difficulty in fine work]. [Results] group D, it was difficult or somewhat difficult to apply make-up due to inconvenience. As for skin care, lotions and sunscreens were frequently used, and in group D, the rate of all-in-one type was the highest at 67%. Concerning makeup content, most of the women answered that they used eye makeup, while the majority of the subjects used foundation, painted eyebrows, and applied lipstick. [Conclusions] Physical changes caused by disease affect body image, and wearing makeup is thought to improve self-efficacy and QOL.

P1-184

A survey regarding the timing of preconception care for female rheumatoid arthritis patients of child bearing age

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Conflict of interest: None

[Objective] We studied the timing of preconception care (PCC) for female rheumatoid arthritis (RA) patients of child bearing age (WoCBA). [Methods] We received consent from 38 WoCBA RA patients at our clinic that were included in this study. [Results] 69% of these patients visited their gynecologist because they experienced gynecological diseases. They received cervical cancer screening (82%), breast cancer screening (58%), and had received an HPV vaccine (5%) and rubella vaccine (37%). At the time of RA diagnosis, 58% of patients were confirmed by their physicians to want to become pregnant, and 53% of patients were aware of their fertility and miscarriage rates. 55% of patients were unmarried and 57% had no desire to marry. The type of pregnancy of patients who had been pregnant was spontaneous (38%), planned (38%), or fertility treatment aided (25%), and the time between the desire to raise a child and conception was often 1-2 years (50%). 76% of patients who had never been pregnant (55%) wanted to become pregnant, with options for fertility treatment (69%). Most WoCBA RA patients wished they had received PCC at the time of their RA diagnosis (41%). [Conclusions] PCC in RA patients should be implemented in accordance with RA diagnosis, changes in RA therapy, and life events.

P1-185

Effects of Joint Ultrasound (US) on Patient Satisfaction and Physician Treatment

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Conflict of interest: None

[Objective] In this study, we investigated the patient's satisfaction after US, and investigated the changes in doctors' treatment after US. [Method] Of the 407 patients who underwent US, 274 who cooperated with the questionnaire were tabulated and investigated. [Result] 270 (98.5%) responded that they were satisfied with the US. The most common reason for being satisfied was "because I could understand the condition of the examination site" (222 people), followed by "because I could talk to the US practitioner" (185 people). As a result of investigating the change in treatment after US, 94 cases (41%) continued treatment, 70 cases (30.6%) intensified treatment, and 14 cases (6.1%) with dose or drug reduction. [Conclusion] It was shown that US gave sufficient satisfaction to patients, and that explanation during the procedure increased satisfaction. Physicians changed their treatment after US (approximately 40%), and there was some discrepancy between the treatment change predicted from clinical findings and the actual treatment change after US. US is useful when physicians consider treatment policy and is necessary to increase confidence in policy changes.

P1-186

Implementation of management the drug on perioperative patient with rheumatoid arthritis by nurses

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Conflict of interest: None

[Objective] We investigated nurses' implementation of drug management, including bDMARDs and tsDMARDs, for perioperative patients with rheumatoid arthritis (RA) [Methods] The subjects were nurses registered with the Japan Rheumatism Foundation and working at hospitals for RA care in the last 3 years. An online questionnaire on medication management and symptoms observation (2483 questionnaires) was distributed and 368 responses were received. The differences between nurses engaged in outpatient work (group O; OG) and those engaged in ward work (group W; WG) were compared. [Results] 165 subjects (75 in OG and 90 in WG) with valid responses were included in the analysis. The rate of nurses who observed their preoperative discontinuation of drugs was 96% in OG and 100% in WG. The rate of nurses who observed patients with diabetic or respiratory disease taking corticosteroids (CS) in OG was significantly lower than that in WG (69% vs 89%; 48% vs 78%; $p<0.05$). [Conclusions] Nurses were highly likely to identify the perioperative discontinuation of drugs in both the outpatient and ward-based groups. On the other hand, CS administration in patients with diabetes and respiratory complications was observed more frequently in the ward-based group.

P1-187

Challenges from a questionnaire on awareness of retinopathy in patients taking hydroxychloroquine (HCQ)

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Conflict of interest: None

[Objective] Early detection of retinopathy is important because it is believed that retinopathy progresses even after the drug is discontinued in patients who develop retinopathy while taking HCQ. This study sought to determine the extent to which patients on HCQ medications actually understand and practice the need for regular eye examinations and retinopathy, and to examine the guidance and support needed. [Methods] Questionnaires were sent to 17 patients taking the HCQ at our hospital. [Results] Thirty systemic lupus erythematosus (SLE) patients (We administered a questionnaire to 17 (mean age: 51 ± 13.1 years) who were taking HCQ, and received 16 responses. Thirteen patients (81%) responded that they regularly visit an ophthalmologist. 14 patients (87%) knew that retinopathy can occur while taking HCQ, and 5 patients (31%) knew what retinopathy looks like. [Discussion] This study revealed that the majority of our HCQ patients understood the risk of retinopathy from taking HCQ and visited their doctor regularly, while 20% of the patients did not visit their doctor regularly and lacked understanding of the symptoms of retinopathy. In addition to the current guidance, it is necessary to prevent and detect retinopathy through the use of unique tools and support programs.

P1-188

Safety and efficacy of monotherapy with biologic agents among patients with elderly onset rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate whether monotherapy of biologic (B-) DMARDs with intensive commitment by rheumatoid arthritis (RA) care nurses contributes to safer and more effective management among patients with elderly-onset RA (EORA). [Methods] From 2015, we retrospectively reviewed consecutive 43 EORA patients (≥65 year-old) received a single-agent treatment with B-DMARDs under examinations of health condition by RA care nurses. [Results] The mean age were 79 years. They had an average of 13 swollen joints. Mean HAQ and RAPID3 were 1.1 and 13.7, respectively. The comorbidities included cerebrovascular diseases (n = 11), HBV infection (n = 14), pulmonary diseases (n = 18), diabetes mellitus (n = 8), and dementia (n = 5). They were treated with abatacept (n = 24), etanercept (n = 8) or tocilizumab (n = 11). Of them, 34 received in-hospital administration of B-DMARDs. After the mean follow-up of 31 months, all the parameters were improved. The cumulative continuation rate was 80% and 75% at 2 and 3 years, respectively. No serious infections were observed. Two patients died from cardiac diseases. [Conclusions] Monotherapy of B-DMARDs seems effective and safe for EORA. It is considered that safety confirmation by RA care nurses contributed to 'no serious infections'.

P1-189

Survey of Patients with Rheumatoid Arthritis Using Subcutaneous Injectable Formulations of Biologic Agents-For the purpose of building a support program for patients with rheumatoid arthritis-

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Conflict of interest: None

[Objective] It is important to clarify the support program for patients so that the patient can self-manage while dealing with the disease. Currentry, Patients support programs have not been established, nurses individual's experience notice or individual support is done by the suit from patients. Therefore, in order to establish the support program, we conducted the fact-finding such as the changes, and the like of an image and the feeling for the self- management. [Methods] We conducted questionary survey to the patients who obtained an agreement. [Results] We obtained an answer from 109 patients. Confirmation is a required item, and, at the biological agents preparation induction, physical information, family constitution and support system status, the degree of the strength of the anxiety control advisability of the self- management. The procedure of the self-care became the confidence by repeating the number of times, and the anxiety was reduced, too. Regardless of the patient's medical history and treatment history, it is necessary to tell the remedial instructions from a medical person regularly. Also, we established the window which patients could talk about, and the need to support in the situation of patients in total was suggested.

P1-190

Results of Patient Satisfaction Survey of Clinical Path Admission for Induction of Biologic Agents for Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We have been conducting educational hospitalization as a clinical pathway when introducing biologic agents to patients with rheumatoid arthritis (RA). In this study, we investigate the influence of patient background on patient satisfaction with the path admission. [Methods] We evaluated the satisfaction of 12 RA patients (pass group) who were admitted to our department from April 2022 for pass hospitalization on a total of 20 items on a 80-point scale, and analyzed the association with patient background. [Results] The 10 patients who responded to the questionnaire were divided into an elderly group and a younger group to compare patient satisfaction. The elderly group tended to have lower average scores than the younger group. In addition, the satisfaction score of one patient who was admitted to the path hospital for a change of biologic agent was lower than the mean score. [Conclusions] Satisfaction with the overall clinical path admission is low in the elderly group and improvement should be considered.

P1-191

Analysis of pregnancy and delivery in patients with rheumatoid arthritis in the last decade

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Conflict of interest: None

[Objective] We retrospectively investigated pregnancy and delivery in patients with rheumatoid arthritis (RA) in the last decade. [Methods] This study included 11 women, with 15 pregnancies and 14 childbirths, from 2009 to 2018. We analyzed their age at pregnancy, disease duration, DAS-28CRP (4), medication, adverse event during pregnancy period. We divided 4 women into biologics (BIO) group (including biologics used before pregnancy) and non-BIO group (not using biologics). We analyzed by Student t-test as a statistical exam. [Results] their mean age at pregnancy was 32.5 years-old (27-39), mean disease duration of RA was 5 years (0.6-9). DAS28CRP (4) at pre-pregnancy and after delivery were 5.5±2.2 and 4.3±1.0 in total (p<0.01), 5.7±2.2 and 4.3±1.0 in BIO, 3.1±3.1 and 4.6±1.0 in non-BIO. There were 10 births at BIO group and 5 births at non-BIO group. After confirming the pregnancy, biologics had been stopped in all cases and prednisolone (PSL) have been administrated or kept for 8 of them in BIO group, csDMARDs had been stopped in 3 cases and they used PSL in 3 pregnancies. There were 3 premature births and 7 low birth weight infants. [Conclusions] During pregnancy period in the patients with RA, their disease activity had been worse in both BIO group and non-BIO group.

P1-192

A case of pregnancy complicated by SLE and APS in which preconception care was important

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Conflict of interest: None

[Case] 33-year-old, female, X-10 years, diagnosed with SLE and APS, X-3 years, became pregnant, but thrombocytopenia appeared at 14 weeks gestation, prednisolone (PSL) was increased and heparin was started, but miscarriage occurred at 16 weeks gestation. The placenta showed fibrinoid necrosis of the desmoid vessel wall and multiple infarcts, APS was suspected; 1 year later, SLE was remitted, pregnancy occurred, and heparin was started immediately. Preconception care was provided by obstetrics and gynecology and internal medicine. Fetal growth slowed from about 28 weeks, and at 32 weeks, the patient was diagnosed with fetal growth retardation and admitted to the obstetrics and gynecology department for management. There was no recurrence of the primary disease, but thrombocytopenia progressed, and a baby girl weighing 1609 g was delivered by cesarean section at 33 weeks and 3 days gestation. [Discussion] In this case, heparin intervention early in pregnancy was important. Antiphospholipid antibodies are known to cause placental damage, and it is important to recognize the condition and provide preconception care. [Conclusion] In pregnancies complicated by collagen disease, it is important to share an adequate preconception care and treatment plan during pregnancy.

P1-193

The prevalence and details of preconception counseling in women with systemic lupus erythematosus: a scoping review

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Conflict of interest: None

[Objective] Preconception counseling in women with systemic lupus erythematosus (SLE) is recommended as a part of preconception care. This study aimed to comprehensively summarize the prevalence and details of preconception counseling in women with SLE. [Methods] We conducted a scoping review using five literature databases. We used search terms related to “SLE”, “counseling” and “preconception care”. We summarized the prevalence and details of preconception counseling from included studies descriptively. [Results] A total of 1904 articles were identified, and 14 studies were included in the review. The median of participants in primary studies was 125.5. The range of the prevalence of preconception counseling was 32% to 95%. Eight studies reported those who counseled patients. In addition to rheumatologists, participants were counseled by doctors in other specialists, such as obstetricians and gynecologists, nephrologists and general physicians. Only one study reported details of preconception counseling in the article. [Conclusions] Most studies were conducted on as a small-scale with a large variation in the prevalence of preconception counseling. We found that various specialists contributed to preconception counseling; however, the details of counseling were rarely reported.

P1-194

Current and future issues of preconception care outpatient service at Tokyo Metropolitan Tama Medical Center

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Conflict of interest: None

[Objective] To investigate the current status of preconception care (PCC) outpatient service at our hospital. [Methods] Twenty-nine patients seen from November 2019 until October 2023 were examined for age, diagnoses, presence of autoantibodies, the organ affected, medications, purposes for the visit, and changes in understanding and feelings after the visit. [Results] The median age of the patients was 32. The diagnoses or positive autoantibodies included systemic lupus erythematosus in 15 patients, antiphospholipid antibodies in 10, anti-SS-A/Ro antibodies in 9, rheumatoid arthritis in 8. The affected organs were kidney in 6 patients, central and peripheral nerves in 2. Twenty-six patients wanted to know pregnancy course in patients with rheumatic diseases and 3 requested drug counseling. Sixteen patients reported improved understanding, and 13 reported unchanged understanding after the visit. Positive feelings toward pregnancy were increased in 13 patients, unchanged in 8, decreased in 8 after the visit. [Conclusions] While the PCC outpatient service has the potential to improve patients’ understanding of pregnancy-related issues, there may be a need to consider continued services in terms of better understanding and feelings in patients.

P2-001

Analysis of the clinical variables associated with negative discordance, in which patients with RA rate the global assessment of disease activity (PGA) lower than their attending physician’s (PhGA), based on NinJa 2014 and 2018

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Conflict of interest: None

[Objective] We previously reported that positive discordance (PosD), i.e. PGA>PhGA by 3 on 10-cm VAS, was associated with age, pain and functional impairment (Int J Rheum Dis 2018). The purpose of this study is to analyze the clinical significance of negative discordance (NegD, PGA<PhGA). [Methods] To analyze the clinical variables associated with NegD, we examined the data of 13,945 RA patients registered in *NinJa* 2014 whose joint counts were available. We analyzed the radiographic progression in RA patients registered in both *NinJa* 2014 and 2018. [Results] The proportion of RA patients classified into PosD, concordance, and NegD was 14.7%, 84.5%, 0.8%, respectively. There were no significant differences in age or disease duration among the three groups, but the prevalence of male patients was significantly high (19.9%, 16.5%, and 28.8%, respectively). The levels of TJC, SJC, and DAS28 were high in NegD group, while those of PGA, pain, and mHAQ were low. The proportion of patients with progression of radiographic stage in the period from *Ninja* 2014 to *Ninja* 2018 was significantly higher in the NegD group (33.3%). [Conclusions] NegD was shown to be associated with progression of joint destruction. Therefore, we should pay attention to this rare but important discordance status.

P2-002

Comparative Study of Elderly-onset Rheumatoid Arthritis Patients and Younger-onset Rheumatoid Arthritis Patients by Age Group of Onset in ACPA-positive Cases

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Conflict of interest: None

[Objective] Among rheumatoid arthritis (RA) patients, the proportion of elderly-onset RA (EORA) patients is increasing. In this study, we investigated the characteristics of ACPA-positive elderly patients with EORA by comparing their age of onset with that of patients with juvenile onset rheumatoid arthritis (YORA). [Methods] We included 467 elderly patients (EORA: 67.5%, YORA: 32.5%) out of 711 ACPA-positive RA patients treated at our hospital from January to December 2021. Age at onset was divided into 6 groups. Age, disease duration, ACPA, RF, disease activity, inflammatory response, and KL-6 were compared in each age group. [Results] The EORA group was older, had shorter disease duration, and higher ACPA than the YORA group. The complication rates of respiratory disease and hypertension were higher in the EORA group than in the YORA group, but the rate of patients with a history of orthopedic surgery was higher in the YORA group, which had a longer disease duration, and there was little difference in disease activity. [Conclusions] In the present study, ACPA, a risk factor for poor prognosis and interstitial pneumonia, was higher in the ACPA-positive EORA group than in the YORA group, but disease activity did not differ significantly by treatment.

P2-003

Comparison of Elderly-Onset Rheumatoid Arthritis Patients and Younger-Onset Rheumatoid Arthritis Patients: Five-Year Course of 219 ACPA-Positive Older-Onset Rheumatoid Arthritis Patients at our Hospital

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Keiyu Orthopedic Hospital

Conflict of interest: None

[Objective] In this study, we compared the age stratification of EORA and YORA in elderly RA patients who had been continuously observed for 5 years. [Subjects] The 219 elderly RA patients who had been followed up for 5 years since January 2016 were divided into 3 groups. The results of the study were compared with the results of the EORA and YORA studies over a 5-year period. [Results] The median values of DSA28ESR and RF tended to increase in both EORA and YORA cases, ACPA tended to decrease in YORA cases and increase in EORA cases, and the lymphocyte count tended to increase in the cases with high susceptibility to infection with less than 1000/μL. The proportion of patients with lymphocyte counts of 1000/μL or less and at risk of infection tended to decrease in YORA and increase in EORA, respectively. The use of biologic agents and JAK inhibitors tended to increase in both EORA and YORA over the 5-year period, and the use of MTX tended to increase in group A and decrease in the older age group (75 years and older). [Conclusion] There were discrepancies in ACPA and lymphocyte counts between EORA and YORA in the same age group, suggesting that EORA patients with more complications need to be more careful about infections than YORA patients.

P2-004

Relationship between development of frailty and decreased grip strength in rheumatoid arthritis patients - T-FLAG study-

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Conflict of interest: None

[Objective] Decreased grip strength is one of the diagnostic criteria for frailty. The purpose of this study is to investigate whether the change in grip strength reflects the development of frailty in rheumatoid arthritis (RA) patients. [Methods] Of 522 RA patients who visited us for two consecutive years in 2021 and 2022 (T-FLAG study), there were 157 patients who were non-frailty at the survey start (2021) and had decreased grip strength one year later (2022). Frailty was defined as 8 or more scores of the Kihon Checklist (KCL). Multivariable logistic regression analysis was performed to determine the odds ratio (OR) for the development of frailty. [Results] Of 157 patients, 23 patients (14.6%) had a decreased grip strength of 20% or more. After one year, KCL was 6.6±4.4/4.1±3.0 points (decreased grip strength of 20% or more/less than 20%), the proportion of frailty was 39.1/10.4%, and grip strength was 13.1±6.2/22.3±7.6 kg ($p<0.05$). The development of frailty was significantly associated with decreased grip strength of 20% or more (OR: 5.13). [Conclusions] The diagnostic criteria of frailty for decreased grip strength is less than 18 kg in women, and 20% correspond to about 4 kg. A decrease in grip strength exceeding 4 kg suggested the development of frailty in RA patients.

P2-005

The impact of lower/small joint involvement on pain VAS is smaller than that of upper/small joint in RA - Analysis based on NinJa 2019 using joint index vectors

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Conflict of interest: None

[Objective] Upper joint involvement (x index) was shown to contribute to circumvention of PGA-PhGA discordance (Int J Rheum Dis 25: 1020, 2022), using JI vector (J Big Data 5: 37, 2018). The purpose of this study was to analyze the effect of affected joint distribution on PGA and pain VAS. [Methods] We performed a multiple regression analysis involving 13,653 patients with RA whose joint data were available in *NinJa* 2019. [Results] Pain was the main determinant of PGA, followed by mHAQ. Multiple regression analysis was performed using pain as an objective variable, and mHAQ, CRP, and JI vector (x, y, z) as explanatory variables. To further explore the effects of affected joint size, we replaced the JI vector with JI (tenderness) of upper/large joint (UL), upper/small (US), lower/large (LL), and lower/small (LS). UL and LL had almost equally strong effects on pain, followed by US, but LS had the least effect. Similar results were obtained with swollen indices. [Conclusions] The effect of LS-joint involvement on pain is smaller than that of US-joint involvement. It is suggested that RA patients are relatively less aware of LS joints, and may not complain to their physicians. It is necessary to pay attention to US-joint involvement, which is not included in DAS28 evaluation.

P2-006

Th17 cells expressing CD83 enhance the Tc17 response in psoriasis

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Conflict of interest: None

[Objective] Psoriasis is an autoimmune chronic inflammatory skin disease, and Th17 cells play a central role in its pathogenesis. Recently, Tc17 cells have been reported to be associated with the progression and worsening of psoriasis. We found that pathogenic Th17 subset has a strong Tc17 induction capacity. However, the molecular mechanism remains unclear. Therefore, we focused on CD83, a $CD8^+$ T-cell activating molecule, to elucidate the mechanism of induction and activation of Tc17 cells by Th17 cells. [Methods] $CCR6^+CD4^+$ and $CD8^+$ T_{EM} cells were sorted from peripheral blood mononuclear cells of healthy volunteers by flow cytometry. These cells were cocultured with or without recombinant human CD83 Fc chimera protein (sCD83) to inhibit CD83 function. The cell-cell contact between $CD4^+$ and $CD8^+$ T cells was inhibited using Transwell. [Results] sCD83 and Transwell prevented the proliferative activation of $CD8^+$ T cells, and did not affect the cytokine profile of cocultured $CD8^+$ T cells. A neutralization of IL-17A by adding IL-17Ra to coculture inhibited Tc17 cell induction. [Conclusions] Th17 cells may be involved in the pathogenesis of psoriasis by activating $CD8^+$ T cells through two pathways, direct contact via CD83 and through the production of IL-17A.

P2-007

Monocyte-derived Langerhans cell-Like dendritic cells induce psoriasis-related molecules after stimulation with toll-like receptor ligands

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Conflict of interest: None

[Objective] Investigating the necessary factors inducing monocyte-derived Langerhans cell-like dendritic cells (Mo-LCs) and the relationship between the Mo-LCs and the pathogenesis of psoriasis. [Methods] Mo-LCs were induced by stimulating monocytes with immobilized Notch ligands, TGF-β1, and GM-CSF. The Mo-LCs were compared with the dendritic cells derived from monocytes (Mo-DCs) and macrophages (Mφs) in the analysis of IL-23 expression by PCR and DLL4 expression by FACS after stimulation with toll-like receptor (TLR) ligands. [Results] Immobilizing Notch ligand on uncoated plates significantly induced Mo-LCs. We also found that DLL1 and DLL4 had a significantly higher rate of differentiation induction than the other Notch families and conventional Mo-LC inducers. The Mo-LCs were found to express significant amounts of IL-23 and DLL4 in response to the TLR ligands compared with Mo-DCs and Mφs. [Conclusions] We established a new method to generate Mo-LCs. We also found that the Mo-LCs induced by DLL1 and DLL4 express IL-23 and DLL4, which are related to the pathology of psoriasis, in response to the TLR ligands. Our results indicate that Mo-LCs are involved in the pathogenesis of psoriasis via Notch signaling of DLL1 and DLL4 or TLR signaling pathway.

P2-008

Clock gene Bmal1 controls expressions of inflammatory mediators in RA-FLS

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Conflict of interest: None

[Objective] We previously reported that the mRNA expressions of MMP-3, CCL2, IL-6, IL-7 and IL-15 in rheumatoid arthritis fibroblast-like synovial cell (RA-FLS) were controlled by Bmal1. In this study, we examined the mRNA expressions of MMP-9, MMP-13, TIMP-1, TIMP-2, TIMP-3 and RANKL in RA-FLS under conditions of RNA silencing of Bmal1. [Methods] RA-FLSs were transfected with small interfering RNA (siRNA)/Bmal1, and stimulated with TNF-α (0, 20 ng/ml), IL-1β (0, 20 ng/ml), IFN-γ (0, 20 ng/ml) and soluble IL-6 receptor (0, 100 ng/ml) for 0 - 32h, respectively. Subsequently, the mRNA expressions of MMP-9, MMP-13, TIMP-1, TIMP-2, TIMP-3 and RANKL in RA-FLS were analyzed by qPCR. [Results] The mRNA expressions of MMP-9 and RANKL were down-regulated by silencing Bmal1 expression. [Conclusions] Results suggested that Bmal1was involved with the pathogenesis of RA by regulating the expressions of MMP-9 and RANKL in RA-FLS.

P2-009

Combination therapy targeting CDK6 and TNFa in vitro and in vivo

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Conflict of interest: None

[Objective] CDK6 is a cell cycle regulator at G1 phase, and its inhibitor (C6I) has been reported to attenuate the proliferation of TNFα-induced RASFs and significantly inhibited the progression of arthritis without myelosuppression in CIA. The aim of this study was to evaluate anti-arthritic potentials of C6I in combination with Etanercept (Enb). [Methods] TNFα-induced RASFs and CIA mice (DBA/1J) were treated with C6I and/or Enb. After RASFs were stimulated for 24 h with TNFα, the inhibitors were added and then cultured for another 24 h. Cell viability was detected using a CCK-8 assay. CDK4, CDK6 and IL6 mRNA levels in RASFs were measured by qPCR. From 25 days after 1st immunization, the efficacy of combination therapy was determined by arthritis score and incidence in mice CIA. [Results] C6I combined with Enb significantly reduced cell viability ($p<0.05$). mRNA levels of CDK6 and IL6 were upregulated with TNFα stimulation. Only CDK6 showed a significant decrease in combined treatment group ($p<0.001$). Furthermore, CIA were markedly suppressed in combined treatment group ($p<0.05$). [Conclusions] Our results suggest that the mechanism of CDK6 inhibition should be differ from anti-arthritic effects of TNFα inhibitor. Combination of the both inhibitors might be effective for RA treatment.

P2-010

Investigation of angiogenesis inhibitory effect by Janus kinase inhibitors

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Conflict of interest: Yes

[Object] The Janus kinase (JAK)/signal transducer and activator of transcription (STAT) signaling pathways play an important role in angiogenesis. The present study aimed to compare the therapeutic effects and mechanism of tofacitinib, baricitinib, and peficitinib on angiogenesis induced by vascular endothelial growth factor (VEGF). [Methods] Human umbilical vein endothelial cells (HUVECs) were treated with 20 ng/mL VEGF, including various doses of tofacitinib, baricitinib, or peficitinib (0.1 μM, 1 μM, 5 μM). After 48 h, the viability, migration, and tube formation of the HUVECs were evaluated. Additionally, STAT3 phosphorylation in HUVECs stimulated with 50 ng/mL VEGF and the suppression by JAK inhibitors were evaluated using western blotting. [Results] Tofacitinib, baricitinib, and peficitinib suppressed VEGF-induced cell viability and tube formation. VEGF-induced cell migration was suppressed by tofacitinib and peficitinib but not by baricitinib treatment. VEGF-induced STAT3 phosphorylation was inhibited by tofacitinib and peficitinib, but not baricitinib. [Conclusions] VEGF-induced angiogenesis in HUVECs was suppressed by JAK inhibitors, especially tofacitinib and peficitinib. The JAK3/STAT3 signaling pathway may be essential for VEGF-induced angiogenesis.

P2-011

Therapeutic potential of plant-derived microRNA for rheumatoid arthritis

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) should be treated in the early stage to prevent joint destruction. microRNA (miRNA)s, non-coding RNA, regulate gene expression. Abnormal expressions of miRNA induce human diseases and several miRNAs such as miRNA-146, 155, and 223 were reported in RA pathogenesis including synovitis. miRNA has the potential to be drugs but problems such as drug delivery and cost still remain. Plants also have miRNAs which is same seed sequences so that plant-derived miRNA could function in human body. This study aimed to examine the potential of plant-derived miRNAs to treat RA. [Methods] Expression analyses of miRNAs derived from vegetables using human miRNA microarray chips were conducted. Proliferation and migration assays of RA synovial fibroblast (RASF)s with or without extracellular vesicle (EV) from vegetables were performed. [Results] miRNA microarray revealed that vegetables had miRNAs with the same sequence as human miRNAs. RASF could uptake immunofluorescence-labeled EV from vegetables. EVs from ginger could reduce cell proliferation and migration in RASF with TNFα. [Conclusions] Recent reports showed plant-derived miRNA could function in the human body. Plant-derived miRNA has the potential to be new drugs for RA treatment.

P2-012

The South Soya Intractable Disease Medical System Project: Shared-medical treatment by general physicians and rheumatologist in depopulated areas: its effectiveness and safety

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Conflict of interest: None

[Objective] Establish an environment where RA patients can safely receive specialized medical care in their familiar area even if the nearest rheumatologist is more than 100 km far away. [Methods] A rheumatology outpatient clinic was set up at the Esashi-city National Health Insurance Hospital, and a rheumatologist of our hospital provided medical care once every 3 or 6 months (=Outpatient A). In cooperation with the National Health Insurance hospitals in Esashi, Hamatonbetsu, and Nakatonbetsu, RA or collagen disease patients were treated in outpatient A, and general physicians at the 3 hospitals routinely provided treatment based on the prescribed treatment policies. Twenty-three consecutive patients with RA who visited Outpatient A from June 1 to September 30, 2012, and a total of 151 consecutive patients with RA who visited our hospital (outpatient B) during the same period were compared for the next 54 months. [Results] After 54 months, the average SDAI values in outpatients A and B were 9.7±5.6 and 7.8±5.8, respectively. 88.6%. The incidence of serious infections was 0.09/person-year and 0.07/person-year. [Conclusions] In this project, shared-medical treatment by general physicians and rheumatologist showed certain efficacy and safety in the treatment of RA patients.

P2-013

Patient reported joint pain are useful for understanding the difference of disease assessment between patient and physician

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Conflict of interest: None

[Objective] Patient visual analog scale (VAS) is the hardest outcome for the achievement of SDAI/CDAI remission. Therefore, understanding precise information about patient surrounding circumstances is quite important. We sometimes experience that patient VAS and physician VAS are quite different. We suspect patient reported so called “pain joints” including uncomfortableness, stiffness, limitation of range of motion might be different from physician reported swollen/tender joints. From this point of view, we compared the distribution between patient reported pain joints and swollen/tender joints. [Methods] In clinical practice, when above 50-point differences between patient VAS and physician VAS are observed, we compared patient pain joints with swollen/tender joints. [Results] We found two major patterns between patient pain joints and swollen/tender joints in 60 RA patients. 1) Patient pain joint dominant pattern- plenty number of patient pain joints with high patient VAS and low physician VAS. 2) Physician swollen/tender joint dominant pattern- a high number of swollen/tender joints with high physician VAS and low patient VAS. [Conclusions] Patient joint pain may be helpful for patient-physician communication for therapy.

P2-014

Effects of medication adherence on disease activity and treatment satisfaction in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To examine the effect of medication adherence on disease activity and treatment satisfaction in patients with rheumatoid arthritis (RA). [Methods] We evaluated medication adherence using the Drug Attitude Inventory-10 (DAI-10) in RA patients (n=70) who were followed up for at least 26 weeks in our hospital from October 2020 to August 2022. DAI-10≧5 was defined as good adherence, and patients were divided into two groups, DAI-10<5 and DAI-10≧5, and Patient Satisfaction Level. [Results] Mean age was 63.8 years, 52 (74.2%) were female, 44 (62.9%) were RF positive, 46 (65.7%) were anti-CCP antibody positive, 60 (85.7%) were using methotrexate (MTX) at 26 weeks and 14 (20.0%) were using biological agents. In the two groups of DAI-10<5 and DAI-10≧5, there were no significant differences in age, gender, or type of drug used between the two groups, but the CDAI (3.60 vs 1.10, p=0.008), DAS28CRP (2.10 vs 1.48, p=0.005), and HAQ (0.28 vs 0.00, p=0.013), Patient Satisfaction Level (76.00 vs 94.00, p=0.003), and significantly lower disease activity and higher treatment satisfaction in the DAI-10≧5 group. [Conclusions] Adherence to medication is important for controlling disease activity and improving treatment satisfaction in RA patients.

P2-015

Factors associated with the improvement of QOL score in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study is to clarify the factors that affect the improvement of QOL score in patients with RA. [Methods] We retrospectively evaluated 788 RA patients from January 2019 to March 2019. To analyze the improvement of QOL after 2 years, we divided into two groups of improvement group and non - improvement group. [Results] Baseline disease activity was TJC 1.4, SJC 0.8, CRP 0.53 mg/dl and SDAI 6.67. Corticosteroids, MTX and biologics were used in 41%, 72%, 34% of patients, respectively. After 2 years, 207 patients (26.3%) improved the QOL score, although, 302 patients (38.3%) remained unchanged and 279 patients (35.4%) worsened. As for factors contributing to QOL improvement, short disease duration (11.8 years vs 14.74 years, p=0.0082), early RA stage (p=0.0275), high SDAI (7.97 vs 6.25, p=0.0010) and low psychological anxiety (HADS) (p=0.0128) were extracted. In RA treatment, use of MTX, bDMARDs, tsDMARDs and corticosteroids were not significant for QOL improvement. Furthermore, in the QOL improvement group, SDAI, HAQ-DI and HADS were significantly improved. [Conclu-

sions] Our data indicated that improvement of QOL in RA was strongly correlated with RA disease activity and the importance of appropriate treatment for patients with high disease activity.

P2-016

Examination of EuroQol 5 dimensions 5-levels (EQ-5D-5L) questionnaire items affecting quality of life scores of Rheumatoid arthritis (RA) patients attending our department

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Conflict of interest: None

Background: Last year, we reported changes in quality of life (QOL) scores using the EQ-5D-5L were associated with disease activity in a study of RA patients attending our department. Many patients with decreased QOL scores despite treatment were identified, and it is important to know which factors affected QOL scores in these patients to develop a treatment plan to improve patients' QOL. Objective: To identify the EQ-5D-5L questionnaire items that influence the decrease and increase of QOL scores and to provide material for QOL improvement. Methods: QOL scores in 2019 were compared with those in 2018, patients who decreased or increased were selected, and changes in the selection level of the questionnaire items were examined for each patient. Results: Among patients whose QOL scores decreased, 27.3% selected "mobility", 20.4% selected "self care", 27.3% selected "usual activities", 41.2% selected "pain/discomfort", and 21.3% selected "anxiety/depression. On the other hand, among patients whose QOL scores increased, 29.3% selected "mobility", 19.3% selected "self care", 31.5% selected "usual activities", 57.5% selected "pain/discomfort", and 30.5% selected "anxiety/depression. Conclusion: Improvement of pain/discomfort was considered important for QOL improvement.

P2-017

Analysis of clinical factors which are involved in VAS scale in patients with rheumatoid Arthritis

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Conflict of interest: None

[Objective] We examined the involvement of clinical factors in VAS scale of RA patients. [Methods] 38 untreated RA patients (m: 16, f: 22), 65 years old (average) were enrolled. We analyzed the involvement of clinical factors in patient's pain VAS (VAS-p), patient's global VAS (VAS-g) and physician's global VAS (VAS-d) before and after treatment, using multiple regression analysis (step wise method). We focused on clinical factors, such as tender joint counts (TJC), swollen joint counts (SJC), CRP, ESR, HAQ-DI, interval since onset to first visit, morning stiffness (MS), trigger point counts (TPC) of fibromyalgia, VAS-p and VAS-g. [Results] In regard to results in six VAS scale, adjusted R-square in multiple regression analysis were more than 0.750. Statistically extracted clinical factors (t value>2, $p<0.05$) were below. Before treatment, VAS-g, SJC and interval were involved in VAS-p. Interval, MS and VAS-p were involved in VAS-g. VAS-p and VAS-g were involved in VAS-d. One year after treatment, VAS-g was involved in VAS-p. VAS-p was involved in VAS-g. SJC, TPC and VAS-g were also involved in VAS-d. [Conclusions] Different factors were more closely involved in each VAS scales mutually than inflammatory markers.

P2-018

A Study of Correlation between RAPID3 and SF-36 in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] SF-36 is a comprehensive measure of health-related quality of life (QOL), and its eight subscales provide physical and mental summary scores (PCS, MCS). RAPID3 is a disease activity index composed of patient-reported outcomes only and correlates with other disease activity indices. This study aims to investigate the association between RAPID3 and SF-36. [Methods] We statistically evaluated the correlation between SF-36 and RAPID3, DAS28-CRP, CDAI in 193 RA outpatients. Multivariate analysis of factors associated with summary scores was also performed. [Results] Correlation coefficients between RAPID3, PGA, SF-36 were higher than those between RAPID3 and CDAI for all items, especially for PF, RP, BP, PCS related to physical function (ρ = -0.62, -0.57, -0.71, -0.66). Correlation coefficient between MCS and RAPID3 was low (ρ = 0.22); PCS decreased significantly with worsening RAPID3 ($p<0.05$), while no significant difference was found for MCS. In multivariate analysis, age (95%CI -0.23 to 0.07, $p<0.05$) and MDHAQ value (95%CI -16.9 to -12.9, $p<0.05$) were significantly associated with PCS. [Conclusions] RAPID3 correlated with the SF-36 subscale as well as other disease activity indices, and was particularly useful in assessing physical-related QOL.

P2-019

Proposal of Japanese-style vegetarian diet therapy to rheumatoid arthritis

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Conflict of interest: None

[Purpose] Recently, pharmacotherapy is emphasized, and nutritional therapy is not seriously considered in the treatment of rheumatoid arthritis (RA). The nutritional therapy is reported to decrease RA disease activity, however, the dangers of strict vegetarian diets has been pointed out. The purpose of this study was to educate RA patients with a less strict Japanese-style vegetarian diet as a nutritional therapy. [Methods] RA patients of outpatient clinic in our university were included from April 2021 to March 2022 in the study. "Plant-based diet score", developed to evaluate Japanese-style vegetarian diet in Japanese patients with inflammatory bowel disease, was utilized in this study. [Results] Six RA patients were scored on the vegetarian score at least twice. The scores improved significantly after the first instruction ($p=0.008$). The scores seemed to increase with each successive instruction. Qualitative evaluation of each patient showed that each patient had a different pre-therapy status, and a different response to the therapy. [Conclusions] A simple method for nutritional therapy using the "Plant-based diet score", which evaluates the Japanese-style vegetarian diet, may be an effective educational method of nutritional therapy for RA patients.

P2-020

Association of a FAM13A variant with interstitial lung disease in Japanese rheumatoid arthritis

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) occasionally occurs in rheumatoid arthritis (RA) and confers a dismal prognosis. We previously reported that a single nucleotide variant (SNV) of *MUC5B* was associated with ILD in RA. However, the pathogenesis of ILD in Japanese RA patients could not be explained solely by this SNV, because its frequency is extremely low in the Japanese population. Here, we examined whether a different idiopathic pulmonary fibrosis susceptibility SNV might be associated with ILD in Japanese RA. [Methods] Genotyping of rs2609255 [G/T] in *FAM13A* was conducted in 208 RA patients with ILD and 420 without chronic lung disease using TaqMan assays. [Results] A significant association with usual interstitial pneumonia (UIP) in RA was detected for *FAM13A* rs2609255 under the allele model (P=0.0092, Pc=0.0276, odds ratio [OR] 1.53, 95% confidence interval [CI] 1.12-2.11) and recessive model for the G allele (P=0.0003, Pc=0.0009, OR 2.63, 95% CI 1.59-4.32). *FAM13A* rs2609255 was significantly associated with UIP in male RA (P=0.0043, OR 3.65, 95% CI 1.52-8.73) under the recessive model for the G allele. [Conclusions] This study is the first to document an association of *FAM13A* rs2609255 with ILD in Japanese RA, implicating it in the pathogenesis of UIP.

P2-021

Pulmonary function measured on spirometry in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To examine the pulmonary function in patients with rheumatoid arthritis (RA) compared to patients with osteoarthritis (OA). [Methods] We included 113 patients with RA and 851 patients with OA who underwent total knee arthroplasty at our hospital from June 2010 to December 2021. A propensity score matching (PSM) was performed to reduce the confounding between the groups of patients. These confounding adjustments included age, gender, body mass index (BMI), smoking status, and respiratory illness. After PSM, 105 patients remained in each group. Outcome measures included vital capacity (VC), vital capacity percent predicted (%VC), forced expiratory volume in 1 second (FEV_1), forced expiratory volume in 1 second percent predicted (FEV_1%), peak expiratory flow (PEF), and type of spirometric pattern (restrictive or obstructive). [Results] FEV_1 and PEF in patients with RA was significantly lower than that in patients with OA. Additionally, the percentage of respiratory disorders in patients with RA was higher than that in patients with OA. [Conclusions] Pulmonary function in patients with RA was lower than that in patients with OA.

P2-022

Antibodies against serum anti-melanoma differentiation-associated gene 5 in rheumatoid arthritis patients with chronic lung diseases

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Conflict of interest: None

[Objective] Chronic lung diseases (CLD), including interstitial lung disease (ILD) and airway disease (AD), are common complications of rheumatoid arthritis (RA). Rheumatoid factor (RF) and anti-citrullinated peptide antibody are reported to be associated with CLD in RA patients. The presence of anti-melanoma differentiation-associated gene 5 antibodies (MDA5 Abs) is associated with clinically amyopathic dermatomyositis developing into rapidly progressive ILD. However, few studies on anti-MDA5 Abs in RA have been published. Here, we analyzed the association of anti-MDA5 Abs with CLD complications in RA. [Methods] Anti-MDA5 Abs were quantified in sera from RA patients with or without CLD. [Results] Anti-MDA5 Ab levels were higher in RA patients with AD than without (mean±SDM, 4.4±2.4-vs. -4.0±4.2 [%], P=0.0001). AUC values of anti-MDA5 Ab and RF ROC curves were similar in RA patients with or without CLD (0.578, 95%CI 0.530-0.627 and 0.579, 95%CI 0.530-0.627, respectively, P=0.9411). [Conclusions] Anti-MDA5 Abs were associated with AD in RA patients and could represent a biomarker for CLD, similar to RF. The involvement of anti-MDA5 Abs in the pathogenesis of AD in RA is proposed.

P2-024

A case of rheumatoid arthritis with organizing pneumonia requiring introduction of a biologic agent to reduce PSL

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Conflict of interest: None

[Case] A 60-year-old man developed cough and fever on June 6, X. CT showed bilateral pneumonia, and antimicrobial agents were administered with a diagnosis of bacterial pneumonia, but the patient did not respond. He visited the hospital because of left elbow pain that began on June 14. Swelling was observed in the left wrist joint and bilateral knee joints, and joint ultrasonography revealed significant synovial thickening and PD signal in the knee joint. he was determined to be organic pneumonia preceding rheumatoid arthritis (RA). he started treatment with PSL 30 mg/day, and his symptom promptly improved, but when the dose was reduced to PSL 25 mg/day, he experienced joint pain, and MTX was introduced. The dose was then increased to 14 mg of MTX and csDMARDs were added in an attempt to reduce the PSL, but he had strong joint pain and difficulty reducing the dose below 15 mg of PSL. When TCZ 162 mg/2w was introduced, his symptoms improved and the PSL's dose was reduced to 6 mg. [Discussion] Although it has been reported that RA associated with OP does not correlate with RA disease activity, the patient and two other patients with RA preceded by OP also had difficulty in reducing PSL. For RA patients with preceding OP, RA disease activity may be high.

P2-025

A case of rheumatoid arthritis with marked improvement of interstitial lung disease after introduction of tocilizumab

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Conflict of interest: None

[Case] A 63-year-old woman was referred to our department in January X because of persistent morning stiffness and polyarticular pain. He had elevated CRP 4.4 mg/dl, RF 17.7 U/ml, and MMP-3 109.4 ng/ml. He met the ACR/EULAR 2010 rheumatoid arthritis (RA) classification criteria, and was diagnosed with RA. The patient was also aware of shortness of breath and SpO_2 was decreased to 93% (room air). CT showed diffuse ground glass opacity mainly in both lower lung fields, and it was determined that the patient had interstitial lung disease (ILD). In February X, tocilizumab (TCZ) was introduced, and the arthritis disappeared thereafter. Although she did not receive regular corticosteroid administration, her

dyspnea gradually disappeared after TCZ was introduced, and a CT scan in February X + 1 year showed that the ground glass opacity had almost disappeared and KL-6 had decreased to within the standard value. She continues to receive TCZ and is in remission, and her ILD has not flared up. [Clinical Significance] Although RA-ILD has been reported to be present in approximately 28-67% of RA patients using HRCT, there is no established treatment for RA-ILD, and reports of cases with clear improvement of RA-ILD after TCZ introduction are very rare. Therefore, we hereby report.

P2-026

A case of leukocytoclastic vasculitis during tocilizumab use

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Conflict of interest: None

[Case] 66-year-old male [Current medical history] He developed seronegative RA at the age of 45 years. He was treated with PSL and SSZ at another hospital. Due to poor activity control, he was referred to our hospital at age 55 and started intravenous tocilizumab (TCZ) (8 mg/kg/month). The patient was well controlled but withdrew from TCZ at the age of 61 years due to economic reasons and relapsed at the age of 64 years. However, 10 months later, purpura, blisters, and ulcerations appeared on her toes. Skin biopsy of the purpura revealed leukocytoclastic vasculitis, neutrophil infiltration of blood vessels, nuclear dust, and fibrinoid necrosis. No systemic symptoms such as fever, general malaise, or weight loss were observed. There was no joint swelling or tenderness, and the patient remained in clinical remission (DAS28-ESR: 0.92). Based on these findings, a diagnosis of TCZ-induced vasculitis was made. [Clinical Significance] Vasculitis is an important complication of RA. bDMARDs have greatly improved the prognosis of RA, but TNF inhibitors have been reported to induce vasculitis. On the other hand, there are few reports of vasculitis induced by anti-IL-6 receptor antibodies in RA patients. We report a case of leukocytoclastic vasculitis during TCZ use at our hospital.

P2-027

A case of rheumatoid arthritis with methotrexate-associated lymphoproliferative disease successfully treated with sarilumab

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Conflict of interest: None

A 70-year-old woman with rheumatoid arthritis (RA) was first treated with methotrexate (MTX). Due to insufficient effect, tocilizumab (TCZ) was introduced. Remission was maintained for 5 years. Since joint symptoms worsened, prednisolone (PSL) was added and TCZ was switched to golimumab (GLM). Despite relief of joint pain, CRP gradually increased. Computed tomography showed bilateral axillary lymphadenopathy and splenomegaly. MTX and GLM were discontinued. A right axillary lymph node biopsy resulted in a diagnosis of Hodgkin's lymphoma (methotrexate-associated lymphoproliferative disease: MTX-LPD). Chemotherapy was started because discontinuation of MTX alone did not lead to improvement. A total of 6 courses were performed, during which the joint symptoms subsided. After chemotherapy termination, the articular symptoms were exacerbated. The PSL dose was increased and furthermore sarilumab (SAR) was started. The joint involvements tended to ameliorate 2 weeks later. Thereafter the PSL was gradually reduced. Hodgkin's lymphoma has also not relapsed. It is often difficult to treat RA with MTX-LPD. SAR could be a useful option like this case.

P2-028

Clinical outcome in patients with rheumatoid arthritis switched to sarilumab after tocilizumab failure

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Conflict of interest: None

[Objective] The present study retrospectively assessed the efficacy of sarilumab in patients with rheumatoid arthritis (RA) who failed to respond to treatment with tocilizumab. To evaluate the efficacy and safety of therapy by switching to SAR in RA patients who had previously received tocilizumab. [Methods] A retrospective study of 10 RA patients who did not respond to tocilizumab was conducted. DAS28-ESR, SDAI, and CDAI. The effects of tocilizumab to sarilumab switch were evaluated at 12, 24 and 52 weeks after switching. [Results] Nine patients who had been treated with tocilizumab were switched to sarilumab. One patient who had been treated with tocilizumab previously were switched from JAK inhibitor to sarilumab. Treatments with disease-modifying antirheumatic drugs before the switch, especially methotrexate (MTX), was maintained. There was a reduction from baseline in DAS28-ESR, SDAI, and CDAI values at 12, 24 and 52 weeks. In one patient, the WBC decreased and the liver function increased, the dose of MTX was reduced and the effect became insufficient after 9 months, and sarilumab was changed. One patient developed a common cold, but sarilumab was temporarily interrupted and continued. [Conclusions] Switching from tocilizuma to sarilumab improved response to therapy.

P2-029

The efficacy of Tocilizumab therapy in rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy in tocilizumab therapy with rheumatoid arthritis (RA) and tapering of methotrexate. [Methods] This study comprised 50 patients with rheumatoid arthritis intolerant to biologic DMARDs. Patients received tocilizumab therapy with methotrexate for 12 months. The outcomes were assessed with the disease activity during 12 months study period, using the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate (DAS28 ESR) and Clinical Disease Activity Index (CDAI). [Results] DAS28ESR (from 3.3 to 1.5) and CDAI (from 4.5 to 0.3) decreased significantly from baseline to Week 52. DAS28ESR Remission achieved in 39 cases at Week 52. Tocilizumab monotherapy was also effective with RA patients of in adequate response to antiTNF inhibitor therapy. The retension rate of tocilizumab at 52 weeks was 90%. The average dose of methotrexate tapered from 5.6 mg to 3.2 mg. The average dose of glucocorticoid also tapered from 1.4 mg to 0.3 mg. [Conclusions] These results suggested that tocilizumab therapy is effective in patients with RA of an inadequate response to other biologic DMARDs.

P2-030

Study of the patients with rheumatoid arthritis who were treated with Sarirumab as a second or subsequent bDMARD

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Conflict of interest: None

[Objective] To Study of the patients with rheumatoid arthritis who were treated with Sarirumab as a second or subsequent bDMARD. [Methods] There were 7 patients with RA in this study. The number of patients that Sarirumab was used with 2nd bDMARD was 3, with 5th bDMARDs was 3, with 6th bDMARDs was 1. Age was 60.6±8.2 and duration of RA was 15.3±9.9 years. The number of Stage II was 3 and Stage IV was 4. DAS28 was 5.0±1.1. We investigated survival rates, treatment efficacy and adverse events of Sarirumab. [Results] The survaival rate of Sarirumab was 71% at 3 month, 71% at 6th month and 36% at 10 month. There was no adverse event requiring discontinuation. In the continuation cases, 1 case was good response and 3 cases were moderate response. [Conclusions] Although it was a small number of cases, the efficacy of sarilumab as a second and subsequent bDMARDs was confirmed.

P2-031

Dose-reduction effect of glucocorticoid and/or methotrexate after introduction of sarilumab treatment in rheumatoid arthritis

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Conflict of interest: None

[Purpose] To investigate the dose-reduction effects of glucocorticoid (PSL) and/or methotrexate (MTX) after the introduction of sarilumab (SAR) in rheumatoid arthritis (RA). [Methods] The clinical and laboratory findings of 19 RA patients who introduced SAR at our hospital were investigated. Twelve patients who continued SAR for more than 52 weeks were divided into 2 groups whether they could discontinue PSL and/or MTX after the initiation of SAR (continuation group and discontinuation group), and the clinical characteristics at the time of SAR initiation were compared. [Results] Mean age at the initiation of SAR was 64±10 years, and the mean time from diagnosis to initiation of SAR was 64 months. The significant improvement in DAS28 (3)-CRP was observed 4 weeks after initiation of SAR, and the PSL dosage was significantly reduced 12 weeks after initiation of SAR. A comparison of the clinical and laboratory findings at the initiation of SAR between the 2 groups showed that the dosage of PSL, the number of swollen joints, and DAS28 (3)-CRP were significantly higher in the continuation group. [Conclusion] Although PSL and MTX doses can be reduced after the introduction of SAR in RA, careful dose reduction may be warranted in patients with high disease activity at the initiation of SAR.

P2-032

Review the efficacy of Sarilumab to Rheumatoid arthritis in our department

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Conflict of interest: None

[Objective] Sarilumab (SAR) was approved for rheumatoid arthritis (RA) in 2018, we will review its efficacy in our department five years after its release. [Methods] In this retrospective, single-center study, patients diagnosed with RA who fulfilled ACR/EULAR in 2010 criteria, and who were treated with subcutaneous SAR 200 mg every two weeks were included. We analyzed their baseline characteristics at SAR initiation, disease activity after SAR treatment, and continuation rate of SAR. [Results] 21 patients were analyzed in this study. The median age was 74 years, the median disease duration was 30.0 months. 13 (61.9%) patients had been treated with bDMARDs. Patients had high disease activity with a median DAS28-CRP of 4.5 and median DAS28-ESR of 5.3, and intermediate disease activity with a median CDAI of 18.0. Of the 20 patients whose CDAI could be evaluated during this period, 10 (50.0%) patients achieved low disease activity criteria of CDAI≦10 at 4 weeks, 15 (75.0%) patients at 8 weeks, and 14 (70.0%) at 12 weeks. The median duration of SAR exposure was 14.0 months, and the SAR continuation rate was 85.7%. 3 patients who discontinued were due to ineffectiveness. [Conclusions] Most patients have been controlled disease activity early after SAR use, with a high continuation rate.

P2-033

A report of two cases of rheumatoid arthritis with injection site reactions to both tocilizumab and sarilumab

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Conflict of interest: None

[Case 1] 54-year-old female was diagnosed with RA and started salazosulfapyridine treatment. Due to inadequate response, changed to subcutaneous injection of sarilumab (SAR). It was discontinued after the 4th injection due to injection site reaction (ISR). She was switched to subcutaneous injection of tocilizumab (TCZ), but the ISR was observed again at the first injection. Changed to TCZ infusion, no adverse events have been observed and disease activity has improved, and treatment is ongoing. [Case 2] A 65-year-old woman was diagnosed with RA and started methotrexate treatment. Etanercept (ETN) was started due to insufficient response to treatment. Due to the arthritis in both hands flared up, she was switched to SAR subcutaneous injection, but an ISR was observed at the fourth injection. The patient was switched TCZ subcutaneous injection, but the ISR was observed again at the first injection. The patient was switched to oral baricitinib, and treatment has continued with no further adverse events and improvement in disease activity. [Clinical Significance] ISR are not uncommon as an adverse reaction to subcutaneous injections of biologic agents for RA. We report two cases of RA in which ISR occurred with both TCZ and SAR. It should be explained to the patient in advance.

P2-034

Usability and Acceptability of a New Autoinjector Device and its Associated App in Japanese Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Objectives] CLICWISE® is a reusable autoinjector with dose-dispensing cartridge for subcutaneous self-injection of biotherapeutics, approved for patients with rheumatoid arthritis (RA) and other diseases. ClicWise can connect to an optional app (ClicNote) to track injections and treatment data. This study assessed patient opinion data on ease of use and usability of the device and app. [Methods] Japanese patients (≧18 years old) with RA each received training for the device, performed simulated injections, and completed questionnaires evaluating the device and app. Responses were recorded as Likert scale ratings from 1 (extremely negative) to 7 (extremely positive), and the percentage of negative (1-2), neutral (3-5), and positive (6-7) ratings for each category were determined. [Results] 75 patients (88% female) participated. Mean scores (% positive responses) were: ease of device use 6.34 (83.1%), device usability effectiveness 6.36 (85.3%), benefit of device features 6.42 (85.5%), device form factor 5.88 (69.9%), and app 6.05 (72.9%). Mean estimated time for training a patient to use the device/cartridge was 11 min. [Conclusion] Japanese patients responded positively to the device/app across all categories, indicating its suitability for self-administration of biotherapeutics.

P2-035

Experience with biosimilars for RA patients in an orthopedic clinic

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Conflict of interest: None

[Purpose] At our hospital, we have introduced Etanercept-BS (ETN-BS) since November 2019 and Adalimumab-BS (ADM-BS) since April 2021 to RA patients who wish to receive them. [Subjects and Methods] ETN-BS was used in 34 cases (14 males, 20 females, average age 60.7 years). ETN 5/tocilizumab 1) and 3 patients changed from JAK inhibitors. Starting doses were 25 mg once weekly for 20, 25 mg twice weekly for 13, 50 mg once weekly for 1, and combined with MTX for 24 patients. ADM-BS was used in 3 cases (3 females), and 1 case was changed from the previous ADM. We investigated the continuation status and usefulness of these cases. [Results] ETN-BS was continued in 24 cases and discontinued in 10 cases (3 cases changed to other biologics). All cases of change from the previous ETN were continued. In 25 patients who were able to continue administration for 12 weeks, changes in DAS28-CRP mean value were 3.74 before administration, 2.53 at week 4, and 2.12 at week 12 after administration, showing an improvement. ADM-BS was continued in 2 patients, and the previous ADM change patient was able to continue without changing the administration interval. [Conclusion] Biosimilars may be an option for RA patients who require biologics, and information is expected to be provided to patients.

P2-036

Biological DMARD mono therapy without oral DMARDs for the treatment of elderly-onset rheumatoid arthritis

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Conflict of interest: None

[Objective] To assess the efficacy and safety of biological DMARD (Bio) mono therapy without oral DMARDs for the treatment of elderly-onset rheumatoid arthritis (EORA). [Methods] We retrospectively analyzed all the EORA patients who were treated with biological DMARD mono therapy without oral DMARDs concerning for the treatment-related comorbidity since July 2015. Initial glucocorticoid (GC) administration was allowed, while patients was determined as treatment failure if GC could not tapered off within 3 months. [Results] Total 135 cases (101 female, 34 male) were identified. Mean age was 77, Duration from disease onset to the initial treatment was 10 weeks (median). ACPA positivity was 39%, rheumatoid factor positivity was 47%. Initial GC was administered in 52 cases. As the 1st Bio, abatacept, etanercept, tocilizumab, and golimumab was used. In case of insufficiency, another Bio was applied. Mean follow-up period was 24 months. Caplan-Meyer survival analysis showed the 1, 2, 3 years treatment success rate was 79%, 69%, 69%, respectively. Cumulative insufficiency rate was 24% at 3 years. Cumulative serious adverse events rate was 11% at 3 years. [Conclusions] Bio-monotherapy may be effective and safe for the patients with EORA and multi-morbidity.

P2-037

Actual use of biological DMARDs in the Elderly Patients with Rheumatoid Arthritis at our hospital

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Conflict of interest: None

[Objective] To explore the characteristics of elderly RA patients treated with biologic agents in our hospital. [Methods] RA Patients aged 65 years or older who received a biologic agent within 2021, will be selected based on medical records, and their age, MTX dose, PSL dose, DAS28-CRP, concomitant DMARDs, and the number of biologic agents used will be identified. Changes at 6 months after induction will then be checked. We will also examine whether there are differences in each of these items for each formulation, and explore what contributes to the choice of formulation. [Results] There were 48 RA patients received a biologic agent within 2021. MTX was used in 31% of patients at an average dose of 8.9 mg/week, and PSL was used in 19% at an average dose of 5.9 mg/week. Other DMARDs included IGR, SASP, Tac, BUC, and ACT, which were used in 63%, 54%, 17%, 10%, and 2%. The 6-month retention rate, was 70%, with a decrease in MTX and PSL doses. TCZ had the highest number of inductions, followed by GLM. The mean age at induction was 76 years for TCZ, and more patients switched to IL-6 inhibitors than to TNFα inhibitors. [Conclusion] Elderly patients with rheumatoid arthritis treated with biologic agents in our hospital have been reduced in the course of treatment with other drugs.

P2-038

Decreasing methotrexate dose after remission in case of rheumatoid arthritis patients who had MTX plus BIO: a clinical course observation

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Conflict of interest: Yes

Objective: MTX is important as a first-line in treating RA. On the other hand, it is also important to reduce MTX to reduce side effect of MTX, especially lymphoproliferative disorder (LPD), but the timing to decrease of MTX is not known in present. In patients with rheumatoid arthritis (RA) that maintained remission by MTX plus Biologic DMARD (BIO) and got their consent, the clinical course after decreasing MTX was evaluated respectively. **Methods**: Subjects were 60 patients who had MTX plus BIO from March 2014 to September 2018. Baseline characteristics were Mean age 57.3 years, mean duration of illness 76.0 months, mean use period of BIO 38.4 months. Changes in the remission rate of DAS28-ESR, SDAI, and CDAI at 208 W were analyzed. **Results**: 14 of 60 patients relapsed due to MTX reduction or withdrawal. But remission rate of DAS28-ESR, SDAI, and CDAI at 0 W were 96.7%,98.3%,100.0%, and remission rate of DAS28-ESR, SDAI, and CDAI at 208 W were 75.0%,84.6%,84.6%. The treatment goal is maintained in many cases after decreasing methotrexate dose of MTX at 208 W. **Conclusion**: This study shows the possibility that decreasing methotrexate dose after remission in case of rheumatoid arthritis patients who had MTX plus BIO might be a useful option after REM.

P2-039

Two RA cases of GI perforation

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Conflict of interest: None

[Case 1] A 76 y.o. female was diagnosed as RA on 2005 and treated with MTX. On 2010, because of high RA activity, CyA and ST regimen was started, she complaint diarrhea which proved due to amyloid deposition in small intestine. Amyloidosis also caused renal proteinuria. TCZ treatment was started on 2012 with successfully. After at just 100th times infusion of TCZ, she was transferred to our hospital because of diverticular perforation. [Case 2] A 72 y.o. female was diagnosed to have RA and treated with MTX at nearest hospital on 2008. On next year, thyroid enlargement cause dyspnea due to air way stenosis, she was transferred to our hospital. Thyroid mass was proved to MTX-LPD which was occurred at her Hashimoto thyroiditis. MTX-LPS, resolved only discontinuation of MTX. Active RA was treated with Biologics and JAKis from 2012, TCZ-ETN-CZP-ABT -GOL-TOFA, every biologic or JAKi was with only partial effect. Baricitinib was started on September 2018, RA relieved dramatically. But she was admitted for our emergent ward because of perforation and operated successively. [Conclusions] In Case 1. Perforation occurred after 100th time infusion. In case 2, TCZ and TOFA did not caused diverticular perforation. Causes of perforation might be multifactorial not only simple IL6 inhibition.

P2-040

Are you a good physician when you treat a patient with rheumatoid arthritis after another physician treated with biological agent? -A case series of elder patients treated with biologics-

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Conflict of interest: None

[Objective] To treat elder patients with rheumatoid arthritis (RA) by biological agents (biologics) appropriately. [Methods] Two cases are shown here, who were treated rheumatoid arthritis by biologics. [Results] (Case 1) 93 years old female. She had been treated with tocilizumab, following with etanercept and was taking 5 mg oral prednisolone. She admitted our hospital because of severe low back pain due to osteoporotic vertebral fracture. Romosozumab was selected and oral steroid was reduced. (Case 2) 72 years old female. She visited our hospital introduced by another physician, who writed “Disease activity is stable by infliximab and methotrexate”. Her knee, shoulder and wrist joits were swollen and painful and serum CRP level was 6.15 mg/dl. Golimumab was selected then. [Conclusions] About 20 years have passed since biological agents for RA was introduced in Japan. In highly-aged society, biologics require to use properly.

P2-041

About half of RA patients who progress to D2TRA in less than 10 years after onset begin during menopause

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Conflict of interest: None

[Objective] To determine the actual status of D2TRA. [Methods] Of 226 women with RA who used biologics and Jaki since 2005 (mean number of drugs: 2.09/patient), 65 (29%) who used ≧3 drugs were defined as having D2TRA; these patients were examined. [Results] According to the onset age, 226 patients included 2 (1%) at age 0-17, 77 (35%) at age 18-44, 74 (34%) at age 45-59, 34 (14%) at age 60-69, and 32 (15%) at age ≧70; and the numbers (%) for 65 patients with D2TRA were 0, 29 (46%), 20 (31%), 11 (17%), and 4 (6%). Disease duration (years) for 65 patients (%) was 0-9 in 16 (25%), 10-19 in 19 (29%), and ≧20 in 30 (46%). For 16 patients with D2TRA for <10 years, the onset age was 0-17 years in 0; 18-44, 3 (20%); 45-59, 7 (46%); 60-69, 4 (27%); and ≧70, 1 (7%). 6 out of the 7 menopausal patients discontinued the first drug due to poor response. Mean CRP during the first drug change was 0.196 (0.02-0.53). [Conclusions] Half of D2TRA <10 years were menopausal onset; in this age group, there was a tendency to change the drugs despite not having high CRP. As pain and stiffness can occur due to menopause, changing RA drugs alone may not relieve symptoms. pVAS is improved by the combined use of hormone replacement therapy (HRT) for csDMARDs. For menopausal RA, the concomitant use of HRT is necessary.

P2-042

A study of rheumatoid arthritis in a cancer-bearing state with continued biologic therapy

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Conflict of interest: None

[Purpose] Biologic agents (BIO) are generally not used in patients with cancer. We investigated rheumatoid arthritis (RA) patients who continued to receive BIO at the patient's strong request, although they were in a cancer-bearing state. [Methods] In the past few years, there have been 3 patients with cancer who continued to receive BIO. The situation of each case was reviewed. [Case 1] An 84-year-old woman started tocilizumab (TCZ) thrapy at the age of 74. She underwent resection of common bile duct cancer at age 75, and TCZ administration was continued until 2 months before her death. [Case 2] A 79-year-old man started infliximab (IFX) therapy at the age of 66, and switched to abatacept (ABT) at the age of 72 due to weakening of the effect of IFX. At the age of 77, gastric cancer was confirmed, but surgery was not indicated. ABT was continued until 2 months before his death. [Case 3] A 70-year-old man started TCZ at the age of 61, and switched to ABT at the age of 63. Gastrectomy was performed, but the cancer recurred, metastasized. The patient was on ABT for 1 year in a cancer-bearing state until 5 months before his death. [Conclusions] We believe that BIO therapy in the oncological state is also necessary to relieve anxiety about RA recurrence.

P2-043

Long-term bDMARD treatment in Patients with Rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the treatment status of patients with rheumatoid arthritis (RA) receiving bDMARD for more than 5 years in daily practice. [Methods] We retrospectively analyzed 20 patients with RA who had received bDMARD for more than 5 years, including switching bDMARD, as of April 2022. Patient characteristics, disease activity, administration period, adverse events, and switching were evaluated. [Results] We included 7 males and 13 females. The mean age and RA duration were 61.3 years and 10.4 years, respectively. MTX was used in 76.5% (mean 6.7 mg). PSL was used in 35.3%. Mean DAS28CRP at baseline was 3.80. The bDMARDs used at first were IFX: 7, ETN: 8, ADA: 2, GLM: 3. Mean administration period was 9.0 years, mean administration period of the first bio was IFX: 9.6 years, ETN: 9.5 years, ADA: 8.5 years, GLM: 6.9 years. 16 patients (80%) continued the first bio. Mean DAS28CRP at last observation was 2.67, remission/low disease activity rate was 28.6%/14.2%, respectively. There were no adverse events, and switching was due to secondary failure and patient convenience. [Conclusions] Patients received first bio for a relatively long period. In terms of disease activity, even in cases which tight control was not achieved, patient satisfaction was considered to be relatively high.

P2-044

A retrospective study of peficitinib for rheumatoid arthritis

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Conflict of interest: None

[Objective] To examine the efficacy of peficitinib on rheumatoid arthritis and the reasons of discontinuation. [Methods] We retrospectively reviewed 12 of the 15 RA cases treated with peficitinib at our hospital for which analysis was possible. [Results] Background: 9 females, 3 males, mean onset age 62.5 years (47-79 years), disease duration 61.9 months, Steinbrocker stage I/II/III/IV: 2/0/8/2 cases, class 1/2/3/4: 0/5/5/2 respectively. History of administration of biologics/JAK inhibitors (mode of action): none/4, 1/3, 2/2, 3/2, 4/1 (mode/case). Outcome: CDAI: HDA/MDA/LDA/Remission, 7/2/2/1 cases at start, 2/2/5/3 cases after 12 months, respectively. 5 cases were continued, 6 cases discontinued (3 primary failure, 1 secondary failure, 2 adverse events), and 1 were transferred to other clinic. Of the 7 patients with 0-1 prior molecular target drugs, 5 patients were continued, 1 patient discontinued treatment, and 1 patient experienced an adverse event. Of the 5 patients who have received 2-4 prior treatments, one was continued, but 3 cases were ineffective, and one had adverse events. [Conclusions] In cases with 0-1 previous molecular target drugs predominant cases revealed effective, but in most of cases with 2 or more therapies were ineffective.

P2-045

Baricitinib Monotherapy and Timing to Begin

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Conflict of interest: None

[Objective] Baricitinib (BAR) monotherapy continuation group from the BAR monotherapy group of the RA-BEGIN study for the MTX naïve patients, safety and efficacy were the best in the phase 3 study and the long-term continuation study. **To focus on BAR monotherapy and examined timing to start of BAR.** [Methods] Eighty-seven patients were enrolled (78 female, mean age 66.3 years, mean disease duration 15.2 years, antiCCP antibody positive rate were 92%). DAS28-CRP mean 4.9, SDAI mean 34.2, and CDAI mean 32.8 at the time of the BAR start. Forty-five patients started with BAR monotherapy. Forty-two patients started BAR with preceding MTX, but reduced MTX by 2 mg when they achieved LDA in the evaluation period every 4-12 weeks. [Results] At 12 weeks in the monotherapy group, remission patients changed from 0 to 19 (Boolean remission 12). In the MTX combination group, remission patients changed from 0 to 15 (Boolean remission 5). Adverse events occurred in 16 patients of MTX combination group (herpes zoster 7), in 5 patients of BAR monotherapy group (herpes zoster 1). [Conclusions] BAR should be started as monotherapy early onset of RA to draw the efficacy and safety.

P2-046

Efficacy and safety of baricitinib in the patients of rheumatoid arthritis

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Conflict of interest: None

[Objective] We report the usefulness and safety of baricitinib. [Meth-

ods] Baricitinib was introduced to 2 males and 10 females with a history of use of MTX and TNF inhibitors for rheumatoid arthritis, with an average age of 73. Treatment effects were evaluated using (DAS28, CRP, ESR, RF, MMP3) at 12 weeks. [Results] For cases in which side effects such as hair loss appeared with MTX and TNF inhibitors, and it became difficult to continue an administration, TNF inhibitors could be completely switched by stopping or reducing MTX. And, since the target age was a little old, who was started at half the dose. In 8 out of 12 cases sufficient effect was observed even at half dose. In one case, half-dose of baricitinib uncreased CRP, and the symptoms was relieved by the normal dose. [Conclusions] Baricitinib is an oral drug that is easy to introduce to patients who are reluctant self-injection. And It could be administered to patients in remission, hypoactive, and elderly patients without side effects, despite being a renal metabolite. And a sufficient effect could be obtained in a half- dose. However, baricitinib has a shorter lead-in and follow-up periods than other drugs, and side effects and effects may not be recognized, so it is necessary to pursue safety and efficacy in the future.

P2-047

Efficacy of Upadacitinib in rheumatoid arthritis patients

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Conflict of interest: None

[Object] To investigate the efficacy of Upadacitinib in rheumatoid arthritis patients. [Methods] 19 Rheumatoid arthritis patients who were treated with Upadacitinib from April 2020 and could follow more than 24 weeks were recruited. Efficacy in disease activity scores and adverse events were investigated. [Results] There were 4 men and 15 women. Mean age was 69.5±19.6 years old, and mean disease duration 7.2±10.2 years. Mean DAS28-CRP were, baseline: 3.60±1.56, after 4 weeks: 2.41± 1.43, after 12 weeks: 2.21±01.18, after 24 weeks: 1.70±0.80, which improved from baseline. There were no herpes zoster. [Conclusions] Upadacitinib was effective in rheumatoid arthritis treatment.

P2-048

Efficacy and safety of one-half dose Upadacitinib in patient with rheumatoid arthritis in a routine care

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Conflict of interest: None

[Objectives] Upadacitinib (UPA) 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 UPA begun at one-half dose (7.5 mg) in RA patients in a routine care. In this study, we investigated the efficacy of UPA in RA patients. [Methods] RA patients treated with UPA for longer than 24 weeks were included in this study. We retrospectively reviewed the efficacy (DAS28-CRP), discontinuation of UPA therapy and adverse event in one-half dose (7.5 mg group) and typical dose (15 mg group), respectively. [Results] ten (7.5 mg group) and six (15 mg group) patients were included in this study. Mean age was 76 and 65 years old and concomitant methotrexate rates are 50% and 67% (7.5 mg and 15 mg groups, respectively). Mean DAS28-CRP was 3.8 and 5.2 at baseline, and 1.4 and 1.7 at 24 weeks (7.5 mg and 15 mg groups, respectively). The number of patients who withdrew from UPA was none in both groups. Two event of herpes zoster was reported in 7.5 mg group (increase dose case). [Conclusion] One-half dose (7.5 mg) as well as Typical dose (15 mg) of UPA was effective in RA patients in a routine care. This study provides support for the possible use of one-half dose of UPA in RA patients.

P2-049

Comparison of Postoperative Improvement Assessment of Micro-Endoscopic Lumbar Laminectomy in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Lumbar spinal canal stenosis caused by rheumatoid arthritis is associated with more joint destruction and spinal deformity than degenerative diseases, and decompression surgery alone may have difficulty in improving symptoms. We compared the achievement of minimal clinically important difference (MCID) using patient-reported outcomes in this study. [Methods] Patients who underwent micro-endoscopic lumbar laminectomy for lumbar spinal canal stenosis at our institution were included. The following patient-reported outcomes were compared in 70 patients in the degenerative disease group (N group) and 11 patients in the rheumatoid arthritis group (R group). [Results] In pre- and postoperative comparisons of each group, ODI, EQ5D, and COMI were significantly improved in group N ($p < 0.01$, <0.01, <0.01) and ODI and COMI were significantly improved in group R ($p < 0.01$, <0.01) after surgery. However, there was no significant difference between the two groups in any of the outcomes with respect to achievement of MCID. [Conclusions] Micro-endoscopic lumbar laminoplasty was as effective in patients with rheumatoid arthritis as in those with degenerative diseases.

P2-050

Safety and Patient-Reported Outcomes of Ultrasound-Guided Synovial Needle Biopsy in arthritis patients

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Conflict of interest: None

Objective: To investigate the safety and patient-reported outcomes (PROs) of ultrasound (US)-guided synovial needle biopsy in arthritis patients. Background: Recently it has been shown that synovial biopsy is safety and also has been suggested that the histological evaluation of the synovium is useful for the diagnosis of arthritis and the disease phenotype in the Western countries. In this study, we performed US-guided synovial needle biopsy at the onset or exacerbation in arthritis patients, and investigated the safety of synovial biopsy and evaluated the PROs in pain, swelling, and stiffness by 0-100 mm VAS (visual analog scale). Subjects and Methods: US-guided synovial biopsies were performed under local anesthesia in a total of 33 arthritis patients. An 18G biopsy needle was inserted in swollen joint (16 wrist, 16 knee, and 1 ankle joint) to obtain synovial tissue. Results: No adverse events occurred in the 33 patients who underwent US-guided synovial needle biopsy. Histopathological analysis confirmed that inflammatory and fibrous synovium was obtained. There was no worsening of VAS with biopsy. Conclusion: PROs after US-guided synovial needle biopsy in arthritis patients showed no worsening of VAS, and the safety of synovial needle biopsy was shown.

P2-051

Clinical study of Rheumatoid arthritis patients aged over 90 years who had a joint replacement surgery in the past

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Conflict of interest: None

[Objective] The number of RA patients aged over 90 is increasing due to the extension of the average life expectancy of Japanese people and the progress in the treatment of RA. In this study, we performed a clinical review of RA patients aged over 90 years who underwent total joint replacement in the past. [Methods] Six patients (2 male, 4 female) who were undergone joint replacement surgeries in the past were studied until September, 2022. Duration of disease, surgical site and number of years since surgery, medical history, and current drug therapy were examined. [Results] The average age was 92.1 y.o. (90-96 y.o.). Average disease duration is 30.8 years (19-44 years). Nine were TKA, two were THA, and two were TEA. 15.1 (7-31) years have passed since the operation. There

was no revision surgery. All patients use steroids (prednisolone 3-10 mg/d), 2 cases of salazosulufapyridine, Methotrexate was used in one case. Etanercept was used in one case, and Abatacept in one case. 3 cases of gastric cancer, 1 case of colorectal cancer. [Conclusions] Not only are RA therapeutic drugs progressing, but the design and materials of artificial joints have also improved, and cancer treatment outcomes have improved. Should be considered to enable management of good ADL future.

P2-052

Three cases of difficult diagnosis and treatment with abnormal signal areas on spine MRI

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Conflict of interest: None

[Objective] We report three cases in our hospital in which it was difficult to determine the diagnosis and treatment based on the clinical course and imaging studies. [Case] The cases are three women aged 56, 69, and 70 who were referred to our department between 2018 and 2022. A 56-year-old woman had inflammatory low back pain and alternating gluteal pain, whereas two others had only nonspecific low back pain. None of the 3 patients had extra-articular symptoms, palmoplantar pustulosis, or skin findings suggestive of psoriasis. CRP and ESR were positive, but rheumatoid factor, anti-CCP antibody, and HLA-B27 were negative. Only one patient had bone marrow edema of the sacrum by MRI and bone erosion of the sacroiliac joint by CT. In all three cases, signal changes in the vertebral body angles scattered in the thoracolumbar vertebrae and bone marrow edema in the vertebral bodies were confirmed. No intervention was done. [Clinical Significance] If there are abnormal signals on the spine MRI, but it is difficult to differentiate and the diagnosis cannot be made, it is important to consider the pros and cons of treatment based on the progress, and to accumulate clinical experience.

P2-053

Three cases of Spondyloarthritis complicated with other autoimmune diseases

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Conflict of interest: None

[Introduction] We report three cases of spondyloarthritis (SpA) with autoimmune diseases that are rarely complicated. [Cases] Case 1: A 64-year-old woman. She was diagnosed with sarcoidosis by lung lymph node biopsy. Morning stiffness (MS), inflammatory lumbar back pain (IBP), and bone marrow edema in sacroiliac joints and abnormal accumulation in bilateral shoulder and sacroloac joints appeared. Diagnosed SpA and initiated DMARDs and adalimumab. IBP, and joint pains were relieved. Case 2: A 56-year-old woman. She was diagnosed with mixed connective tissue disease and interstitial pneumonia at the age of 40. Treated with tacrolimus from 54 years old. MS, polyarthralgia, increased CRP, psoriasis appeared. Diagnosed with psoriatic arthritis and initiated secukinumab (SEC). Joint pains improved. Case 3: A 70-year-old man. He had IBP, plantar fasciitis and postrenal renal failure. Increased serum IgG4, sacroiliac arthritis, abnormal accumulation in sternum, clavicle, and sacroiliac joints, bilateral swelling of parotid and submandibular glands. Diagnosed with SpA and IgG4-related disease and initiated SEC. Plantar fasciitis disappeared. [Conclusions] These cases suggest that it is necessary to consider the combination of SpA for osteoarticular symptoms with autoimmune diseases.

P2-054

Administration experience of Upadacitinib for three cases with Psoriatic arthritis

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Conflict of interest: None

[Objective] We report three cases with psoriatic arthritis (PSA) using upadacitinib (UPA). [Methods] We investigated patient background, blood test results (CRP, ESR, ALP, MMP-3, WBC, RBC, hemoglobin, rheumatoid factor, ACPA), and DAPSA (disease activity index forpsoriatic arthritis) as activity assessment. [Results] (Case 1) 42 year old male. He was diagnosed with PsA at age 31, and started treatment with methotrexate (MTX). Though we increased MTX up to 10 mg/week, no improvement of his joint symptoms was observed, and started UPA administration. (Case 2) 72 year old female. She was diagnosed with PsA, and started treatment with MTX. Though MTX + certolizumab pegol (CZP) co-therapy inhibited her polyarthralgia and occipital dermatitis, we switched to UPA due to the lack of efficacy of previous treatments. (Case 3) 75 year old female. Though we increased MTX up to 6 mg/week, no improvement of her polyarthralgia and dermatitis of trunk and extremities were observed, and started UPA administration. All three cases showed improvement in blood tests and DAPSA. The therapeutic effect of switch case, compared with naïve cases, was slow. [Conclusions] UPA administration against PsA (switch and naïve case) was remarkably effective for a short time.

P2-055

Two cases of axial spondyloarthritis that became less severe by IL-17A inhibitor

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Conflict of interest: None

[Case 1] 57 year-old-man. He had been treated with steroid as PMR since January X. But, he got pain at left waist and left clavicle, April. He went to our department for treatment of relapsing PMR. There was no abnormality on X-ray. For ruling out of malignant tumor, he got a PET-CT and there were concentration at left sternoclavicular joint and left sacroiliac joint. MRI showed left sacroiliac arthritis. We suspected PAO, but he had no skin symptom. We started Ixekizumab, and his symptoms became less severe. [Case 2] 44 year-old-woman. She had been treated by MTX as RA since Y-4. She got pain at cervical region, lower back, both knees and anterior chest, april Y. There was not abnormal finding at lumber spine and sacroiliac arthritis, but inflammatory finding at cervical spine on MRI. We found accumulateons at cervical region, both sternoclavicular joints and sacroiliac joint on bone scintigraphy. There was enthesitis at both knee joints on ultrasonography. We suspected PsA, but she had no skin symptom. We started Secukinumab, and her symptoms became less severe. [Discussion] PAO and PsA are diseases that often lead to skin symptom. We suspected PAO and PsA preciding arthritis. There was not peripheral arthritis, but sacroiliac arthritis and vertebritis. We started IL-17A inhibitor as ax-SpA and got the effect.

P2-056

Osteomalasia in a patient with inflammatory bowel disease- a case report-

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Conflict of interest: None

Joint symptoms associated with inflammatory bowel disease have been reported to occur in about 5%. We report one case that was considered to be osteoarticular symptoms due to osteomalacia. The patient was a 44-year-old man, who developed Crohn's disease at the age of 17 and was treated with infliximab at the age of 30. Multiple rounds of ileum have been surgically treated, most recently laparoscopic ileal anastomosis resection at the age of 43. Subsequently, 6 Hb anaemia persisted and he was given feinject. Six months later, severe pain in the right dominant bilateral heel appeared and was examined for the first time in our department. No adherentitis was observed, and no obvious arthritis was observed. MRI revealed extensive strong inflammatory findings in the calcaneus, and other mild inflammatory findings in the surrounding joints. Serological studies were CRP 1.3 mg/dl, Hb 9.2 g/dl, RBC 3.89 million, Ca4.5 mg/dl, P0.9 mg/dl, and ALP213 U/L. Bone mineral density decreased to 65% in the

lumbar spine and 72% in the femur, and the FGF23 decreased to 144 pg/ml. This was considered to be a case in which we osteoarthrologists considered the possibility of developing osteoarticular symptoms due to osteomalacia in cases where long-term anemia is treated for inflammatory bowel disease.

P2-057

A case with SAPHO syndrome/pustulotic arthro-osteitis (PAO) initially diagnosed as recurrent mandibular osteomyelitis

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Conflict of interest: None

A forty-one year-old female initially visited a dental clinic because of left jaw pain, who initially received the pulpectomy. Since mandibular bone lysis and sclerotic change were found by the CT scan, the diagnosis of osteomyelitis was made. Although antibiotics and hyperbaric oxygen were effective, it was recurred after 6 months. Although any bacteria was not detected by the culture, the same treatment was reintroduced. Afterwards, the accumulation was found on the right sterno-costal joint by the bone scintigraphy and the inflammation in the clavicle, sternum, bilateral first to third ribs and sterno-costal joints by MRI. Then, she was referred to our clinic and found to have a previous history of palmoplantar pustulosis and swelling and tenderness around the left mandible and right sterno-clavicular and right acromioclavicular joints but no skin changes including pustlosis by the exam. Based on Benhamou's and Sonozaki's criteria, she was diagnosed as SAPHO/PAO. However the previous treatment was mildly effective for the mandibule, sterno-costal arthritis was still. Teriparatide and NSAIDs plus methotrexate were started but discontinued due to side effects. The sterno-costal lesions were finally improved after GUS was started. No recurrence of was observed.

P2-058

A case of HLA-B24-negative axial spondyloarthritis (axSpA) diagnosed with onset of bilateral uveitis and markedly effective with adalimumab (ADA)

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Conflict of interest: None

46 years-old man, who had been annoyed by back pain, went to an osteopathic clinic. In June of X-1, he visited an orthopedic clinic because he developed polyarthralgia. Loxinon started. Foggy vision appeared in April, year X. He visited an ophthalmologist and diagnosed with uveitis, and treated with steroid. In May, he was referred to our hospital due to the suspicion of an underlying disease. No symptoms of Behcet's disease, no BHL on chest X-ray. There was no swelling in the joints. Although the range of motion increased after oral loxonin administration, forward bending was limited (Schober test positive). His symptoms improved with exercise. CRP 4.70, ANA<40, RF and ACPA normal, ACE normal, HLA-B27 negative. X-rays of the spine showed no significant changes, but bilateral bone sclerosis and narrowing of the joint space were observed on sacroiliac joint X-rays, and MRI showed high signals on T1-weighted and T2-weighted fat suppression images, hypointense on the T2 coordination image was also compatible with sacroiliac arthritis. AxSpA with uveititis was diagnosed. According to ASAS/EULAR recommendations, ADA was started in July. The symptoms and ADL were rapidly improved. A single injection showed a remarkable effect, with DASBAI 6.5→2.6, BASMI 6→3, and CRP 4.70→0.27.

P2-059

A case of pediatric pustulotic arthro-osteitis patient successfully treated with tonsillectomy

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Conflict of interest: None

[Case] 14 years old, female [Chief complaint] Right knee pain, right ankle pain. [History] She had blisters and pustules on both palms and foot pads. Moreover she had pain in her right knee and right ankle. There was no history of skin disease or collagen disease, and no history of tonsil treatment or dental treatment. [Findings] She had no anterior chest wall pain, but tenderness in the right knee and the right foot, with a PalmoPlantar Pustulosis Area Severity Index (PPPASI) score of 19.5. MRI also showed extensive bone marrow edema (BME) around the right tibial tuberosity. In addition Sanger sequencing analysis of all exons and adjacent introns of IL36, IL36RN, CARD14, and AP1S3 was performed. [Clinical Course] Because of the exacerbation of both skin rash and arthralgia by tonsil massage, bilateral palatine tonsillectomy was performed six months after the onset of the disease. The pain in the right knee and ankle improved promptly after the surgery. Four months after surgery, PPPASI score was 4.7 and MRI showed improvement of the BME. [Clinical Significance] There have been very few reports of pediatric pustulotic arthro-osteitis (PAO) patients. We report here a rare case of pediatric PAO patient whose symptoms improved after tonsillectomy.

P2-060

A case of palmoplantar pustulosis osteoarthritis with the heel enthesitis in the absence of anterior chest wall lesions

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Conflict of interest: None

[Case] A 47-year-old female was referred to the Department of Dermatology of this hospital a month ago, and diagnosed with palmoplantar pustulosis. She had upper and lower limb pain mainly in the heel area, and was referred to our department. She had tenderness in the distal interphalangeal (DIP) joints of both hands and the Achilles tendon and plantar fascia attachments of both feet. A X-ray showed a narrowed fissure, erosion and osteogenesis at the DIP joint, and osteophyte formation at the Achilles tendon and plantar tendon attachments of the calcaneusand. She had no anterior thoracic wall lesions, but was diagnosed palmoplantar osteoarthritis (PAO) according to the revised Sonozaki criteria. After starting treatment with celecoxib 200 mg/day, her upper and lower limb pain showed a rapid improvement. Since then, she has been undergoing the same treatment without relapse. [Clinical Significance] Although anterior thoracic wall lesions are characteristic of PAO, there are a few cases of PAO without the lesions. In such cases, lesions are reported to be found in the spine, sacroiliac joint, long bones, mandible, but there are few reports of cases with enthesitis. In this report, we described a rare case of PAO with the heel enthesitis.

P2-061

A case of pustulotic arthro-osteitis with various joint lesions

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Conflict of interest: None

A 74-year-old woman visited our hospital with right knee pain. Right knee joint swelling and mild pustular lesion on the plantar of left foot that was diagnosed with palmoplantar pustulosis by dermatologist were noted. There were no other joint pain and inflammatory low back pain. Venous blood sample showed that CRP was 0.2 mg/dL, MMP3 was 353 ng/mL, CCP was < 0.6 U/mL, RF was 4.4 IU/mL, and HLA-A24, A26, B51, B62 were positive. Joint space narrowing in right knee of lateral, bony proliferation at distal phalanx, and osteosclerosis of bilateral sacroiliac joints were found in X-ray or CT. MRI showed high-intensity areas in STIR at bilateral sacroiliac joints, and at inferior corner of 5-7th thoracic vertebral bodies. No enthesitis or synovitis were found in joint ultrasonography. In this case, we start celecoxib, and total knee arthroplasty was performed for

right knee. Pustulotic arthro-osteitis (PAO) was a rare disease involving the skin and joint comorbidity, most often affecting the anterior chest wall. A rare case with mild skin lesions but strong axial lesions in multiple bone is reported. It is important to distinguish PAO from spondyloarthritis, because so treatment methods such as biologics differ depending on disease.

P2-062

A case of juvenile psoriatic arthritis complicated by aortitis and IgA nephropathy

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Conflict of interest: None

A 15-year-old female. She had uveitis 3 years before hospitalization. She had back pain in the spinous processes of the lower thoracic and lumbar vertebrae and nail pitting and papules on both thighs. Blood tests showed CRP 13.0 mg/dL, negative for RF and antinuclear antibodies. Urinalysis revealed hematuria and cylindruria. MRI of the sacroiliac joint showed high short tau inversion recovery (STIR) signal in the left sacral superior anterior region. The patient met the CASPAR criteria and was diagnosed with juvenile psoriatic arthritis (JPsA) with sacroiliitis and uveitis. Furthermore, CT angiography showed dilation and circumferential thickening of the abdominal aorta, and FDG-PET/CT revealed increased FDG uptake in aortic arch and abdominal aorta. Renal pathology showed no proliferative changes or sclerotic lesions in the glomeruli but IgA and C3c deposition with immunostaining. We started mPSL pulse therapy followed by PSL 1 mg/kg/day, methotrexate, and infliximab. [Discussion] It has been reported that patients with PsA and psoriasis are at increased risk of cardiovascular disease, especially in the cases with sacroiliitis, which are associated with aortic vascular inflammation. Here we report a complication of JPsA, aortitis, and IgA nephropathy with a literature review.

P2-063

Rate of positive serum RA-related markers in patients with severe knee osteoarthritis

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Conflict of interest: None

[Objective] The diagnosis of rheumatoid arthritis (RA) is difficult in seronegative elderly patients, especially those with radiographic knee osteoarthritis (KOA). Positive ratios of RA-related serum markers in the general population is not well understood. The purpose of this study was to investigate the rate of positive biomarkers for the diagnosis of RA in patients with severe KOA. [Methods] Hospital records of 223 consecutive patients with radiographic severe KOA who had undergone primary total knee arthroplasty (TKA) were analyzed. Preoperative CRP, ESR, MMP-3, and RF as well as ACPA measured 1 week postoperatively, were collected from electronic medical records. Positive rates and gender differences for each item were examined. [Results] The overall rate of positivity for serum RA-related marker were as follows: ACPA, 1.3%; RF, 6,7%; CRP, 12.1%; ESR, 25.1%; and MMP-3, 40.3%. There was a significant difference between males and females for MMP-3 (27.5 vs 44.2%, respectively; $p<0.05$). [Conclusions] There are cases among those with severe KOA that present with abnormalities in RA-related serum markers. There are also cases of KOA requiring TKA that may meet the 2010 RA classification criteria.

P2-064

Activation of fibrinolytic system may promote cartilage degeneration through the activation of MMP-1 in osteoarthritic knee joints

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Conflict of interest: None

[Objective] We reported that the OA knees with synovial flare may undergo rapid disease progression with the rise in the concentrations of urokinase (uPA) and PIC in synovial fluid (SF). In this study, we attempted to elucidate the mechanism (s) underlying this rapid progression by evaluating MMP-1 activity. [Methods] SF samples were obtained from the OA knees with synovial flare twice in the middle of flare (F) and after the resolution of flare (AF). SF samples were also collected from 15 OA knees treated non-surgically. SF samples were collected from another 6 OA knees with no synovial pain, which were incubated with or without purified uPA. Proteins were extracted from the synovial tissues from 16 OA knees. [Results] In the SF samples from the flare knees, concentrations of uPA and PIC, and MMP-1 activity were higher in F compared to AF in most knees. Among the SF samples from end-stage OA knees, there was a positive correlation between the PIC concentration and MMP-1 activity. Among the extracted proteins, a positive correlation was found between the activities of plasmin and MMP-1. [Conclusions] The results of this study suggested that in OA knees, MMP-1 may be activated in synovial fluid or within the synovium by plasmin, which could be involved in disease progression.

P2-065

Alteration in DNA methylation mechanisms in a rat model of osteoarthritis of the hip

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Conflict of interest: None

[Objective] This study aimed to investigate the methylation mechanism in the synovial tissue of the rat hip joint in a monoiodoacetate (MIA)-induced OA model. [Methods] SD rats were used to create the MIA group (n=6), in which 2 mg of MIA + 25 μl of sterile saline was administered to the right hip joint, the Sham group (n=6), in which only 25 μl of sterile saline was injected, and the Control group (n=6), which was untreated. Pain behavioral evaluation and radiographic evaluation were performed at 2 and 4 weeks. Histological changes and gene expression of DNA methylation-related enzymes (Dnmt 1, 3a, 3b, Tet 1, 2, 3) in the synovial tissue were assessed at 4 weeks. [Results] Pain thresholds were significantly lower in the MIA group than in the other groups. The radiographic assessment revealed a narrowing of the joint space and the migration of the femoral head in the MIA group. Histological evaluation clarified osteoarthritic changes in the MIA group. In the synovial tissue, gene expression of Dnmt 3a and Tet 1 was significantly increased in the MIA group. [Conclusions] In the MIA group, the gene expression of Dnmt 3a and Tet1 was significantly up-regulated in synovial tissues. This suggests that alterations in the epigenetic mechanisms may be involved in the onset and progression of OA.

P2-066

Secondary osteoarthritis of knee in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] In recent years, patients with rheumatoid arthritis (RA) often have osteoarthritis of knee. This study investigated relationship between the site of osteophyte formation in the knee and the patients' background. [Methods] The 644 knees of RA patients were enrolled. Osteophyte grades of medial and lateral femur and medial and lateral tibia were

evaluated. We categorized as follows: ML group, medial and lateral progression; M group, medial progression; L group, lateral progression; and N group, no progression. The patients' background of ML, M, and L groups were compared with those of N group. [Results] The mean observation period was 4.7 years. Prevalence of ML, M, L, and N groups were 55 knees (8.5%), 78 knees (12.1%), 63 knees (9.8%), and 448 knees (69.6%), respectively. The factors associated with progression of osteophyte grades were BMI (ML: 24.2, N: 22.1) and DAS28-ESR at follow-up (ML: 2.8, N: 2.4) in ML group, age (M: 67.1, N: 59.8) and baseline MMP-3 (M: 170.5 ng/mL, N: 93.9 ng/mL) in M group, age (L: 66.5, N: 59.8), baseline DAS28-ESR (L: 3.4, N: 2.8) and MTX use (L: 57.1%, N: 70.8%) in L group, respectively. [Conclusions] Our results suggest that the factors of associated with progression of osteophyte differ depending on the site of knees in RA patents.

P2-067

Research of the need for dose adjustment due to changes inrenal function in patients receiving long term Hydroxychloroquine (HCQ) treatment

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Conflict of interest: None

Object: HCQ is used as the standard treatment for SLE, but there are concerns about retinal toxicity. It was recommended not exceed 5 mg / kg of actual body weight and dose reduction with renal dysfunction but renal function changes overtime due to SLE itself and drug-related adverse events. In this study, we investigated the changes in renal function of patients receiving long-term HCQ at our hospital to know the necessity of dose reduction. Method: 93 have been receiving HCQ for more than 3 years were examined for age, sex, height, weight, HCQ dosage, renal function etc. retrospectively from the medical records. Result: The median age was 50 years, 82 females, Ht 157 cm, Wt 55 kg, Cr 0.7 mg/dL, eGFR 71, HCQ dose per actual body weight 4.2 mg/kg/day, classification of CKD G1/G2/G3/G4 17/51/23/3 each. After 3 years, 15 cases had improved renal function, 9 had worsened, and 2 were recommended to reduce. Consideration: It is important to support patients not only at the time of drug initiation but also periodically to confirm that the HCQ dosage is appropriate.

P2-068

Predictors for the efficacy of hydroxychloroquine in patients with systemic lupus erythematosus receiving the maintenance therapy

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Conflict of interest: None

[Objective] To identify predictors for the efficacy of hydroxychloroquine (HCQ) in treatment of rash, arthritis and systemic symptoms such as fatigue in systemic lupus erythematosus (SLE) patients. [Methods] We reviewed our SLE patients receiving the maintenance therapy who started HCQ for rash, arthritis or fatigue between Mar 2016 and Sep 2021, and then conducted multivariate logistic regression analysis to identify predictors for the response to HCQ. [Results] Forty-five SLE patients were extracted in our review. The age was 41.7±15.1 years, the male-female ratio was 7:38, and the disease duration was 8.6±8.7 years. At the start of HCQ, the prednisolone (PSL) dosage was 5.1±3.0 mg/day, anti-dsDNA antibody was 15.2±25.6 IU/mL, C3 was 87.2±24.7 mg/dL, CRP was 0.30±0.49 mg/dL, and antibodies to Sm, RNP and SS-A were positive in 12, 21 and 34 patients, respectively. Improvement was obtained in 17 patients three months after the start of HCQ in the physician global assessment. The multivariate analysis identified PSL dosage (odds ratio (OR) 0.65), positivity of anti-SS-A antibody (OR 0.07) and CRP (OR 15.5) as significant predictors for the response to HCQ. [Conclusion] Lower PSL dosage, absence of anti-SS-A antibody and CRP elevation could predict the efficacy of HCQ in SLE patients.

P2-069

Effect of Hydroxychloroquine on glucocorticoid reduction in stable SLE

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) has been shown to suppress SLE recurrence, protect organs, and improve prognosis, but its use in Japan has been short and the significance of starting administration during the stable phase in unclear. [Methods] Seventeen patients with stable SLE who had not changed their GC dosage for more than 6 months at our outpatient clinic. The primary outcome was a mixed-effects model of GC dosage at 6 and 12 months after HCQ administration. [Results] Mean age 53 years, female 88%, duration of SLE 14 years, mean GC 7.3 mg (PSL equivalent), 41% on concomitant immunosuppressive drug, C3 94 mg/dl, C4 17 mg/dl, anti ds-DNA antibody positive rate 47%, SLEDAI-2K 3.0. 12 months after starting HCQ (mean 4.7 mg/kg), GC significantly decreased ($p<0.001$). Mean GC (PSL equivalent) at 6 and 12 months after HCQ was 4.0 mg and 3.4 mg, respectively. [Conclusions] We believe that the addition of HCQ may increase the possivility of GC reduction in SLE patients who have achieve low disease activity.

P2-070

A case of systemic lupus erythematosus treated with multidisciplinary therapy for severe heart failure due to myocarditis

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Conflict of interest: None

[Case] A-20-year-old female presented with dyspnea after catching a cold one month before admission to our hospital. She was diagnosed with acute heart failure with a left ventricular ejection fraction of 15% and transferred to our hospital. She was managed with a ventilator and percutaneous ventricular assist device. A large amount of pericardial effusion was observed, and an endomyocardial biopsy showed lymphocytic myocarditis. She was diagnosed with systemic lupus erythematosus (SLE) based on butterfly rash, positive antinuclear antibody, positive anti-ds-DNA antibody, hypocomplementemia, and proteinuria. She was treated with methylprednisolone pulse therapy and plasma exchange (PE) therapy. With improved cardiac function, she was weaned to the ventilator and ventricular assist device management. A renal biopsy revealed lupus nephritis type IV. Hydroxychloroquine and mycophenolate mofetil were added. She was discharged from the hospital after the remission of lupus nephritis and recovery of EF to 50%. [Clinical Significance] This case is the rare report of severe SLE complicated by myocarditis treated with PE therapy.

P2-071

A case of elderly-onset SLE with acute myelocytic leukaemia treated with combination therapy with venetoclax and azacitidine

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Conflict of interest: None

[Case] A 66-year-old man with developmental disorder. SASP started in X-5 years with a diagnosis of serologically positive RA. X-2 years, he first came to our hospital with the appearance of purpura and ulceration of the tips of his fingers in winter. He was diagnosed with elderly-onset SLE based on pancytopenia, hypocomplementaemia, positive direct Coombs test, skin biopsy showing C3 and IgG deposition along basement mem-

brane and no atypical cells or chromosomal abnormalities on bone marrow puncture. Joint symptoms, haemoptysis, purpura of the fingers in winter were persistent under treatment. In July X, fever, night sweats and the appearance of myeloblasts in the peripheral blood were observed. Bone marrow biopsy confirmed the diagnosis of acute myelocytic leukaemia. Bone marrow transplantation was difficult due to the patient's age and lack of awareness of the disease, and combination treatment with venetoclax and azacitidine was initiated. The myeloblasts in the peripheral blood disappeared rapidly and the patient has progressed without recurrence of joint symptoms or skin rash. [Discussion] The combination of venetoclax and azacitidine is a novel therapy approved for acute myeloid leukaemia, but its impact on patients with collagen disease is unknown.

P2-072

Successful treatment of refractory thrombocytopenia by thrombopoietin receptor agonist in a patient with systemic lupus erythematosus accompanying anti-phospholipid syndrome

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Conflict of interest: None

[Case] A 52-year-old female with a 41-year history of systemic lupus erythematosus (SLE) was referred. At the onset of SLE, she presented with malar rash, arthritis, and diffuse lupus nephritis. She had deep vein thrombosis induced by anti-phospholipid syndrome (APS). In her forties, prednisolone (PSL) was increased to 60 mg/day because of the disease flare. Then, the PSL was tapered, but immunosuppressants were not started because of recurrent respiratory infections accompanying bronchiectasis. Hydroxychloroquine was started for thrombocytopenia, but was not effective. At the referral, her platelet was 2×10^4/μL. Although PSL was increased from 9 mg/day to 30 mg/day, her platelet did not increase. Considering her persistent hemoptysis, romiplostim was started in spite of the coexisting APS. The drug was started at the minimum dosage and was gradually increased to maintain the platelet above 10×10^4/μL. Her hemoptysis disappeared without thrombosis. [Clinical Significance] Administration of thrombopoietin receptor agonists (TPO-RAs) in patients with APS is associated with thrombosis, and thrombosis developed in patients with normal platelet counts have been reported. Our case was successfully treated with the TPO-RA without thrombosis by titrating the drug vigilantly.

P2-073

A Case of life-threatening SLE Treated in a Remote Island

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Conflict of interest: None

A 34-year-old woman presented with one month duration of anorexia, progressive inability to move and bilateral leg edema. She had been socially withdrawn since her late teenager. Vital signs on arrival showed fever, tachycardia, and hypoxia. Physical examination revealed decreased breath sounds in both the lungs, and bilateral leg edema. Laboratory tests revealed renal dysfunction, hypocomplementemia, hypoalbuminemia, and cytopenia. Urinalysis revealed proteinuria and glomerular red blood cells. Radiography showed bilateral pleural effusions, and transthoracic echocardiography indicated pulmonary hypertension. Prednisolone 1 mg/kg and diuretics were administered. Antinuclear, anti-dsDNA, anti-Smith, and anti-U1RNP antibodies were positive. Renal biopsy revealed type IV lupus nephritis, and right-sided heart catheterization revealed pulmonary hypertension. Cerebrospinal fluid analysis revealed elevated IL-6 level and positive anti-neuronal cell and anti-NR2 antibodies. Mycophenolate mofetil, tacrolimus, hydroxychloroquine, belimumab were administered. Endothelin receptor antagonist (macitentan) and PDE inhibitor (tadalafil) alleviated her symptoms. This case illustrates challenges in treating life-threatening case of SLE on a remote island. We reviewed the literature on NPSLE.

P2-074

Feasibility of glucocorticoid-free maintenance therapy for systemic lupus erythematosus

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Conflict of interest: None

[Objective] To investigate feasibility of glucocorticoid-free maintenance therapy for systemic lupus erythematosus (SLE) [Methods] Disease activity was assessed with the British Isles Lupus Assessment Group (BILAG) index. Remedies in the remission induction phase and maintenance phase were retrospectively analyzed. [Results] Thirty-one patients (female 29) were enrolled. The average age and disease duration were 50.2±15.2 yr., 9.1±7.5 yr., respectively. Including 9 patients with lupus nephritis (LN), 21/31 patients had organ domain scores of ≥1A, and 22/31 patients had severe disease activity in one or more organs or moderate disease activity in two or more organs measured by the BILAG index as organ domain scores of ≥1A or ≥2B, respectively. Remission induction therapy with glucocorticoids was administered in 25/31 patients, and 21/31 (68%) patients maintained remission without glucocorticoids. Of the 22 patients with BILAG ≥1A or ≥2B, 20 patients had remission induction therapy with glucocorticoids, and 13 patients (57%) including 4 patients with LN maintained remission without glucocorticoids. [Conclusions] The majority of patients with severe or moderate disease activity of SLE can maintain remission without glucocorticoids.

P2-075

A case of systemic lupus erythematosus with Epstein Barr Virus reactivation

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Conflict of interest: None

The patient is a 58 years old man. 20 years ago, he developed SLE upon fever, erythema, a positive lupus band test, but he interrupted commuting to hospital. On Y/19/X he had a headache, and following day, fever, neck pain, and edema of extremities appeared, and he visited our department on 27. On admission, he also had polyarthralgia, and pale erythema on the upper back, which spread to the whole body within a few days. Because of anti-DNA antibodies and multiple lymphadenopathy, we performed skin biopsy and lumbar puncture to rule out malignant lymphoma. Atypical lymphocytes were found in CSF and skin tissue, and we added lymph node biopsy. There were no findings for malignant lymphoma, but many EB virus positive cells. We found 1.0×10^5 virus copies per mL whole blood. Bone marrow biopsy and flow cytometry results were negative for chronic active EBV, and we treated him with PSL and IVCY for SLE. The clinical symptoms improved quickly and atypical lymphocytes disappeared after treatment. EBV infection is proposed as a contributing agent in the development or exacerbation of SLE, as more than 99% of patients with SLE infected with EBV. SLE with EBV activation as in this case, it is difficult to distinguish it from malignant lymphoma or CAEBV, and careful diagnosis is necessary.

P2-076

A case of hypothyroidism with pericardial, thoracic and abdominal effusions requiring differentiation from serositis associated with SLE

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Conflict of interest: None

[Case Presentation] The patient was a 33-year-old woman. Her symp-

toms were fever and arthralgia 4 years ago. Laboratory tests showed leukopenia, positive anti-RNP antibody, and hypocomplementemia, but no diagnosis was made. At that time, thyroid hormone was started for hypothyroidism. Later, she was diagnosed with SLE due to alopecia and progression of hypocomplementemia, but she refused drug therapy. She stopped coming to the hospital, and gradually developed fatigue, alopecia, and leg edema. She visited the hospital due to respiratory distress and was noted to have a large amount of pericardial and thoracoabdominal effusion. After pericardial drainage, 500 ml of serous fluid was obtained. Blood tests showed pancytopenia and elevated CK. Hypocomplementemia had not worsened, while hypothyroidism was worsening. After thyroid hormone replacement therapy, pericardial and thoracoabdominal effusions decreased. Pancytopenia did not improve, and hydroxychloroquine was started. [Clinical Significance] SLE is often complicated by hypothyroidism. Fatigue, alopecia, leg edema, CK elevation, pericardial and thoracoabdominal effusions are common findings in both diseases, but the pathology is different. We discuss the differences in pathology and the management of complicated cases.

P2-077

Clinical features of 6 cases of SLE with cervical cancer or dysplasia

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Conflict of interest: None

[Background] It is known that SLE has a high risk of complication of cervical cancer. It has been pointed out that there is a relationship between immunological abnormalities due to SLE or treatment and human papillomavirus (HPV). [Purpose] To analyze these cases of SLE with cervical cancer or dysplasia, clarify the clinical characteristics, and raise awareness of the importance of HPV vaccines, screening, and cervical cancer risk. [Results] The ages at diagnosis of cervical cancer or dysplasia ranged from 32 to 44 years, and the duration of SLE ranged from 4 to 27 years. Two had moderate dysplasia (CIN2) and were followed up, two had severe dysplasia (CIN3) and had cervical conization, and two had cervical cancer and underwent total hysterectomy. Glucocorticoids were taken orally from 0 mg to 12.5 mg/day of PSL, immunosuppressants had been administered with AZA in 3 cases, TAC in 1 case, and HCQ in 4 cases. [Clinical Significance] With accumulation of case reports such as our one, it is important that clinicians are aware of the risk of cervical cancer or dysplasia in SLE patients, and encourage patients to take screens and cervical HPV vaccines. In addition, if cervical dysplasia is observed, careful follow-up is required in cooperation with gynecologists.

P2-078

A case of neuropsychiatric systemic lupus erythematosus previously diagnosed schizophrenia manifested by impaired consciousness during close examination of pulmonary aspergillosis

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Conflict of interest: None

[Case] A 57-year-old woman. She had been treated with schizophrenia and eating disorder for several decades. She was suspected to have lung cancer and underwent a close examination. Glucocorticoid pulse therapy was administered, because of Hashimoto's encephalopathy was suspected. After that, she was diagnosed with systemic lupus erythematosus and NPSLE due to positive antinuclear antibody, anti-dsDNA antibody, anti-Sm antibody, anti-ribosomal P antibody, hypocomplementemia and high IL-6 levels in CSF. Lupus nephritis was also suspected because of urine protein and hematuria. After treatment with glucocorticoid, consciousness gradually improved. Chronic lung aspergilloma was diagnosed by bronchoscopy. Neuropsychiatric Symptoms (dysuria, constipation, and dysphoria) was suspected caused by NPSLE, were improved with intravenous cyclophosphamide pulse therapy. [Clinical Significance] The possibility that some of her psychiatric symptoms, which had been treated for many years as schizophrenia, were caused by NPSLE could not be ruled out. When treating a patient with neuropsychiatric symptoms of any kind, the possibility of NPSLE should not be ruled out even in the presence of a diagnosis of another disease, and active examination and therapeutic intervention are important.

P2-079

Systemic lupus erythematosus manifesting as persistent enteritis

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Conflict of interest: None

A 16-year-old girl manifested persisting lower abdominal pain with diarrhea following transient skin rash in extremities. Laboratory data in the neighboring hospital showed hypoalbuminemia with proteinuria, and computed tomography (CT) with contrast enhancement demonstrated comb and target signs suggestive of edema ascribable to severe enteritis, ascites, hydronephrosis and diffuse hypertrophy in the bladder wall. Based on positive results of anti-DNA, anti-Sm and anti-nuclear antibodies, she was diagnosed as having systemic lupus erythematosus (SLE) with enteritis and cystitis in our hospital. Prednisolone (PSL) at a dose of 60 mg/day quickly relieved her clinical symptoms in parallel with improvement of CT findings. A transient exacerbation was seen while tapering PSL, but she has been in good general condition after commencement of hydroxychloroquine and tacrolimus in addition to PSL following steroid pulse therapy. Lupus enteritis is a rare visceral manifestation of SLE producing non-specific clinical symptoms, such as abdominal pain and diarrhea. We should consider lupus enteritis as a possible diagnosis when abdominal symptoms are persistent, particularly in young female patients.

P2-080

A case of drug-induced lupus erythematosus caused by etanercept biosimilar (ETN-BS)

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Conflict of interest: None

[Case] A 78-year-old woman with an 18-year history of RA was referred to our hospital due to a skin rash and fever. She has been treated with MTX and tacrolimus for long term but developed pancytopenia in 3 months ago. Then MTX was discontinued. Since pancytopenia was improved, ETN-BS and tacrolimus was started in 2 months ago. Antibiotic therapy in previous doctor was ineffective. Chest computed tomography showed ground-glass opacity. Erythematous macules with desquamation appeared mainly on sun-exposed areas. Blood examinations revealed pancytopenia (WBC 2,400 /μL, Hb 8.2 g/dL, Plt 28,000 /μL), positive antinuclear antibody (320x, homogeneous pattern), low complement (C3 25 mg/dL, C4 3 mg/dL), negative anti ds-DNA IgG antibody and positive anti ss-DNA IgG antibody. Then we diagnosed the drug-induced lupus caused by tumor necrosis factor (TNF) inhibitors. After discontinuation of ETN-BS, arthralgia worsened and skin rash and pancytopenia did not improve. The patient's clinical conditions improved promptly after starting PSL 20 mg, There was no relapse even after tapering of PSL. [Clinical Significance] Patients using TNF inhibitors should be aware of the possibility of drug-induced lupus.

P2-081

A case of systemic lupus erythematosus with hoarseness possibly caused by cricoarytenoid arthritis at onset

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Conflict of interest: None

[Case] A 46-year-old woman had been suffering from arthralgias of the whole body joints for which methotrexate were ineffective for 3 months. She developed hoarseness and was referred to our hospital a month later. Ultrasound examination showed no space occupying lesion in her neck. Recurrent nerve palsy was negative because laryngoscopy revealed movement of the laryngeal region, but the vocal folds were suspected to be open and fixed due to poor mobility of the cricoarytenoid joints.

Concerned about airway obstruction, we started prednisolone (PSL) at 30 mg/day. Hoarseness was improved in two weeks and vocal cord movement had normalized. On the second examination, she was diagnosed with systemic lupus erythematosus based on polyarthritis, bilateral pleurisy, lymphocytopenia, glomerular hematuria, antinuclear antibodies 2560x (homogeneous pattern), positive anti-ds-DNA antibodies, and hypocomplementemia. Renal biopsy also revealed lupus nephritis class III. She received remission induction therapy with high-dose PSL, mycophenolate mofetil and hydroxychloroquine, and achieved a remission. [Conclusions] Few studies have reported about cricoarytenoid arthritis in SLE. However, we cannot rule out the possibility of SLE when we encounter a patient presenting with hoarseness.

P2-082

A case of systemic lupus erythematosus combined with protein-losing enteropathy and pseudo-pseudo Meigs syndrome

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Conflict of interest: None

59-year-old woman presented with loss of appetite, abdominal distention, and lower leg edema. An ovarian mass, ascites and elevated CA-125 in serum and ascites were pointed out, but ascites cytology was negative and ovarian mass is not cause of ascites retention. Protein-losing enteropathy (PLE) was diagnosed by scintigraphy. Systemic lupus erythematosus (SLE) was suspected from positive antinuclear antibodies, hypocomplementemia, positive anti-phospholipid antibody, and ascites retention due to serositis. A disease with pleural and abdominal ascites occurred due to ovarian fibroma and disappeared by remove of tumor is called Meigs syndrome. It is also called pseudo-Meigs syndrome that pleural and abdominal ascites is presented by ovarian tumors expect fibromas. On the other hand, pseudo-pseudo Meigs syndrome (PPMS) is a rare manifestation of SLE, defined by presence of ascites, pleural effusion and elevated CA-125 level in the absence of ovarian tumor. She was diagnosed with SLE combined with PLE and PPMS, and intravenous treatment of methylprednisolone 60 mg/day was started. Ascites decreased and hypoalbuminemia improved gradually after treatment, and she was discharged after 9 weeks of treatment. Her we reported a case of SLE with PPMS and PLE, based on past a few case reports.

P2-083

A case of SLE with protein-losing gastroenteropathy after ovarian tumor resection

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Conflict of interest: None

We reported a case of SLE that developed due to protein-losing gastroenteropathy (PLE) immediately after ovarian tumor resection. A 25-year-old female patient underwent laparoscopic ovarian encephalomectomy for a right ovarian mature cystic teratoma in December X. Nausea and diarrhea appeared on the second postoperative day. On CT scan, intestinal edema of the small and large intestine and large amount of pleural effusion were observed. We diagnosed her as PLE based on hypoalbuminemia, leakage of RI from the intestinal tract on protein leak scintigraphy, ANA160, positive for anti-Sm antibody, positive for aPL, hypocomplementemia, and hemolytic anemia, glomerulonephritis. Steroid pulses were administered, followed by PSL 1 mg/kg/day, HCQ 200 mg/day, and MMF 2 g/day, achieved LLDAS. After 1.5 years of surgery, PSL 3 mg/day, HCQ, and MMF were treated. Discomfort on her back, polyarthritis, and hemolytic anemia were found. Right ovarian tumor was detected by CT. SLE activity increased at the time of recurrence of the ovarian tumor. Discussion: We suggested that hypoalbuminemia and pleural effusion associated with SLE could lead to PLE, pseudo-pseudo Meigs' syndrome, and so on.

P2-084

A case of systemic lupus erythematosus in which protein-leaking gastroenteropathy caused May-Thurner syndrome

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Conflict of interest: None

A 47-year-old woman with systemic lupus erythematosus 28 years ago and lupus nephritis type V 7 years ago was treated with prednisolone (PSL) 1 mg, mycophenolate mofetil 1 g, hydroxychloroquine 200 mg and tacrolimus 3 mg, and his symptoms were generally stable, although he still had hypocomplementemia. 1 month earlier, a thrombus appeared in the left femoral vein to the common iliac vein, and he was diagnosed with May-Thurner syndrome and started on Reveroxin. He was suspected to have protein-leakage gastroenteropathy and was admitted to the hospital for a thorough examination. Protein leak scintigraphy suggested protein leakage from the duodenum to the jejunum, so PSL 50 mg was started. Protein S/C was decreased but improved with treatment, and venous thrombus, which remained unchanged after 1 month of anticoagulation therapy, showed a tendency to shrink 2 weeks after the start of PSL treatment. Clinical Significance: The loss of fibrinolytic factors from the intestinal tract due to protein leakage gastroenteropathy is thought to have led to the formation of a large venous thrombus. We report a case in which PSL therapy was effective in treating a venous thrombus that had not improved with anticoagulation therapy.

P2-085

Clinical characteristics of gastrointestinal lesions in patients with systemic lupus erythematosus: A retrospective single-center study

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Conflict of interest: None

[Objective] To clarify the clinical characteristics of gastrointestinal (GI) lesions in patients with systemic lupus erythematosus (SLE). [Methods] We performed a retrospective analysis of SLE patients treated at our single center between 2012 and 2022 who suffered from GI lesions associated with SLE. [Results] Nine patients with SLE were identified. Of these, six had lupus enteritis, one had protein-losing gastroenteropathy, one had lupus peritonitis, and one had appendiceal perforation. The median age was 50 years, and eight patients were female. Six patients had other organ diseases, such as lupus nephritis; however, two patients had only GI lesions as the initial manifestation of organ damage. The mean SLE Disease Activity Index score at GI onset was 15. While two patients had pathologically confirmed vasculitis or ischemic enteritis, the others did not. Eight patients were treated with high-dose steroids; two received a combination with intravenous methylprednisolone, three received intravenous cyclophosphamide, and one patient spontaneously improved. Eight patients improved; however, one died of serious infections during treatment. [Conclusions] Diverse manifestations were observed, and various treatment intensities were administered for GI lesions in SLE patients.

P2-086

The achievement of lupus low disease activity state (LLDAS) and Its related factors in patients with systemic lupus erythematosus (SLE) in clinical practice

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Conflict of interest: None

[Objective] In recent years, the treat-to-target principle in SLE has been proposed, and Lupus Low Disease Activity State (LLDAS) is one of the treatment targets in SLE. On the other hand, the reduction of glucocorticoid dosage is associated with the risk of SLE relapse. This study exam-

ined the frequency of LLDAS achievement in our hospital and the association between LLDAS achievement and SLE relapse. [Methods] Seventy-nine patients (73.8%) met the LLDAS; LLDAS was achieved in 64.3% of patients with a history of SLE relapse and 84.3% without a history of relapse. In particular, patients with a history of lupus nephritis relapse had a lower LLDAS achievement rate than those without a history of lupus nephritis relapse (52.6% of patients with nephritis relapse and 78.4% of patients without a relapse). (Relapse of SLE: odds ratio 0.410, p=0.056; Relapse of lupus nephritis: odds ratio 0.305, p=0.026). [Conclusions] In our study, LLDAS was achieved in 73.8% of SLE patients, and to achieve LLDAS, therapeutic strategies to prevent disease relapse during the disease, especially renal disease relapse, are needed.

P2-087

The effect of shared decision making to LLDAS achievement in systemic lupus erythematosus: TRUMP2-SLE

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Conflict of interest: None

[Objective] Although the importance of shared decision making (SDM) in systemic lupus erythematosus (SLE) is mentioned in EULAR recommendation, there is a little evidence about its clinical efficacy. Here we examined the effect of SDM to Lupus Low Disease Activity State (LLDAS). [Methods] Patients were enrolled at 5 facilities in Japan. We considered the association with SDM scale SDM-Q-9 at enrollment and LLDAS one year later. Binary logistic regression analysis was conducted with age, sex, disease duration, SLEDAI, physician global assessment, treatment, major organ dysfunction, complications, and adverse events at enrollment as moderator variables. [Results] 316 patients were analyzed (age 45.7±14.1 years old, female 88.0%, median SDM-Q-9 76 [62-89]). We classified patients into high SDM group (SDM-Q-9 score≧76) (n=172) and low SDM group (SDM-Q-9 score≦75) (n=144). In high SDM group, ciclosporin was used more commonly (2.4% vs. 7.6%, p=0.034) but there were no significant differences in the other parameters and LLDAS (high SDM group vs. low SDM group: 36.7% vs. 38.7%, p=0.80). Binary logistic regression analysis did not identify SDM-Q-9 at enrollment as an independent factor for LLDAS one year later (p=0.99). [Conclusions] We couldn't show the effect of SDM on LLDAS in this study.

P2-088

Clinicl study of pregnancy in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] SLE usually develops in WoCBA, therefor management of disease control is desired for pregnancy. The purpose of this study is to investigate the changes in disease activity, treatment, effects on pregnancy and delivery during pregnancy in SLE patients. [Methods] We retrospectively investigated 29 SLE patients (46 pregnancy) who have got pregnant since April 2009 till December 2021 in our hospital. [Results] The average age at pregnancy was 35.4 years old. Thirty-five patients were treated with GC (PSL6.6 mg/day), and 12 patients were concomitantly administered immunosuppressants. The average SLEDAI was 6, BILAG was 1. Thirty-six patients were planned pregnancy and 2 patients were complicated hypertensive disorders of pregnancy. Twenty-seven babies were birth in full term, 6 were in premature, 9 were miscarry and 1 were born dead. The group of full term birth were treated with lesser doses of GC (PSL 4.4 mg/day) than the group of non-full term birth (PSL6.6 mg/day). Five patients had moderate flare of SLE, they were controlled only by increased GC. [Conclusion] Although the pregnancy complications for maternal were few, non-full term birth were increased in our hospital. It indicated the importance of pregnancy after controlling the disease by reducing the GC as much as possible.

P2-089

Scleroderma-like immune-related adverse event (irAE) caused by atezolizumab administered in a patient with lung squamous cell carcinoma

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Conflict of interest: None

[Case] An 83 years old man had been treated with atezolizumab for lung cancer for two years. One month before, pruritus in trunk and limbs, and painful edema in lower legs were appeared. At his first visit, skin sclerosis was observed in his fingers to forearms, dorsum to lower legs, and trunk, however abnormal nail fold capillaries and Raynaud's phenomenon were not observed. Antinuclear antibody and systemic sclerosis (SSc) specific autoantibodies were all negative. Skin biopsy from his forearm revealed dense collagen deposition with inflammatory cell infiltration mainly consist of lymphocyte in dermis. We diagnosed him as SSc like immune-related adverse event (irAE). Topical steroid therapy was not effective, and he was treated with oral PSL 25 mg/day (0.5 mg/kg/day). One month after, modified Rodonan's total skin thickness score (mRSS) was improved from 38 points to 31 points. However, further improvement was not seen, and PSL was gradually reduced and ceased. [Clinical Significance] In this case, skin sclerosis started from legs and rapidly extended to the trunk. His symptoms were not typical of SSc, and we diagnosed him as SSc like irAE. Since atezolizumab induced scleroderma was very rare skin irAE, we will report this case as an important case need to differentiate from SSc.

P2-090

A case of mixed connective tissue disease with drug-induced perimyocarditis due to tacrolimus

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Conflict of interest: None

A 64-year-old woman had general malaise, edema, finger joint pain, and progressive weight loss. She came to our hospital, suspected to mixed connective tissue disease (MCTD) based on myalgia, elevated CK, positive for anti-U1-RNP antibody. In addition echocardiography revealed right heart stress findings, and cerebrospinal fluid examination revealed coexistence of aseptic meningitis. Based on these examination, she was diagnosed with MCTD. Treatment was started with prednisolone (PSL) 40

mg. Since myogenic enzymes did not decrease, tacrolimus (TAC) was added. However, after 10 days starting TAC, she was noticed chest pain and electrocardiogram (ECG) showed extensive ST-segment elevation. In addition elevation of myocardial enzymes were also found, From these results she was diagnosed with perimyocarditis due to TAC. After discontinuation of TAC, colchicine was started. The patient's course was good and ECG findings were normalized. Azathioprine (AZP) was started for myositis. We experienced a case of TAC induced perimyocarditis with MCTD patient. Perimyocardial myocarditis is a common complication of MCTD, however drug induced perimyocardial should be considered like this case. Herein, we report other cases of pericardial myocarditis caused by TAC experienced at our hospital.

P2-091

Two cases of systemic sclerosis-associated skin sclerosis and interstitial lung disease treated with rituximab

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Conflict of interest: None

A double-blind, investigator-initiated, randomized, placebo-controlled trial showed the efficacy of rituximab (RTX) with skin sclerosis and interstitial lung disease (ILD) in patients with systemic sclerosis (SSc), and RTX was approved for the treatment of SSc in 2021. We present two SSc patients treated with RTX. Case 1 is a 53-year-old woman having skin sclerosis, pulmonary hypertension, and ILD. Tests for disease-specific antibodies were negative. She was diagnosed with SSc when she was 51 and treated with prednisolone, cyclophosphamide, and nintedanib. However, skin sclerosis progressed and she was treated with RTX. After the treatment, skin sclerosis did not worsen and ILD did not improve. There was no adverse event. Case 2 is a 56-year-old woman having skin sclerosis and ILD. Anti-Scl-70 antibodies were positive and she was diagnosed with SSc when she was 53. She was treated with nintedanib, but it was discontinued due to liver injury. She was treated with RTX due to the progression of ILD. After the treatment, skin sclerosis improved. She developed infusion reactions at the first dose. In our cases, one patient improved skin sclerosis, and ILD was not improved in both patients. Further cases are needed to determine the best use of RTX.

P2-092

A case of mixed connective tissue disease with recurrent hypersensitivity pneumonitis

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Conflict of interest: None

The patient is a 44-year-old woman. She was diagnosed with MCTD based on Raynaud's phenomenon, swelling of the fingers, positive anti-U1-RNP antibody, polyarthritis, leukopenia, dermatosclerosis, and Interstitial lung disease (ILD). The patient had an exacerbation of ILD and was treated with prednisolone (PSL) 20 mg/day and tacrolimus. 2 years later, she was repeatedly hospitalized for pneumonia, and hypersensitivity pneumonitis (HP) was suspected. So she was treated only with antigen avoidance, which resulted in rapid improvement of the pneumonia. Bronchoalveolar lavage showed findings consistent with HP, and she was diagnosed with HP. She has been treated with PSL, azathioprine, belimumab, and hydroxychloroquine for the skin rash associated with MCTD, but has been hospitalized 15 times due to difficulty in identifying the antigen for HP. ILD associated with MCTD has many clinical and pathological similarities to HP, and the diagnosis of HP may be difficult to make under concomitant immunosuppressive drugs, including steroids. However, HP can be considered in cases that are relieved by antigen avoidance.

P2-093

A case of refractory erythema nodosum complicated with systemic sclerosis

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Conflict of interest: None

[Case] A 77-year-old woman. 10 years ago, she had Raynaud's phenomenon, continuous fever, and arthralgia. The blood test showed that antinuclear antibody was positive at 1:640 with discrete-speckled pattern and all specific antibodies were negative. 9 years ago, erythema nodosum (EN) occurred on her lower extremities. She was treated with non-steroidal anti-inflammatory drugs, colchicine, prednisolone (PSL), and methotrexate (MTX), but relapses of EN occurred several times a year. One year ago, skin biopsy revealed her diseases were systemic scleroderma and EN. She was treated with sildenafil and hydroxychloroquine, but these drugs showed only a partial effect. She was added on etanercept 50 mg, after skin lesions fade immediately and PSL was able to be finished. [Discussion] EN is a disease with a good response to treatment and a good prognosis. In case of insufficient effect, some detailed examinations, including a biopsy, are essential for diagnosis. Treatment for refractory cases includes case reports such as immunosuppressants, and TNFα inhibitor is one. It will be necessary to keep an eye on whether or not. [Clinical Significance] It is rare that EN is complicated with a scleroderma, which makes difficult to diagnose and treat.

P2-094

New clinical syndrome centered on centromere antibody-positive localized scleroderma systemic sclerosis

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Conflict of interest: None

[Objective] Anti-centromere antibody positive limited cutaneous systemic scleroderma (lcSSc) tends to be neglected because of the mild range and degree of skin symptoms compared to diffuse cutaneous type. However, it progresses chronically and complicates severe organ dysfunction and merges many other autoimmune diseases. [Methods] 124 patients who had hospitalized in our outpatient clinic from 2012 to 2022 were enrolled. All patients met the American College of Rheumatology classification criteria for lcSSc. We assess their clinical characteristics and data. [Results] Female were 109 (88%). Mean age was 67.2 years old. The duration between onset of Raynaud phenomenon and first visit was 8.5 year. Clinical characteristics; Incidence of Raynaud phenomenon and sclerodactylia were 76 and 88%. Organ damages; interstitial pneumonia, pulmonary hypertension, PBC, Sjogren syndrome, Hashimoto's disease were 44%, 34%, 45%, 51%, and 39%, respectively. Complications with other autoimmune diseases were rare. [Conclusions] Anti-centromere antibody positive lcSSc is a clinical syndrome which predominantly occurs in females, and complicates interstitial pneumonia, pulmonary hypertension, primary biliary cirrhosis, Sjogren's syndrome, and Hashimoto's disease at extremely high rates.

P2-095

No suppressive effect of calcineurin inhibitors on relapse of anti-synthetase syndrome

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Conflict of interest: None

[Objective] To clarify the therapeutic effect of calcineurin inhibitors (CNI) on relapses of anti-synthetase syndrome (ASS). [Methods] Participants were consecutive ASS patients who received the first induction ther-

apy in our department. Relapse was judged to occur when physicians decided to intensify the therapy for ASS. The Data on clinical features were collected by reviewing medical records. [Results] 44 patients (PM/DM: 26/18, ILD: 44, myositis: 32) were enrolled in this study. ILD and myositis were complicated in 44 and 32 patients, respectively. Anti-EJ, Jo-1, PL-12, and PL-7 Abs were detected in 11, 22, 6, and 5 patients. Relapse was 53 episodes in 21 patients (myositis only: 39.6%, ILD only: 33.9%, myositis, and ILD: 26.4%). No differences were found in relapse rates among patients treated with PSL alone (58.3%), those with PSL+CNI (58.3%), and those with PSL+CNI+MMF (56.3%). The relapse frequently occurred in patients with anti-EJ and Jo1 Abs (EJ: 72%, Jo-1: 55%, PL-12: 16%, PL-7: 0%). Patients with anti-EJ and Jo1 Ab relapsed at high frequency under additional CNI therapy (Jo-1: 66.7%, EJ: 50%). [Conclusions] The specificity of ARS Abs was associated with relapse. CNI might have little effect on preventing relapse.

P2-096

A case of anti-melanoma differentiation-associated gene 5 (MDA5) antibody-positive dermatomyositis complicated by interstitial lung disease (ILD) that presented with symptomatic myositis and was found to be co-positive for anti-Zo antibody

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Conflict of interest: None

Introduction; Anti-MDA5 antibody-positive dermatomyositis is characterized by clinically amyopathic dermatomyositis, frequently associated with rapidly progressive ILD. Anti-Zo antibody-positive dermatomyositis is rare. We report a case of dermatomyositis associated with symptomatic myositis and ILD, in which both anti-MDA5 and -Zo antibodies were positive. Case; A 64-year-old woman developed erythema on the extensor surface of the PIP MCP joints of both hands and on the front of the neck, face, and both upper eyelids in September of X year. In October of the same year, skin ulceration was observed on the extensor surfaces of the 2nd and 3rd DIP joints, and was found to be positive for anti-MDA5 antibody. A CT scan confirmed ILD. MMT4 muscle weakness in the proximal muscles of the extremities, mildly elevated creatine kinase and aldolase, and T2 high signal areas on MRI in the buttocks and thighs were observed. This was partly atypical for anti-MDA5 antibody-positive dermatomyositis, found to be anti-Zo antibody-positive. Discussion; Anti-MDA5 antibody-positive dermatomyositis presenting as symptomatic myositis requires consideration of co-positivity of other myositis-related positives. Reports of anti-Zo antibody-positive cases are very few, and this is a valuable case to study its clinical features.

P2-097

A case of dermatomyositis with new 5 anti-ARS antibodies

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Conflict of interest: None

[Background] As anti-aminoacyl-tRNA synthetase (ARS) antibodies, anti-Jo-1, EJ, PL-7, PL-12, KS, OJ, Ha, Zo antibodies are reported. [Case] A 52 years old female had Gottron sign, mechanic's hand, loss of upper limb muscle strength and polyarthritis. CK was 314 IU/L. CT scan showed IP. Though anti-ARS antibodies covered by insurance and myositis specific antibodies were all negative, she was treated with 50 mg prednisolone (PSL) and tacrolimus as a dermatomyositis with IP. Her symptoms improved and PSL was tapered. By immunoprecipitation using her serum and cell line lysate, arginine, leucine, isoleucine, bifunctional glutamate/proline, and lysine-tRNA synthetase were identified. [Discussion] This case had multiple new anti-ARS antibodies with characteristic symptoms. These antibodies will be new markers and help for the elucidation of the mechanisms of myositis specific antibody negative dermatomyositis.

P2-098

Anti-EJ and anti-Ro50 antibody positive dermatomyositis with interstitial lung disease: an autopsy case

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Conflict of interest: None

A 63-year-old Japanese male with a past medical history of myocardial infarction was diagnosed with interstitial lung disease (ILD) associated with dermatomyositis eight years ago. When the ILD worsened, cyclophosphamide (IVCY) was administered in a total of 3000 mg intravenously. The serum was positive for Anti-EJ and anti-Ro52 antibodies. Three years ago, he had an exacerbation of skin rash and ILD and was treated with a total of 1500 mg IVCY and rituximab. However, repeated infections made it difficult to administer further immunosuppressive drugs, and he was discharged with home oxygen therapy. One week before admission, he had dyspnea on exertion and weakness of proximal muscles, and the chest CT showed worsening ILD, and he was admitted to the hospital. Respiratory status once improved with steroid pulses and IVCY 500 mg but worsened again on day 16 of admission. Steroid pulses were added, but there was no improvement and he died. [Discussion] Anti-EJ antibodies, a type of anti-ARS antibody, occur less than 5% of the time in myositis and there are few reports of detailed clinical features. On the other hand, in anti-ARS antibody-positive patients, the prevalence of anti-Ro52 antibodies is not uncommon and has been reported to be up to 50%.

P2-099

A case of recurrent anti-PL-7 antibody-positive dermatomyositis with pericardial effusion successfully treated by addition of mizoribine to tacrolimus and steroid

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Conflict of interest: None

[Case] A 73-year-old female was referred to our hospital because of Gottron's sign, elevated serum CK levels, and rapidly progressive interstitial pneumonia (RP-IP). Anti-PL-7 antibody was detected and she was diagnosed with dermatomyositis (DM). Initiation of 55 mg of PSL and 3 mg of TAC (day 0) resulted in rapid resolution of the IP. High-dose intravenous gammaglobulin therapy normalized serum CK levels. After tapering of PSL to 40 mg (day 54), severe pericardial effusion was noted (day 61). Becasuse neither malignancy nor infectious diseases including tuberculosis which could cause pericarditis were found, and because pericarditis was common in patients with PL-7 positive DM, we considered the pericarditis was due to relapse of DM. As valganciclovir could not be used against concomitant CMV infection for its dermal side effect, MZR, which had been reported to have anti-CMV effect and mild immunosuppressive effect, was employed. After addition of MZR (day 62), the pericardial fluid gradually decreased. PSL was successfully reduced to 5 mg, while maintaining remission. [Clinical Significance] PL-7 positive DM is intractable, and it is not known which immunosuppressant is preferable. This is a valuable case showing the addition of MZR to TAC and steroid led successful result.

P2-100

A case of IVCY for refractory anti-Jo-1 antibody-positive interstitial pneumonia without myositis

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Conflict of interest: None

A 61-year-old woman presented with cough and dyspnea that had been worsening. She was consulted to our department because of multiple pneumonias and positivity for anti-Jo-1 antibody. Physical examination revealed no skin and muscle findings. CK did not elevate, MRI showed no findings. Although she did not meet the diagnosis of polymyositis, she was

started on high-dose steroid therapy and TAC as polymyositis. Oxygenation gradually improved, but the patient required the use of 1 L of oxygen at the time of discharge. TAC was increased and PSL tapering continued, but when PSL was reduced to 15 mg, CRP elevated. CT scan of the chest showed residual pneumonia. She was considered to have refractory interstitial pneumonia, and IVCY was administered, and the CRP and symptoms improved. Some patients with idiopathic interstitial pneumonia do not fulfill the diagnostic criteria for connective tissue disease (CTD), but have features of CTD, called Interstitial Pneumonia with Autoimmune Features (IPAF). Treatment of IPAF is currently individualized, and although it has been reported that IPAF tends to respond well to treatment, the patient in this case was refractory. We report a case of a patient with refractory anti-Jo-1 antibody-positive interstitial pneumonia who had a response to IVCY.

P2-101

A case of polymyositis with high-degree muscle atrophy which was useful by doing rehabilitation

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Conflict of interest: None

BACKGROUND In inflammatory myopathies, some reports mentioned the safety and efficacy of early rehabilitation. CASE PRESENTATION A 66-year-old man presented to his primary care physician for polyarthralgia a year ago. In April of X year, he developed weakness in the lower extremities and consulted a neurologist in our hospital. Neurophysiologic testing was performed for muscle weakness. Neuropathy was negative. In blood test, anti-aminoacyl tRNA synthetase antibodies was positive and serum creatinine kinase (sCK) was elevated (5259 U/l). So, he visited our department with suspicion of inflammatory myopathy. Manual muscle testing grades were 3 or 4 in extrimities and electromyography showed chronic myopathic muscular atrophy. Skeletal muscle CT scan showed severe atrophy of the iliopsoas and in muscle biopsy there was gross fatty degeneration in the left biceps brachii muscle. We diagnosed polymyositis with a chronic course of severe atrophy. We treated systemic glucocorticoids and started rehabilitation at the same time. 3 weeks after treatment, muscle weakness was improved and sCK was normalized. DISCUSSION In autoimmune myositis with severe atrophy, early rehabilitation is effective. CONCLUSION We report a case of polymyositis for which rehabilitatio was effective.

P2-102

Giant cell arteritis remitted spontaneously in a woman with mild dementia

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Conflict of interest: None

[Case Presentation] A 76-year-old lady living by herself was found to have myalgia, fever, and lethargy and was brought to a nearby clinic by her daughter. She had become gradually forgetful and lethargic over several months, which was later diagnosed as Alzheimer's disease (AD). Fever was refractory to NSAIDs and antibiotics. She was diagnosed with polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) afterwards for the presence of compatible symptoms and laboratory data. Considering AD and her reluctance to take treatment, she and her family requested observation approach rather than immunosuppressive therapy. Her disease activity worsened for two months, but showed gradual improvement after a plateau. Her symptoms almost diminished after a year, with inflammatory markers in normal range. [Clinical Significance] Current guidelines strongly recommend against observational and symptomatic approach for GCA and PMR, but old literatures reported several cases in whom the diseases remitted spontaneously or with NSAIDs. Along with the growing number of old people with dementia, we are expected to see more PMR/GCA patients without adequate ability to adhere to treatment; therefore more experiences of observational approach to these diseases need to be built up.

P2-103

A case of giant cell arteritis diagnosed after 4 years of follow-up and in remission with tocilizumab

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Conflict of interest: None

A 70-year-old woman, X-4 years, visited the department of neurology because of headache and fever, and was diagnosed as myotonic headache. However, her headache continued to worsen, and her CRP was as high, so she was admitted to our department. Her pulsatile headache was pulsatile, so giant cell arteritis (GCA) was also a possible diagnosis, but MRI and ultrasonography showed no findings suggestive of GCA. In X-2 years, high fever and wet cough appeared and she was diagnosed with sarcoidosis and the dose of PSL was increased to 40 mg. She was tapered down to 3 mg of PSL. In February X, headache and fever flared up and the dose was increased to 20 mg of PSL, but neither symptoms nor laboratory tests showed improvement. PET-CT showed increased accumulation in the thoracic aorta and echo showed thickening of the temporal artery, which led to the diagnosis of GCA. She was dstarted on tocilizumab, then she went into remission quickly. Conclusion: In cases of recurrent unexplained fever lacking specific symptoms, it is important to consider large vessel vasculitis, and PET-CT may be particularly useful as a diagnostic tool. It should be noted that administration of steroids before a definitive diagnosis may delay early diagnosis.

P2-104

Treatment of giant cell arteritis in our clinical practice and evaluation of the efficacy of tocilizumab

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Conflict of interest: None

[Objective] The efficacy of tocilizumab (TCZ) for giant cell arteritis (GCA) was demonstrated in 2017 and was covered by insurance in Japan. Due to concerns about glucocorticoid (GC) toxicity, the 2021 American College of Rheumatology/Vasculitis Foundation guidelines states that TCZ combination should be considered early in treating new GCA. However, there is no high-quality evidence regarding the timing of TCZ initiation. This study aimed to understand the status of GCA treatment in actual clinical practice and verify the efficacy of TCZ. [Methods] Clinical information on GCA diagnosed in our department after January 2011 was collected retrospectively. [Results] Thirty-one patients were included in the study. 15 of 31 patients relapsed during the observation period (3.9 ± 2.7 years). After relapse, TCZ was added in 9 of 15 patients, and GC was increased in 7 of 9 patients, but GC could be significantly reduced 1 year after TCZ initiation. 4/31 patients were on TCZ before experiencing relapse, with no relapse in all patients during the observation period. Thirteen patients with TCZ had no serious adverse events during the TCZ continuation period. [Conclusions] In our clinical practice, TCZ can be expected to reduce GC and prevent relapse in GCA, regardless of the stage of the disease.

P2-105

Investigation of nerve conduction studies before and after the introduction of mepolizumab in eosinophilic granulomatosis with polyangiitis complicated by mononeuritis multiplex

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Conflict of interest: None

[Object] The mononeuritis multiplex due to EGPA significantly impairs the QOL of patients, but its treatment has not been established. MEP is a drug that has been shown to reduce the steroid dose and prolong the duration of remission in the treatment of EGPA. The interim analysis of

post-marketing surveillance of MEP suggests it may reduce neuropathy. Therefore, we investigated the effects of MEP on multiple mononeuritis. [Methods] Nine EGPA patients were enrolled. We examined the compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) in each case before and after MEP introduction. [Results] In the group, three males and six females were included. Mean age was 56.4 ± 10.6 years, ANCA-positive cases were 5 (56%), and median time to MEP initiation was 244 (95-2045.5) days. Median prednisone dose was 16 (7.5-25) mg at MEP initiation and in 4 cases (44%) immunosuppressants were used. CMAP amplitude improved in 6 cases (67%), decreased in 1 case (11%), and did not change in 2 cases (22%). SNAP amplitude improved in 4 cases (44%) but decreased in 1 case (11%) and did not change in 4 cases (44%). [Conclusions] The combination therapy of MEP and existing treatment may be useful for mononeuritis multiplex complicated by EGPA, but further validation is needed.

P2-106

Corticosteroid Sparing Effect of Mepolizumab in Maintenance Therapy of Severe Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: Yes

[Objective] To evaluate the corticosteroid (GC) sparing effect of mepolizumab in maintenance therapy of severe eosinophilic granulomatous polyangiitis (EGPA). [Methods] Subjects were patients classified as EGPA according to the CHCC 2012 classification criteria and who underwent outpatient care at the Juntendo Hospital between November 2017 and September 2022. This a cross-sectional study including a retrospective search based on medical records. [Results] Thirty-five patients were analyzed. Sixteen patients received mepolizumab. Eight patients were introduced for corticosteroid dose reduction, six for neuropathy, four for exacerbation of asthma attacks, and two for exacerbation of skin ulcers. When corticosteroid doses before and after the introduction of mepolizumab were compared, a median GC sparing effect of 2.0 mg/day (quartile: 0.0-7.1 mg/day) was observed. We achieved withdrawal of GC in 5 cases. The minimum dose in the non-mepolizumab group was 2 mg/day of PSL. [Conclusions] The results of this study showed the possibility of being effective in severe EGPA remission maintenance therapy.

P2-107

Efficacy and safety of avacopan for ANCA associated vasculitis

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Conflict of interest: None

[Objective] We investigated the efficacy and safety of avacopan in patients with ANCA-associated vasculitis (AAV). [Methods] We investigated the disease activity and safety of AAV after 12 weeks of avacopan administration in AAV patients who started administration of abacopan. [Results] Eight AAV patients were treated. Remission induction in 2 cases, relapse in 2 cases, steroid reduction in 4 cases. 1 male and 7 females, age 81.0±5.5 years, disease duration 1.7±0.9 years, all were MPO-ANCA positive at the time of first onset. During administration of abacopan, prednisolone dose of 8.5±4.8 mg/day, immunosuppressants in 5 cases, interstitial lung disease in 7 cases, renal dysfunction in 6 cases. After administration of abacopan, no aggravation of AAV disease activity was observed, and the dose of prednisolone could be reduced without problems in remission-induction and relapse cases. Diarrhea occurred 2 weeks after the start of administration in 1 case, and mild liver enzyme elevation occurred in 1 case after 4 weeks. No significant decrease in blood cells, complement, or IgG was observed. [Conclusions] Avacopan could be introduced into AAV without major side effects, and no exacerbation of disease activity was observed.

P2-108

5 cases of ANCA associated vasculitis treated with avacopan

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Conflict of interest: None

[Objective] Avacopan (AVC) became available in June 2022. Herein, we report 5 cases of microscopic polyangiitis (MPA) patients treated with AVC. [Method] We investigated all cases of MPA patients who were newly introduced AVC in 2022. [Result] Case 1: A 68-year-old woman, who was diagnosed with MPA in 2022. She was treated with glucocorticoid (GC) as remission induction therapy. Two weeks after starting that treatment, she was introduced to AVC. Case 2: A 89-year-old man with MPA for 6 years. He was treated with GC and azatioprine. MPA flared up in May 2022. He was inducted with AVC in June. He improved without increasing GC. Case 3: A 69-year-old man with MPA for 7 years. He was treated with GC and cyclophosphamide pulse as initial remission induction therapy. MPA flared up a year ago, he was treated with rituximab (RTX). MPA flared up in July 2022 again, he was inducted with AVC in August. Case 4: A 89-year-old man with MPA for 15 years. He was treated with GC monotherapy. MPA flared up in September 2022. He was inducted with AVC in that month. Case 5: A 89-year-old man with MPA for a year. He was treated with GC monotherapy. MPA flared up in May 2022. GC was increased and AVC was inducted in July. [Conclusion] All patients were able to continue AVC without severe adverse events.

P2-109

Two cases of treatment effect of digital ischemia with ANCA-associated vasculitis

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Conflict of interest: Yes

[Case 1] A 54-year-old male with a past medical history of angina pectoris presented to breath shortness. The patient had interstitial pneumonia, multiple mononeuropathy, and digital ischemia of right 2nd finger and left 3rd finger. The patient's laboratory data was MPO-ANCA 256 U/ml. The skin biopsy showed lymphocytic infiltrate around blood vessels. We diagnosed this case as digital ischemia with ANCA-associated vasculitis. We treated oral prednisone and monthly IV cyclophosphamide (IVCY). After the initial treatment, these symptoms were improved. [Case 2] A 85-year-old female presented to the hospital with 1 month of worsening discoloration and pain of the left 4th finger and right 3rd finger. The patient had exudative otitis media and hearing loss. The patient's laboratory data was MPO-ANCA 292 U/ml. The skin biopsy showed lymphocytic infiltrate around blood vessels. We diagnosed this case as digital ischemia with otitis media with ANCA-associated vasculitis. We treated oral prednisone and monthly IVCY. After the initial treatment, these symptoms were improved. [Clinical Significance] This time, we report a rare case of MPA with digital ischemia. We considered that digital ischemia is an important organ lesion, because it might be the cause of the decrease of ADL.

P2-110

A case of vanishing bile duct syndrome after avacopan treatment for microscopic polyangiitis

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Conflict of interest: None

A 75-year-old woman. Her chest CT revealed multiple ground-glass shadows and infiltrative shadows in both lungs. She had high levels of MPO-ANCA 53 IU/mL and CRP 5 mg/dL. Thereafter, proteinuria 1.6 g/gCr, and microscopic hematuria with dysmorphic red blood cells persisted. Renal biopsy revealed focal crescentic necrotizing glomerulonephritis, and she was diagnosed with microscopic polyangiitis (MPA). She was treated with methylprednisolone 500 mg for 3 days, followed by prednisolone (PSL) 25 mg. In addition, rituximab and avacopan were administered and urinary protein decreased to 0.5 g/gCr. Thereafter, she was incidentally noted to have liver damage, and jaundice, and was admitted. Her ERCP, CT, and MRI revealed no malignancy, biliary dilatation or gallstones. A liver biopsy showed lymphocytic infiltration of her portal region and obscuring bile ducts. She was diagnosed with drug-induced acute mixed liver injury and vanishing bile duct syndrome. Avacopan and sulfamethoxazole/trimethoprim were stoppped and treated with PSL 40 mg, and ursodeoxycholic acid. [Clinical Significance] Serious liver injury due to avacopan or its concomitant drugs may occur during administration of avacopan for MPA, requiring more careful observation.

P2-111

A case of microscopic polyangiitis with acute cholecystitis treated with abacopan

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Conflict of interest: None

[Case] 74 year old man [Main complaint] fever and muscular pain [Progress] He had fever and thigh muscle pain since June 10, X. He is diagnosed microscopic polyangiitis (MPA) due to elevated CRP and MPO-ANCA 242 U/ml, and skin biopsy results of reticulitis on both lower legs that showed vasculitis with fibrinoid degeneration. He was referred to our hospital on July 13. He also show Peripheral neuropathy and myositis, prednisolone (80 mg) was started. On Y+2, dysrhythmia appeared and head MRI showed new infarcts in the right internal hind leg and the brainstem. On the same day, methylprednisolone pulse was started in addition to anticoagulation therapy, and intravenous cyclophosphamide (IVCY) was also administered on Y+3. Posttreatment, PSL 1 mg/kg, was gradually decreased, and IVCY was repeated at 2-week intervals. On Y+27, epigastric pain appeared and CT scan findings acute cholecystitis. After the 3th IVCY, the cholecystitis did not improve, and on Y+42, abacopan 60 mg/day was started, and on Y+47, the cholecystitis improved. IVCY was deemed ineffective, and rituximab 375 mg/m2 was administered four times. He was discharged on Y+93 days. [Consideration] We experienced a case of MPA with cholecystitis that was successfully treated with abacopan.

P2-112

A case of eosinophilic granulomatous polyangiitis with small bowel perforation after induction therapy with steroid pulse therapy

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Conflict of interest: None

[Case] A 37-year-old man with bronchial asthma, nasal polyps and chronic sinusitis. He visited our hospital with abdominal pain and diarrhea, and was admitted for eosinophilia and CT findings of enteritis and eosinophilic pneumonia. His tissue showed eosinophilic infiltration of the nasal and gastrointestinal mucosa. He was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). He had no peripheral neuropathy, was ANCA-negative, and had a Five-Factor Score of 0. After two courses of steroid pulse therapy, post-treatment with PSL 50 mg/day was started, and the dose was tapered to 35 mg/day. Eight days after discharge, he developed right lower abdominal pain. Intraoperative findings revealed two perforation sites in the small intestine, and histologically confirmed eosinophilia in the intestinal wall around the perforations. He never developed eosinophilia during the course. We plan tapering the dose of PSL in combination with mepolizumab. [Clinical Significance] This is a case of EGPA with small bowel perforation after tow courses of steroid pulse therapy. Ischemia due to vasculitis may cause gastrointestinal perforation, and steroids may not be effective. EGPA with intestinal involvement can develop gastrointestinal perforation even during maintenance therapy.

P2-113

A case of eosinophilic polyangiitis granulomatosa with eosinophilia associated with myocarditis (EGPA) in remission with mepolizumab

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Conflict of interest: None

[Case] 85-y/o woman [Past medical history] Allergic rhinitis [Course] She noticed dyspnea on exertion 1 month ago, and malaise and anorexia 2 weeks ago. Chest X-ray revealed an abnormal shadow and she was presented to our hospital. Physical examination revealed pitting edema in both lower limbs. Blood test showed elevated levels of eosinophil (8919/μL), CRP (4.83 mg/dL), BNP (1695 pg/mL), troponin T (2.22 ng/mL). CT revealed pulmonary edema. Echocardiography revealed LVEF of 54%, and a myocardial biopsy showed an infiltration of eosinophils. LVEF decreased to 40% on the second day. We diagnosed her with EGPA complicated by myocarditis, and she was treated with pulse methylprednisolone (1 g/day for 3 days). We added the mepolizumab (MPZ) from the 23rd day. The treatment led to the improvement of her symptoms and blood test findings. PSL was gradually tapered to 8 mg/day, and her disease status has been stable without relapse. [Discussion] There is a consensus to treat severe EGPA with high dose of glucocorticoids (GC) in combination with rituximab or cyclophosphamide. In our case, we added MPZ because of the good response to GC and the side effects of immunosuppressive therapy. It might be considered that MPZ could be useful in severe EGPA cases that respond well to GC.

P2-114

A case of microscopic polyangiitis refractory to treatment with pulmonary pyogenic disease due to chronic airway infection with mucoid Pseudomonas aeruginosa

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Conflict of interest: None

A 67-year-old woman presented to her previous physician with fever. A CT scan of the chest revealed bronchopneumonia, and she was admitted to the same hospital and started intravenous infusion. However, since her symptoms did not improve, immunogenic pneumonia was suspected and she was referred to our department. On physical examination, purpura was observed on the lower extremities, and biopsy showed inflammatory cell infiltration around blood vessels, leading to the diagnosis of microscopic polyangiitis. Treatment was started with prednisolone (PSL) 50 mg/day and cyclophosphamide 600 mg/2 weeks, and on the 10th day of treatment, multiple nodular shadows appeared in the lungs. TAZ/PIPC was started, and the nodules slowly disappeared. A CT scan of the chest showed massive pulmonary pyogenic disease. The patient was discharged from the hospital after TAZ/PIPC was administered again for 4 weeks, and although structural destruction of the lungs remained, the lung shadows were improved. We experienced a case of microscopic polyangiitis that was difficult to treat due to chronic airway infection with mucoid Pseudomonas aeruginosa. We report the case with literature review.

P2-115

MPO-ANCA-associated hypertrophic pachymeningitis presenting with aortitis due to ANCA-associated vasculitis: a case report and literature review

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Conflict of interest: None

[Case] An 82-year-old man developed anorexia 9 days before. Although the antibiotics were given, high inflammatory responses persisted, and he was hospitalized. On the 4th day, fever and neurological disorders appeared. Brain MRI revealed dural thickening and cerebrospinal fluid revealed protein cell dissociation. Trunk contrast-enhanced CT showed wall thickening abdominal aorta and contrast enhancement of the spinal dura mater. A renal biopsy showed vasculitis in the interlobular artery. Finally, we diagnosed MPO-ANCA-associated hypertrophic pachymeningitis (HP) presenting with aortitis. The symptoms and laboratory findings rapidly improved with steroid pulse and combination with steroids and azathioprine. [Discussion] ANCA-associated vasculitis is the most common in secondary HP, many cases are MPO-ANCA positive, which often have localized lesions in the dura mater. Eight cases of HP with aortitis were reported, including this case. Five were MPO-ANCA positive and one was PR3-ANCA positive. Four had headaches and five had neurological symptoms, which rapidly improved with steroids. All cases with pulmonary and renal lesions were positive for MPO-ANCA. [Conclusions] MPO-ANCA-positive HP might be more likely to develop organ lesions in patients with aortitis, so caution is required.

P2-116

A case of lymphomatoid granulomatosis with multiple nodules in the lung, liver, and kidney during treatment of ANCA-associated vasculitis

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Conflict of interest: None

Case. A 73-year-old woman with fever, increased LDH, and multiple pulmonary, hepatic, and renal masses during maintenance therapy with prednisolone and oral cyclophosphamide for anca-associated vasculitis for 15 years. PET-CT showed FDG accumulation in lung, liver, kidney, stomach, and small intestine. Gastric biopsy revealed a diagnosis of B-cell lymphoma. The patient was treated with THP-COP therapy, but died of bleeding from a small intestinal ulcer. Autopsy revealed necrotic nodules in the lungs, liver, and kidneys, a vasculocentric and vasodestructive lymphocytic infiltrate around the necrotic lesions, and a cluster of Epstein-Barr virus-encoded RNA (EBER)-positive atypical B-cell blasts, which suggested the presence of Epstein -Barr virus (EBV) infection. The small intestinal hemorrhage was thought to be caused by a rupture of degenerative blood vessels. Conclusion. Lymphomatoid granulomatosis is a rare lymphoproliferative disease associated with EBV reactivation. Immunosuppressed status is a risk factor. In the case of multiple masses during the use of immunosuppressive drugs, a biopsy and EBER in situ hybridization of the specimen may be considered in the context of this disease.

P2-117

MPO-ANCA positive granulomatosis with polyangiitis presenting an orbital inflammatory pseudotumor diagnosed by femoral muscle biopsy

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Conflict of interest: None

[Case] A woman in her 70s presented to an ophthalmologist with right eye pain, conjunctival hyperemia, and visual disturbance one year ago. Right conjunctival mass and tumor in the right orbit were diagnosed. She was referred to our hospital because of worsening right eye pain, fever, headache, and positive MPO-ANCA. According to ACR/EULAR 2022 classification criteria for ANCA-associated vasculitis, the patient was classified as granulomatosis with polyangiitis. However, the differential diagnosis including fungal infection and lymphoma had to be excluded. Bilateral thigh muscle biopsies was performed despite that she did not have myalgia or elevated muscle enzymes. Biopsies showed fibrinoid necrosis of small vessels, ANCA-associated vasculitis was confirmed. Fever, headache, and conjunctival hyperemia resolved with the start of prednisolone and rituximab, without relapse for three months. [Clinical Significance] Orbital inflammatory pseudotumor occur in about 10% of patients with granulomatosis with polyangiitis. Most reports are positive for PR3-ANCA, and only few reports of MPO-ANCA positivity. In addition, there have been few reports of muscle biopsy for the diagnosis of vasculitis in recent years, and we report this case because of the novelty of these two points.

P2-118

Microscopic polyangiitis with multi-arterial aneurysm which ruptured in right gastroepiploic artery after remission induction therapy

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Conflict of interest: None

A 64-year-old woman presented pain in bilateral upper and lower limbs and was diagnosed as polymyalgia rheumatica two months before she visited our hospital. Although 10 mg/day of oral prednisolone (PSL) was started, the pain and inflammatory markers did not improve. Then, she admitted to our hospital and was diagnosed as microscopic polyangiitis (MPA) because of positive MPO-ANCA, hematuria and mononeuritis multiplex in lower limbs. At this point, contrast-enhanced (CE) CT didn't show any arterial aneurysm. PSL was increased to 40 mg/day on admission day (AD) 4th. On AD 19th, she suddenly had abdominal pain. CE CT showed pseudoaneurysms in the right gastroepiploic artery and left gastric artery, and revealed that the pseudoaneurysm of the right gastroepiploic artery was ruptured. She had cardiopulmonary arrest (CPA) shortly thereafter, and transcatheter arterial embolization was performed on the artery in parallel with resuscitation. Later, we got the report of renal biopsy on AD 14th which showed pauci-immune crescentic glomerulonephritis with middle size artery inflammation. She was recovered from CPA and receiving induction remission therapy with rituximab. (Conclusion) We experienced MPA with multi-arterial aneurysm which ruptured after remission induction therapy.

P2-119

A case of polyangiitis granulomatosa with cerebral infarction and ventricular fibrillation during remission induction therapy

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Conflict of interest: None

[Case] On November 8, 20XX, a 51-year-old man became aware of edema in his right lower leg and subcutaneous hemorrhage on the posterior surface of his right thigh. Blood tests revealed elevated CRP and PR3-ANCA, and CT scan showed infiltration shadows in both lungs. Blood sputum appeared, which was considered to be alveolar hemorrhage. After close examination, he was diagnosed as GPA, and was treated with steroid pulse therapy and post-treatment with prednisolone 55 mg/day, IVCY and simple plasma exchange. The course was good, but on the 24th day, he had an acute cerebral infarction, the cause of which was unknown. On the 60th day, he developed ventricular fibrillation, and a coronary angiography was performed, but there was no significant stenosis in the coronary arteries, and no obvious cause could be pointed out. On the 75th day, the alveolar hemorrhage flared up again, and IVCY was replaced with rituximab, and the patient has passed without any flare-up of any of the symptoms since then. [Clinical Significance] CNS and cardiac lesions are not common in GPA, but they are important, and their complications

during the course of the disease should be kept in mind again. We report a case, including a discussion of CNS and cardiac lesions in patients with GPA at our hospital.

P2-120

A case of ANCA-associated vasculitis with paravertebral lesions treated with avacopan

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Conflict of interest: None

A 61-year-old woman was admitted to our hospital with a 42-day history of fever and dry cough. Twenty-four days before admission, she developed sensory disturbances in the lateral side of both lower legs and foot, and the ulnar sides of the left hand. Additionally, she developed right foot drop and right hearing loss. Laboratory data showed proteinuria, hematuria, and serum MPO-ANCA titer were elevated at 3915 IU/ml. A renal biopsy revealed crescentic glomerulonephritis. FDG-PET/CT showed soft opacities with FDG uptake in the ventral side of Th4-5 vertebral bodies and the left side of the L5 vertebral body and sacrum. CT-guided biopsy of a paravertebral lesion showed nonspecific inflammation, but no granuloma or necrotizing vasculitis. Avacopan 60 mg/day was started on the 3rd hospital day, and four courses of rituximab 600 mg/week were administered. However, the paravertebral lesions did not improve and the cough persisted. On the 24th hospital day, PSL 20 mg/day was started, and the lesions shrunk and her cough disappeared. A few reports have reported that paravertebral lesions are associated with ANCA-associated vasculitis, especially granulomatosis with polyangiitis. In our case, the effect of avacopan on the lesion was considered to be poor.

P2-121

A case of granulomatosis with polyangiitis (GPA) presenting refractory soft-tissue lesions extending from the base of the skull to the peri-cervical spine

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Conflict of interest: None

In September 20XX, a 56-year-old woman developed fever and neck pain. Because her previous physician suspected PMR, she was started on PSL 20 mg/day in November 20XX, and then she was admitted to our hospital. She had exudative otitis media and mild hearing loss. CT showed right sphenoid sinusitis and multiple nodules with cavities in both lungs. Heterogenous lesions around the base of the skull were found on MRI. Biopsy of the lung and the pharynx showed no specific findings. The lung lesions responded well to steroids, so we made a presumptive diagnosis of GPA although PR3-ANCA was negative. After discharge, the patient was treated with PSL 30 mg/day and MTX. As the shadows beside the skull base also showed a tendency to disappear, the steroid dose was reduced. In November 20XX+1, a new lesion appeared on the right side of C2 on MRI. In January 20XX+2, a subcutaneous mass also developed under the right auricle. Biopsy ruled out MTX-associated lymphoproliferative disorder. In May 20XX+2, she was started on PSL 25 mg/day and rituximab for flare-ups of GPA. 5 months later, that lesion has regressed. GPA with the lesions around the skull base is reported to be rare. A definitive diagnosis might be difficult to make due to negative ANCA or poor histological findings.

P2-122

A case of MPO-ANCA-negative microscopic polyangiitis with pain in the thigh diagnosed by muscle biopsy

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Conflict of interest: None

[Case] 85-year-old male [Present medical history] A 85-year-old male had pain in the thigh in April X. In May he was transferred to our hospital for fever and difficulty walking, and was hospitalized. Creatine kinase and aldolase levels were normal, but STIR MRI of the thigh revealed high-intensity areas in the bilateral quadriceps and adductor muscles. A muscle biopsy was performed at the quadriceps muscle revealed inflammatory cell infiltration and fibrinoid necrosis in the arteriolar wall between muscle tissues, and MPO-ANCA-negative microscopic polyangiitis was diagnosed. He was started on oral steroid treatment with prednisolone 30 mg/day (0.6 mg/kg). After starting treatment, pain in the thigh improved, and he was able to walk, and was discharged from our hospital. [Clinical Significance] Muscle biopsy was considered useful for diagnosing vasculitis in cases with normal muscle deviation enzymes or MPO-ANCA-negative.

P2-123

New Onset of Eosinophilic Granulomatosis with Polyangiitis Following COVID-19 Vaccine

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Conflict of interest: None

1. Case Presentation A 51-year-old man was diagnosed with asthma in X-15. He received the COVID-19 Vaccine in August X and September X. A few days after vaccination, He appeared various symptoms. He was seen at a nearby hospital in October X and then at our clinic. He was admitted to our hospital on suspicion of ANCA associated vasculitis, because of high anti-neutrophil cytoplasmic myeloperoxidase antibody, C-reactive protein and eosinophil count. CT scan showed findings of sinusitis and interstitial pneumonia. We diagnosed a patient with Eosinophilic Granulomatosis with Polyangiitis and started treatment with prednisolone (0.5 mg/kg/day) on day 7 of hospitalization. We also started him on rituximab. After the start of treatment, his symptoms improved. We gave him rituximab once a week for a total of four doses. We tapered off the steroids. The patient was discharged on the 31st day of hospitalization. 2. Discussion and Clinical significance In this study, we experienced the case of Eosinophilic Granulomatosis with Polyangiitis that developed after COVID-19 Vaccine. Since several similar cases have already been reported, it is possible that the COVID-19 Vaccine contributed to the development of the vasculitis.

P2-124

A case of microscopic polyangiitis with only cerebral infarction

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Conflict of interest: None

[Case] 72-year-old male. He visited his local doctor on August 17 because he had a headache in July of X year. Blood tests showed an elevated inflammatory response, which suspect an infection, and he was started on antimicrobial medication. On August 31, he presented with dysarthria and visited his previous doctor. MRI showed multiple cerebral infarctions, and he was hospitalized and started on anticoagulant medication. He was transferred to our hospital on September 5 for examination and treatment of cerebral infarction originating from microscopic polyangiitis (MPA), since MPO-ANCA was 134 U/mL. After transfer, MPO-ANCA was elevated at 240 U/mL, so prednisolone (PSL) 50 mg was started. In addition, Rituximab was then administered, the inflammatory response and MPO-ANCA tended to improve, and MRI showed no new cerebral infarction, and the cerebral infarction lesion was significantly relieved. The patient was discharged from the hospital after the PSL was reduced and 25 mg of azathioprine was added. [Clinical Significance] MPA complicated cerebral infarction is rarely, and the diagnosis is preceded by other organ involvement. We experienced an extremely rare case of MPA with cerebral infarction only, and we discuss the case including the literature review.

P2-125

A case of PR3-ANCA-positive microscopic polyangiitis

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Conflict of interest: None

An 80-year-old woman had fatigue, fever, and weight loss two months prior to the visit to our hospital. One month later, purpura developed and CRP 15.93 mg/dL, urinary protein 3+, and urinary blood 3+ were detected in the laboratory test. Additionally, serum creatinine levels increased from 0.54 to 1.28 mg/dL, the patient was referred to our hospital. Testing for PR3-ANCA was positive (2440 U/mL). Histopathologic examination showed crescentic glomerulonephritis in the kidney and leukocytoclastic vasculitis in the skin, without granulomatous lesions. The diagnosis of microscopic polyangiitis (MPA) was made because the patient did not have lesions in the upper pulmonary tract and lungs. The patient started steroid pulse therapy followed by prednisolone (PSL) 50 mg/day and rituximab (RTX) 375 mg/m2/week for a total of 4 doses, which improved both symptoms and renal impairment. While most Japanese patients with MPA are MPO-ANCA positive, PR3-ANCA positivity is very low; however, as in this case, PR3-ANCA positive MPA is possible. There are few reports on Japanese patients with PR3-ANCA-positive MPA complicated with rapidly progressive glomerulonephritis, and further case accumulation is needed to better elucidate this rare clinical condition.

P2-126

Eosinophilic granulomatosis with polyangiitis presenting severe bilateral ischemic optic neuropathy and multiple cerebral infarctions

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Conflict of interest: None

A 60-year-old man admitted to our hospital with exertional dyspnea, cough and progressive right visual loss for a few days. His medical history was notable for eosinophilic sinusitis. Laboratory data showed elevation of eosinophil, inflammatory marker and MPO-ANCA. Head MRI revealed multiple cerebral infarctions with no symptoms. Ophthalmologic examination revealed bilateral visual loss (right hand motion /left 0.03), and optic nerve MRI showed local contrast effects in the optic nerve papillae and posterior ciliary artery. The diagnosis of EGPA with anterior ischemic optic neuropathy was made. The patient was started on steroid therapy under anticoagulation but failed to respond, so he was treated with mepolizumab and blood eosinophils decreased. On the 10th day of hospitalization, left visual acuity worsened and IVIG and antiplatelet therapy was also started. Her right visual acuity recovered to manual valve but left did not recover. Eosinophilic tissue damage is the main pathogenesis of EGPA, which requires prompt diagnosis and treatment to prevent organ damage and sequelae. Eosinophils have been reported to induce thrombosis via platelet activation due to ETosis. In addition to early detection, it is important to examine therapeutic regimens to suppress ETosis.

P2-127

A case of ANCA-associated nephritis in horseshoe kidney with divergence between urinalysis results and renal-pathological features

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Conflict of interest: None

[Case] 56-year-old male [Medical history] A numbness in both lower extremities appeared. 2 months later, he was diagnosed with lumbar spinal stenosis at a nearby hospital. Preoperative tests revealed Cre 1.4 mg/dL, CRP 13.5 mg/dL, and MPO-ANCA 196 U/mL. ANCA-related nephritis was suspected, but hematuria and proteinuria weren't observed. Because of horseshoe kidney, a percutaneous renal biopsy was considered to be difficult. In the next month, he was admitted to our hospital. [Laboratory findings] Urinalysis: RBC 1-4/HPF, protein 0.4 g/gCre, β2MG 154 μg/L. Blood test: BUN 42 mg/dL, Cre 2.4 mg/dL, CRP 12.8 mg/dL, ANA <40 fold, MPO-ANCA 214 U/mL, PR3-ANCA <1.0 U/mL. [Course] A nerve conduction study suggested mononeuritis multiplex. On day 8, an open renal biopsy was performed, revealing necrotizing crescentic glomerulonephritis and tubulointerstitial nephritis. He was diagnosed with ANCA-associated nephritis. Prednisolone 30 mg and two courses of rituximab were administered, and on day 30, Cre level improved to 1.7 mg/dL and CRP to 0.01 mg/dL. [Conclusion] Although the influence of horseshoe kidney on urinary results is unclear, glomerulonephritis may occur in ANCA-associated nephritis despite poor urinalysis, and renal biopsy should be considered when renal dysfunction progresses.

P2-128

A case of microscopic polyangiitis with multiple venous thrombosis associated with candidemia

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Conflict of interest: None

[Case] We present a case of microscopic polyangiitis (MPA) with multiple venous thrombosis associated with candidemia. The patient was a 81-year-old woman who was diagnosed as MPA with myeloperoxidase-antineutrophil cytoplasmic antibodies (MPO-ANCA) positivity, alveolar hemorrhage and rapidly progressive glomerulonephritis. We treated induction therapy with methylprednisolone pulse therapy, cyclophosphamide and rituximab. Subsequently, MPO-ANCA was negative, and the vasculitis condition was improving. However, during the course of treatment, she developed bacteremia due to central venous catheter infection. A contrast-enhanced CT scan performed for close examination revealed multiple venous thrombi. We treated with anticoagulation therapy under antibiotic therapy, and these thrombi had been disappeared. [Clinical Significance] Venous thromboembolism can be a complication in patients with ANCA-associated vasculitis. It is known that neutrophil extracellular traps (NETs) in vasculitis cause hypercoagulability. Bacteremia also causes coagulation abnormalities due to NETs formation, suggesting that there is a pathophysiological association with thrombogenesis in ANCA. Physicians should consider the possibility of thrombogenesis in AAV patients with bacteremia.

P2-129

A case of ANCA-associated vasculitis with refractory multiple pulmonary nodules

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Conflict of interest: None

An 87-year-old woman. She was diagnosed with ANCA-associated vasculitis (AAV) due to multiple pulmonary nodules, nephritis and positive MPO-ANCA 5 years ago. She improved with prednisolone (PSL) 30 mg/day. She had enlarged multiple pulmonary nodules, which were suspected to be lung abscesses, and was treated with antibiotics 3 years ago. They were effective, and the multiple nodules were reduced. The nodules continued to grow and shrink, and she was hospitalized and treated with intravenous antibiotics four times. One month ago, she got fever again, and was hospitalized due to elevated MPO-ANCA and urinary protein, in addition to worsening multiple pulmonary nodules again. Meropenem was administered and the fever resolved, but CRP did not decrease, and urinary protein and MPO-ANCA increased. According to the diagnosis of AAV flare, the dose of PSL was increased from 3 mg/day to 20 mg/day. CRP rapidly decreased and urinary protein tested negative. In this case, the pulmonary nodules and inflammation did not improve with antibiotics alone, but improved with PSL, suggesting that infection and vasculitis were involved in this case. In this case, we consider that the infection caused aggravation of AAV.

P2-130

A case of acute tubulointerstitial nephritis diagnosed by renal biopsy in a patient with Sjögren syndrome

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Conflict of interest: None

The case is a woman in her 40s who had been suffered from dry eyes and dry mouth several years ago. Two weeks prior to our first visit, the patient was admitted to the previous hospital due to muscle weakness and was diagnosed with hypokalemic periodic paralysis with serum K of 1.7 mEq/L. Subsequently, the cause of the hypokalemia was diagnosed as type 1 renal tubular acidosis associated with Sjögren syndrome, and K supplementation therapy relieved the paralysis. However, during 2 months after her visit to our hospital, renal impairment consistently progressed (serum Cr; 0.81 → 0.93 → 1.03 → 1.16 mg/dL), and a complication of tubulointerstitial nephritis was suspected because of a high level of urine β2-microglobulin (965 μg/L). Renal biopsy revealed inflammatory changes in the interstitium and an inflammatory cellular infiltrate consisting primarily of lymphocytes and plasma cells, leading to a diagnosis of acute tubulointerstitial nephritis. Interstitial fibrosis was moderate and glomerular injury was trivial. Fluorescent antibody method confirmed the deposition of IgA and IgM in the mesangial regions. After one month of treatment with prednisolone for acute tubulointerstitial nephritis, serum Cr and urine β2-microglobulin decreased to 0.86 mg/dL and to 111 μg/L, respectively.

P2-131

A case of sicca symptoms with anti-centromere antibody positivity due to fatty replacement in the labial salivary glands

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Conflict of interest: None

[Background] Labial salivary gland biopsy is essential for diagnosis of sicca symptoms with anti-centromere antibody positivity (ACA). Inflammation in the biopsy indicates Sjögren's syndrome, but fibrosis indicates systemic sclerosis. [Case] The patient was a 75-year-old woman who consulted our clinic because of telangiectasia on her fingers and had tested positive for ACA 8 years ago. She did not have Raynaud's phenomenon, nail abnormality or skin sclerosis. Saxon's test exhibited 1.9 g per 2 minutes, and Schirmer's test showed 5 mm per 5 minutes. Labial salivary gland biopsy revealed marked fatty replacement and only one focus in nine specimens. We concluded that her sicca symptoms were caused by fatty replacement in the salivary glands, not by Sjögren's syndrome or systemic sclerosis.

P2-132

Coexistence of Primary Effusion Lymphoma-like Lymphoma and Hepatic Inflammatory pseudotumor Associated with Primary Sjögren's syndrome

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Conflict of interest: None

An 88-year-old woman visited to our hospital complaining with dyspnea on exertion. She visited our clinic having noticed ocular and oral dryness and Raynaud's phenomenon before 6 years. Anti-SS-A and anti-SS-B antibodies were positive. She was diagnosed with primary Sjögren's syndrome (pSS). She was pointed out multiple solid lesions in liver before one year. On the basis of the histopathological findings of the liver biopsy, diagnosis of inflammatory pseudotumor was made. She felt dyspnea on exertion before 2 weeks. A chest X-ray revealed massive pleural effusion in the right chest. Cytological findings of pleural effusion showed proliferation of atypical lymphocytes with monoclonality, and analysis of cell-surface markers showed CD20 (++), MOM-1 (+), Bcl-6 (+), and CD10 (-). Polymerase chain reaction assay of HHV8 was negative in pleural effusion. She was diagnosed with primary effusion lymphoma (PEL)-like lymphoma (PEL-L) associated with pSS. R-THP-COP therapy was initiated, and the patient was in remission and the inflammatory pseudotumor also resolved. PEL-L is extremely rare in lymphomas associated with pSS. Moreover, there is no previous report of coexistence both of inflammatory pseudotumor and lymphoma associated with pSS within our knowledge.

P2-133

Acute tubulointerstitial nephritis due to Sjögren's syndrome with severe renal failure like rapidly progressive glomerulonephritis

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Conflict of interest: None

[Case] A woman in her 60s visited a local clinic with stomach ache and weight loss two days ago, and was referred to our hospital because renal failure was found. Her past physical examination did not reveal her renal failure. Laboratory tests at our hospital showed severe renal failure (Cr 9.31 mg/dL) and urinalysis abnormalities such as urinary protein (1.18 g/gCr) and occult blood, and we suspected rapidly progressive glomerulonephritis. We performed a renal biopsy immediately, and renal pathological findings showed no glomerular lesions, but severe acute tubulointerstitial nephritis (ATIN) with cellular infiltration in the renal tubulointerstitium, interstitial edema, and tubular obstruction. We used the ACR/EULAR classification criteria for Sjögren's syndrome, evaluation with Schirmer's test and anti-SS-A antibodies confirmed the diagnosis. We attributed her ATIN to Sjögren's syndrome because her medical history did not include a history of infections or use of drugs that could have caused ATIN. After she was treated with steroids, her kidney failure improved dramatically. [Discussion] TIN is known as the most common renal symptom in Sjögren's syndrome patients. However, we report this case because severe renal failure due to primary Sjögren's syndrome alone is rare.

P2-134

Two cases in which differentiation between adult onset Still's disease (AOSD) and angioimmunoblastic T-cell lymphoma (AITL) was difficult

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Conflict of interest: None

[Case 1] A 68-year-old woman with a history of epileptic seizures was transferred to our hospital with convulsions. Her convulsions improved with anticonvulsants, but she had fever, hyperferritinemia, and multiple lymphadenopathies. About a year ago, she had a similar condition, and although bone marrow biopsy, random skin biopsy, and lymph node biopsy were performed, there was no evidence of malignant lymphoma (ML). ML was ruled out, and she was possible AOSD. Repeat lymph node biopsy was performed, steroids were administered. The final biopsy result was AITL, and she died of complications including infection. [Case 2] An 85-year-old woman with seronegative RA was transferred to our hospital with fever. A CT scan revealed multiple lymphadenopathy, and a blood test showed high sIL-2R and ferritin levels. Antibiotic therapy was ineffective, and she had probable malignancies, including ML. A lymph node biopsy was performed and steroids were administered. First biopsy results suggested AITL, but final result was reactive lymphadenopathy. Steroids were effective, and we diagnosed AOSD. [Conclusions] Even with ML, steroids alone may improve the condition to some extent. Lymph node biopsy in AOSD provides few useful findings for diagnosis, but is important for differentiation from ML.

P2-135

A case of Vexas syndrome with myelodysplastic syndrome and Sweet's disease diagnosed during the course of treatment for recurrent polychondritis

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Conflict of interest: None

He had been treated with prednisolone 12.5 mg/day for recurrent polychondritis diagnosed in 5 years ago. 1 year prior to admission, azathioprine was started and stopped after one month due to anemia, and bone marrow biopsy was performed, which led to the diagnosis of myelodysplastic syndrome. He developed fever and skin rash and was admitted to the hospital for close examination. On admission, multiple lymph nodes were observed in the bilateral axillae and inguinal region. A skin biopsy revealed a generalized erythema, which was diagnosed as Sweet's disease. Body temperature was over 39°C every day. He was diagnosed with hemophagocytic syndrome and was treated with steroid pulse followed by post-treatment with prednisolone, which improved his general condition and blood tests. VEXAS syndrome was suspected due to the presence of recurrent polychondritis, myelodysplastic syndrome, and Sweet's disease, and genetic analysis identified the UBA1 gene variant, which led to the diagnosis. VEXAS syndrome is a poor prognosis autoinflammatory disease characterized by recurrent polychondritis, generalized skin rash, high fever, arthritis, and myelodysplastic syndrome caused by an acquired somatic mutation in hematopoietic stem cells of the gene UBA1 involved in E1 ubiquitination.

P2-136

A case report of acute tubulointerstitial nephritis during adalimumab use for complete Behçet's disease

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Conflict of interest: None

[Case Report] A 49-year-old woman presented with fever, aphthous stomatitis, vulvar ulcer, and painful wart since March X-2. Petechial hemorrhages around blood vessels were observed in the fundus of both eyes, and bilateral choroiditis was suspected. She was diagnosed with complete Behçet's disease and started prednisone 60 mg, colchicine and adalimumab. Since January X-1, she has been followed up with colchicine 1.5 mg + adalimumab 40 mg/2 w. At the regular visit in March X, Creatinine increased from 0.86 to 1.59 mg/dl. Suspecting drug-induced renal failure, adalimumab was discontinued in April X. On May 15, X, fever, aphthous stomatitis, and painful induration of the pubic area were observed, and she was admitted to the hospital. A renal biopsy showed mononuclear cell infiltration in the renal tubules and interstitium. She was started on prednisone 30 mg for acute tubulointerstitial nephritis and her renal function and symptoms improved. Adalimumab was suspected as the cause of acute tubulointerstitial nephritis, and it was discontinued. [Discussion] This is a case of drug-induced interstitial nephritis caused by adalimumab during treatment of Behçet's disease. Renal involvement in Behçet's disease is rare, and we report this case with a review of the literature.

P2-137

Acute neuro-Behcet's disease (ANB) with hyperintensity on diffusion-weighted imaging (DWI) and hypointensity on apparent diffusion coefficient (ADC) map

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Conflict of interest: None

Introduction: ANB causes fever, headache, and focal brain symptoms. In brain MRI, the affected lesions are high-intensity areas (HIAs) on FLAIR. DWI and ADC are usually hyperintense, while high DWI/low ADC is rare. Case: A 53-year-old woman with recurrent stomatitis since her teens, vulvar ulcers (47-year old) and erythema nodosum (51-year old) presented with headache 3 days before admission, followed by numbness in her left extremity. Brain MRI revealed HIAs in her pons, occipital, and parietal lobes on FLAIR and DWI. Cerebral lesions were HIAs on ADC, while the pontine lesion was visualized as low-intensity. Blood tests showed an increase in WBC counts (10,800/μL) and CRP (3.5 mg/dL). CSF examination revealed elevated levels of cell count (59 μL: mononuclear-cell predominance), IL-6 (175 pg/mL). She was diagnosed with brainstem encephalitis, and treated with corticosteroids. She was given aspirin, which was discontinued when her brainstem lesion ameliorated on Day 20. This case is unique because brain MRI showed both vasogenic and cellular edema. ADC low signal areas must be differentiated from cerebral infarction in ANB. Future case accumulation would be necessary to clarify the pathophysiology of cellular edema in ANB, and the necessity of antiplatelet treatment.

P2-138

Acute Liver failure in Adult onset Still Disease dramatically treated with tocilizumab

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Conflict of interest: None

Adult onset Still's disease (AOSD) is a systemic inflammatory disorder and hepatic involvement is frequently observed in the course of AOSD such as elevated transaminases and hepatomegaly. But hepatic failure is a rare manifestation of AOSD. We here reported a 40-year-old woman who presented with jaundice in the course of AOSD and 0.8 mg/kg prednisolone therapy was not effective, but tocilizumab administration dramatically improved liver function.

P2-139

Adult-Onset Still's Disease Developed Immediately after COVID-19

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Conflict of interest: None

A 54-year-old woman admitted to our hospital presented with high fever. She noticed high fever before 25 days. Polymerase chain reaction (PCR) assay of SARS-CoV2 obtained from nasal mucosa was positive, and she relieved fever after 3 days. High fever without shaking chill and bilateral shoulder pain appeared, she consulted home doctor 4 days before admission and was pointed to systemic lymphadenopathy, hepatosplenomegaly, and salmon-pink erythema in bilateral thigh. Laboratory examinations showed as following; WBC 16000 /ml, Hb 11.3 g/dl, Plt 19.0 ×104 /μl, GOT 26 IU/l, GPT 41 IU/l, LDH 179 IU/l, ALP 140 IU/l, CRP 8.28 mg/dl, ESR 8 mm, ferritin 2642 ng/ml. ANA and RF were negative. PCR assay of SARS CoV2 was negative. She was diagnosed with adult-onset Still disease (AOSD) and administered 1 g daily of methylprednisolone for 3 days followed by 50 mg daily of prednisolone and cyclosporin A. Her condition improved rapidly. AOSD and COVID-19 share common pathophysiological features such as marked hyperferritinemia and macrophage-activated syndrome as results of excessive activation of innate immunity. AOSD triggered by COVID-19 has been seldom reported. However, activated innate immunity contributes exacerbation of the inflammatory process in a part of patients with AOSD.

P2-140

Cases of adult Still's disease with unfortunate outcomes during Treatment

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Conflict of interest: None

We diagnosed and treated six cases of Adult Still's disease (ASD) from July 2021 to July 2022. We have treated 13 cases ASD in 14 years from 2007 to 2020. Although the abnorm. al frequency of development made us suspect the presence of some kind of trigger, there was no clear relationship between the time of onset and coronavirus vaccination or infection with coronavirus. As a characteristic, it often occurs in elderly people. And comorbidities and general conditions complicated the treatment We present cases that was difficult to treat and died, and discuss the treatment.

P2-141

Two cases of juvenile systemic sclerosis

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Conflict of interest: None

We experienced two cases of juvenile systemic scleroderma (jSSc), a rare disease. Case 1: 14-year-old boy with no medical history. He came our hospital because of skin hardening of the fingers and elevated anti-Scl-70 antibody. Raynaud's phenomenon and capillary abnormalities were observed in both fingers. From the fingertips to the forearms, his skin showed stifness. KL-6 chest CT were slithly abnormal but respiratory function tests were normal. We diagnosed jSSc with localized cutaneous sclerosis, and organ evaluation revealed normal except for mild reflux esophagitis. Case 2: 10-year-old girl with no medical history. At the age of 5, Raynaud's phenomenon was observed in her fingers, blood test showed elevated anti-Scl-70 antibody, and early pattern of scleroderma was observed in the capillary scope, leading to the diagnosis of systemic cutaneous sclerosis jSSc. At age 10, she visited our hospittal for the first time, 3 weeks after PSL and MMF induced. Her skin hardening and dyspnea on exertion slightly improved, KL-6 and %FVC showes no deterioration after the intervention. It is difficult to judge the intervention of jSSc treatment, and it is necessary to accumulate evidence by accumulating cases in the future to establish a guideline for treatment.

P2-142

A specific finding of contrast-enhanced CT in pediatric patient with Behcet's disease complicated with subclavian aneurysm

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Conflict of interest: None

A 11-year-old girl developed fever at night and lose weight for one year. She developed erythema nodosum, abdominal pain, and recurrent oral ulcers for 5 months. One month before visit, she had cellulitis on her lower leg, which resolved with antibiotics. Because of the erythema nodosum persisted, she was admitted to our hospital. Blood tests showed elevated leukocyte counts, CRP level and D-dimer level. Contrast-enhanced CT showed an aneurysmal dilatation in the left subclavian artery and soft shadows surrounding left subclavian artery, right ectopic subclavian artery and superior mesenteric arteritis. HLA-B51 was positive. These image findings and clinical course supported to diagnose with Behcet's disease. She was treated with colchicine, prednisolone and methylprednisolone pulse. Behcet's disease with aortic involvement is an infrequent but is the most common of mortality. Pediatric Behcet's disease usually starts with incomplete clinical phenotype. In this case, the patient was suspected type of Behcet't disease, but treatment was started after vascular involvement were found. We report this case because pediatric Behcet's disease with aneurysm is rare and there are characteristic imaging findings.

P2-143

A case of a 2-year-old boy with PAPA syndrome presenting with pyoderma gangrenosum-like skin lesions caused by refractory perianal abscesses

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Conflict of interest: None

PAPA syndrome is an autoinflammatory disease, caused by gain-of-function mutations in the *PSTPIP1* gene. While PAPA syndrome is reported that usually begins with pyogenic arthritis at a young age and pyoderma gangrenosum and acne appear in puberty, the pathogenesis is not elucidated fully. We report a case of a 2-year-old boy with PAPA syndrome presenting refractory perianal abscesses developed gangrenous pyoderma-like lesions. The boy presented with multiple perianal abscesses one month after birth. After incisional drainage, the abscesses enlarged within a few weeks. At 13 months old, after gastroenteritis, those abscesses formed three anal fistulas. At 26 months old, after part of them was drained again, the surrounding area developed pyoderma gangrenosum-like lesions. His father and uncle took a genetic test because of arthritis and identified a heterozygous mutation of NM_003978.5: c. 688G>A: p. A230T, which was also detected in this boy. [Clinical Importance] A case of a toddler with PAPA syndrome, who presented with pyoderma gangrenosum-like skin lesions, probably due to repeated skin irritations such as incisional drainage and diarrhea. It is suggested that mutation and physical stimuli to the body, that is pathergy, may be factors in the formation of PAPA syndrome symptoms.

P2-144

Two cases of polymyalgia rheumatica successfully treated with antibiotics

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Conflict of interest: None

[Case 1] A 83-year-old male had visited our hospital for chronic heptitis B, type 2 diabetes and hypertension since 6 years ago. He was hospitalized in our hospital because of significant pain in shoulders, upper arms, hip girdle, and thighs for 1 week. Blood examination showed ESR 96 mm/h, CRP 13.84 mg/dl, RF 29 IU/ml, and anti-CCP Ab negative. He was diagnosed with polymyalgia rheumatica (PMR). He was treated with cefoperazone and sulbactam and his symptoms were improved. [Case 2] A 89-year-old female developed severe pain of her neck, shoulders, and upper arms from 1 week ago and was admitted to our hospital. ESR was 105 mm/h and CRP was 11.19 mg/dl. RF and anti-CCP Ab were both negative. She was diagnosed with PMR. She was treated with ceftriaxone and her symptoms were improved. [Discussion] Antibacterial agents is generally ineffective and steroid is the first priority in the treatment for PMR. However, many cases required long-term steroid treatment and adverse effects frequently occurred in elderly patients. Antibiotics therapy may be a useful option in PMR patients with high risk of adverse effects of steroids.

P2-145

Clinical characteristics of latter-stage elderly onset polymyalgia rheumatica

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is more common in the elderly, there have been few studies comparing the clinical features of PMR with those of other diseases. [Methods] We compared the clinical characteristics and complications of patients diagnosed between January 2012 and December 2021 at our hospital using Bird's criteria or the 2012 EULAR/ACR classification criteria. latter-stage elderly onset polymyalgia rheumatica was defined as age 75 years or older. [Results] The mean age was 74.2 years, mean observation period was 46 months, CRP was 8.4 mg/dL, and mean prednisolone dose was 14 mg/day. PMR patients in the >75 years of age group had significantly more history of osteoporosis (P=0.004) and fracture (P=0.005) than those in the <75 years onset group. There were significantly more cases of diabetes at the time of PMR at diagnosis in the group with onset over 75 years (P=0.024). There were no significant differences in sex, deaths, C-reactive protein levels, fractures after PMR diagnosis, or relapse. eGFR was lower in patients aged 75 years or older than in those aged <75 years (P=0.009). [Conclusions] Latter-stage elderly onset PMR have diabetes, renal dysfunction.

P2-146

A case of SAPHO syndrome presented with headache and skull biopsy was performed

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Conflict of interest: None

A 68 year-old woman began to have headaches, and although she was examined by a local orthopedic surgeon and a neurosurgeon, the cause of the headaches was unknown. She began to have left occipital pain and temporomandibular joint pain, and was referred to our hospital. In May, a contrast-enhanced MRI scan of the head revealed multiple enhancing effects in the mandibular head and skull. Multiple pustules began to appear on her soles, palms, and scalp, and his CRP was as high as 10 mg/dL. She was diagnosed as palmoplantar pustulosis by skin biopsy. Since the possibility of osteomyelitis was considered regarding the abnormal enhancement effect in the head on contrast-enhanced MRI, bone scintigraphy was performed in June. The bone scintigraphy showed accumulation in the sternoclavicular joint and hip joint as well as in the skull. From these results, SAPHO syndrome was suspected. A skull biopsy was peformed to prove osteomyelitis. Symptoms of fever and headache were alerted when NSAIDs were started. Although the bone biopsy results did not clearly demonstrate the presence of osteomyelitis, the clinical course was consistent with SAPHO syndrome. We report the various initial findings and course of this case with a discussion of the literature.

P2-147

Upadacitinib Hydrate might be a good choice for cytokine storm like phenomenon for psoriatic arthritis

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Conflict of interest: None

41 year-old man admitted to our hospital due to high fever, polyarthritis, skin lesions and lumbago with high serum CRP value. He had psoriasis from ten years ago, had been treated with Apremilast. He was suspected of infectious arthritis at first in orthpedics department. He had been treated with antibiotis and had drainage from right ankle. However, he had continous fever with negative studies on all the cultures which were taken before the treatments. He was referred to us for unknown fever of origin. He had high serum ferritin (536.9~6001.6 nglml, normal 274.8 ng/ml>), high CRP values and serum IL-6 296 ng/ml (normal 7.0 pg/ml>) with high fever. We suspected of cytokine storm like phenomenon due to psoriatic arthritis. We also diagnosed the cause of fever were partly due antibiotic agent and Celecoxib. We reconfirmed the diagnosis of Psoriasis vulgaris by skin biopsy. We treated him only with Upadacitinib Hydrate 15 mg/day. We had to pose the treatment after giving him it for first four days due to temporary lymphopenia. After its recovery, we restarted the treatment and all symptoms recovered. It might be very useful for cytokine storm like phenomenon, because it regulates mutiple cytokine abnomalitis. It is also easy to control its dosage when side effect might arise.

P2-148

Five cases of palmoplantar pustular arthritis treated with Iguratimod

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Conflict of interest: None

(objectives) we report five cases of pustulotic arthro-osteitis (pao) treated with iguratimod (igu). (case) 2 males, 3 females. palmoplantar pustulosis is diagnosed in all cases by a dermatologist. average age 52.6 years, average bmi 22.8. there are no allergy to metal, tonsillitis in all cases. as for 3 cases, joint symptom developed with cutis symptom. as for 2 cases, joint symptom developed 4 years later, 2 years later after cutis symptom. 3 patients had articulatio sternoclavicularis, and 2 patients had an acromioclavicular joint. the axial lesion was absent in all cases. (results) 3 patients received igu monotherapy. we used bucillamine together in 2 cases. the joint symptom, the cutis symptom remitted in all cases. time to remission is average of 13 weeks. the mean observation period after igu initiation is 35 months. we maintain all cases remission. (discussion) there are reports using antirheumatic, prednisolone, the biological preparation in pao. there is not the typical treatment. igu inhibits nf-κb. igu inhibit a production of inflammatory cytokine (tnf α, il1β, il6, il8, il17, mcp1) due to monocytic/macrophage and synovial cells. it is reported that il-17, il-6, il-8, increase of rankl, decrease in the tgf-β1 we are to become the choice of the treatment for pao.

P2-149

A case of common variable immune deficiency diagnosed due to arthritis

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Conflict of interest: None

A 43-year-old man had had arthritis for 9 months, when he was diagnosed with rheumatoid arthritis (RA). AlthoughNSAID and prednisolone (10 mg/day) were initiated, he was referred to this hospital because of the inefficacy of the treatment. He had past histories of 6 times of pneumonia since his 20's, irritable bowel syndrome, and otitis externa. He had no family history of immunodeficiency. The serum level of CRP was 8.08 mg/dl, and both RF and anti-CCP antibody were negative. He had diarrhea more than 10 times a day. As colonoscopy revealed an ulcer in the ileocecal region, the diagnosis of inflammatory bowel disease was made. Mesalazine was started, however, CRP further increased and thediarrhea continued. The patient was hospitalized. His immunoglobulin levels (IgG, A, M) and B cell number in the blood were below the sensitivity limit. He also had a decreased number of T cells. Thus, he was diagnosed with common variable immune deficiency (CVID). CVID sometimes complicates with autoimmune diseases. Autoimmune diseases can be diagnosed before underlying immunodeficiency is recognized. Complications of autoimmune diseases in CVID are reported to be 20%, and that of RA 1-10%. Detailed history taking is important for the diagnosis of underlying immunodeficiency.

P2-150

Persistent pain in interval period was revealed after remarkable response to colchicine in recurrent mono-arthritis by pseudogout: a case report

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Conflict of interest: None

[Case] The patient was a 75-year-old woman who had acute mono- or oligo-arthritis attack in the left hip and bilateral foot once a month over the past 4 months. Each episode lasted 3 days to a week. She was prescribed 5 to 10 mg of prednisolone 2 months ago and referred to our rheumatology clinic. On her first visit, C-reactive protein (CRP) was 1.13 mg/dl although she did not complain of any arthralgia. X-ray of the knee revealed calcification of the cartilage. We diagnosed recurrent pseudogout and continued low dose prednisolone. The attacks happened thrice in 2.5 months after our referral. She could go mountain-climbing in the interval period, but CRP remained positive. After 6 months from the first episode, she had left knee arthralgia for over 2 weeks and CRP increased to 6.58 mg/dl. Recurrent pseudogout improved drastically by 0.5 mg of colchicine. Three months after colchicine, she noticed persistent pain during mountain-climbing in "her thought" interval period of pseudogout. [Key Message] It is essential to refer to the patient history after remission of acute symptoms. History will rewrite when we take a retrospective glance.

P2-151

A Historical Origin Cohort Study Using J-CANVAS Registry Data on Risk Factors for Cytomegalovirus (CMV) Reactivation During ANCA-Associated Vasculitis (AAV) Treatment

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Conflict of interest: None

[Objective] In this study, we aimed to identify factors that increase the risk of CMV reactivation in AAV patients and to identify populations that require screening tests. [Methods] Patients with first-episode MPA or GPA between January 2017 and June 2020 were included. Patients were classified into two groups according to CMV antigen test positivity or negativity, and were analyzed for age, presence of chronic renal failure and diabetes, CRP, IgG level, lymphocyte count, BVAS at diagnosis (total score and renal score), initial steroid dose, steroid pulse, rituximab or Logistic regression analysis was performed using the following risk factors: CRP, IgG level, lymphocyte count, BVAS at diagnosis (total score and renal score), initial steroid dose, steroid pulse, and presence of rituximab or cyclophosphamide. [Results] Older age at diagnosis (OR 31.5; 95% CI 3.33-298, p=0.001) and higher BVAS Renal score (OR 3.95; 95% CI 1.55-9.84, p=0.017) were significant factors for CMV reactivation up to 48 weeks after treatment. [Conclusions] We report for the first time that patients with AAV and renal impairment at the time of initial therapy require more regular CMV antigen testing.

P2-152

Comparison of autoantibody-positive and -negative groups in 131 cases of TAFRO syndrome registered retrospectively

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Conflict of interest: Yes

[Objective] TAFRO syndrome is a new disease concept of unknown etiology with symptoms of thrombocytopenia, anasarca, fever, bone marrow fibrosis, and organomegaly. In a few recent reports, patients with autoimmune disease might present with TAFRO symptoms. Thus, differentiation of TAFRO syndrome from autoimmune diseases is important to elucidate the pathology. [Methods] We conducted a multicenter retrospective study to establish TAFRO syndrome and 131 patients were registered. We compared the two groups, autoantibody-positive group (n=72) and negative group (n=59), using the Mann-Whitney U test. The autoantibody-positive group included cases with positive antinuclear antibody ≧160 times or disease-specific autoantibodies. [Results] Comparison of data between the two groups showed that the platelet count was significantly lower in the autoantibody-positive group than in the negative group (median 2.85×10^4/μL vs 5.6×10^4/μL, respectively; P=0.000327); and serum ferritin level was significantly lower in the autoantibody-positive group than in the negative group (median 440.4 ng/mL vs 694.0 ng/mL, respectively; P=0.00694). [Conclusions] Autoantibody-positive TAFRO syndrome patients tend to have low platelet counts and a mild ferritin increase, but further analysis is necessary.

P2-153

A case of Sjogren's syndrome complicated with TAFRO syndrome

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Conflict of interest: Yes

We reported a case of Sjogren's syndrome who was treated with TAFRO syndrome and was treated with steroid pulse therapy and cyclosporinA (CyA). Case: A 54-year-old woman. At a local doctor, she was prescribed medicine for xerostomia and dry eye of Sjogren's syndrome. One month before hospitalization, she became aware of bilateral leg edema. Two days before hospitalization, she was suspected nephrotic syndrome due to proteinuria and referred to our department. Pleural ascites efffsion was noted. At the first visit, urine protein was 1.7 g/gCr, serum albumin was 3.0 g/dL, platelet count was 60,000/μL, and CRP was 5.5 mg/dL. We suspected SLE complicate, but antinuclear antibodies and anti-ds-DNA antibodies were negative. resistant to diuretics. Since TAFRO syndrome was suspected from clinical symptoms, bone marrow biopsy was performed and myelofibrosis was found. Treatment was started with PSL 60 mg/day and CyA 100 mg/day was added. Initially, the effect was weak, but after steroid half pulse therapy, diuresis was performed, weight decreased, and edema improved markedly. In addition, platelet count improved slowly. Reduced PSL and discharged. [Clinical Significance] There is no established treatment for TAFRO syndrome, but steroid pulse therapy, CyA, has been effective.

P2-154

A case of refractory polyarteritis nodosa that was complicated with myelodysplastic syndrome and responded to azacytidine

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Conflict of interest: None

[Background] Myelodysplastic syndromes (MDS) are associated with autoimmune diseases in approximately 10-25% of patients. It has been reported that autoimmune diseases associated with MDS often respond to steroids, but sometimes have difficulty of steroid tapering. We report a case of a patient with recurrent polyarteritis nodosa (PN), later found to have MDS, which was controlled by the addition of azacytidine. [Case] 42-year-old male presented with fever, skin rash, myalgia, and arthralgia. His symptoms improved with steroid therapy, but flared-up after tapering off, and was referred to our hospital. A skin biopsy revealed necrotizing vasculitis in the medium-sized blood vessels, and he was diagnosed with PN. WBC levels became decreased, and bone marrow examination was performed, which showed no significant findings. Four months later, his status remained refractory to treatment, and re-examination of bone marrow helped to diagnose as MDS. The disease was subsequently stabilized with addition of azacytidine. [Discussion] As in the present case, when PN is refractory to treatment, even if there is no abnormality in the bone marrow examination at the first time, the possibility of complications such as MDS has to be suspected, and repeated examination should be considered.

P2-155

A case of minimal-change nephrotic syndrome (MCNS) and multiple cerebral sinus thrombosis during treatment for SLE

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Conflict of interest: None

32-year-old woman, suffering from SLE, was admitted with severe headache, vomiting, and leg edema. BT37.0°C, BP132/96 mmHg. She had severe leg edema, no neck stiffness. Urine test: TP4+, RBC3+, UPCR24.2 g/gCRE, Blood test: TP4.6 g/dL, ALB0.9 g/dL, CRE0.60 mg/dL, BUN28 mg/dL, TC536 mg/dL, TG365 mg/dL, LDLc402 mg/dL, WBC13800/μL, HGB13.8 g/dL, $PLT48.5\times10^4$/μL, IgG505 mg/dL, C3 113.0 mg/dL, C4 21.9 mg/dL, CH50 32 U/mL, anti-dsDNA ab -, anti-Sm ab -, anti-ribosomal P ab -, Cerebrospinal fluid test: cell count3/μL, TP16 mg/dL, IL-6 55 pg/mL, IgG 2.1 mg/dL. IgG index 0.05. We did not diagnose her with NPSLE

and her head MRI showed multiple cerebral sinus thrombosis. She had no aPLAb, so we considered that she had thrombosis due to intravascular dehydration resulting from marked hypoalbuminemia. On the other hand, her renal biopsy showed as below, no abnormalities on light microscopy, subepithelial deposition, subendothelial edema, endothelial swelling, increased mesangial matrix were slightly observed in each on electronic microscope, deposits of Ig, C3 and C4 were only ± by immunostaining respectively. So she was diagnosis MCNS, not lupus nephritis. We experienced a case of SLE complicated with MCNS and multiple cerebral sinus thrombosis, such a case have not been reported, and were considered rare.

P2-156

A Case of Peliosis Hepatis Associated with Systemic Lupus Erythematosus Regressed by Immunosuppressive Therapy

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Conflict of interest: None

A 49-year-old female presented to our hospital with one-year history of skin rash in the dorsum of the hands. Blood tests revealed anemia, thrombocytopenia, reduced levels of complement, and elevated level of antinuclear antibody. Since urinalysis showed severe proteinuria at the nephrotic level in the absence of hematuria, she underwent a kidney biopsy and was diagnosed with lupus nephritis (class V). The level of D-dimer was also markedly elevated, and contrast-enhanced CT scan exhibited the large heterogenous mass occupying the right lobe of the liver while there were no signs of thrombosis. MRI findings lead to the diagnosis of peliosis hepatis. Nephritis achieved complete remission by combination therapy with high-dose PSL, TAC, and MMF and HCQ. On the other hand, hepatic mass remained the same size in the first 4 weeks of the induction therapy and significantly regressed with the decreasing level of D-dimer in the following year. Peliosis hepatis can cause severe complications including hepatic failure and hepatic rupture. Prevalence of peliosis hepatis in SLE remains uncertain. Some cases were reported to be aggravated by corticosteroids or immunosuppressants. We report the case of SLE associated with peliosis hepatis that was regressed by immunosuppressive therapy.

P2-157

A Case of Desmoid Tumor with Malignant Transformation after Re-administration of Etanercept

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Conflict of interest: None

[Objective] We report a case of intestinal desmoid-type fibromatosis with malignant transformation. [Methods] A 41-year-old woman with a history of rheumatoid arthritis was treated with MTX and etanercept. At the age of 51, a transverse colon tumor was resected. Pathological diagnosis was a desmoid tumor. A lesion appeared in the right iliopsoas muscle and grew slowly. About a year later, the patient was referred to our department. An incisional biopsy revealed a desmoid tumor. However, after resuming etanercept, the tumor grew again. A second incisional biopsy was performed one year later. The result was a diagnosis of high-grade sarcoma. Radiation therapy was performed. Three months later, she died of the tumor. [Results] Malignant transformation of desmoid tumors has been reported to be caused by multiple surgeries and radiotherapy in the past. Although the frequency of carcinogenesis by tumor necrosis factor (TNFα) inhibition therapy is low, it has been discussed from the beginning. After it was diagnosed with high-grade sarcoma, she died of a tumor. [Conclusions] The resumption of tumor necrosis factor (TNFα) inhibition therapy was thought to cause tumor malignancy.

P2-158

A case of multiple lung masses and endometrial cancer after improvement from anti-MDA5 antibody-positive interstitial lung disease (ILD)

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Conflict of interest: Yes

Case A 78y. o woman was admitted to the hospital 28 months before with fatigue. Skin rash and ILD were observed, and based on anti-MDA5 antibody 5310 ferritin2124 ng/ml, a diagnosis of rapidly progressive ILD due to asymptomatic dermatomyositis (CADM) was made. She was treated with steroid, tacrolimus (TAC), IVCY and IVIg, and overcame the disease. She could reduce PSL to 2 mg, TAC to 2 mg 6 months before. Periodic x-rays showed multiple lung masses. Suspecting lymphoproliferative disease (LPD), TAC was discontinued. A full body search revealed an abnormalities of uteres, biopsy revealed endometrial adenocarcinoma moderately-poorly differentiated. Three months later, a total hysterectomy was performed. After operation, a CT scan showed that the lung mass was reduced and was considered to be LPD. She underwent 6 courses of TC therapy. Discussion ILD with positive anti-MDA5 antibody have a high mortality rate, and intense immunotherapy is used, but relapse is rare and the long-term prognosis is relatively good. CADM can be considered paraneoplastic myositis, some cases showing malignancy after ILD treatment. In addition, strong immunosuppression can cause LPD. It may be considerable to reduse and stop immunosuppressive agents more promptly, as well as to continue to monitor for malignancy.

P2-159

A case of systemic scleroderma with intravascular lymphoma while taking methotrexate

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Conflict of interest: None

A 68-year-old woman was diagnosed with systemic scleroderma in X-4. She began taking MTX 6 mg/week in December X-1, and visited her previous doctor on June 1 because of the onset of fatigue and dyspnea on exertion in mid-May X. She had fever, decreased blood pressure, and red blood cells (RBCs). Fever, low blood pressure, decreased red blood cell and platelet counts, high LDH level (1552 U/L), and hypoxemia were observed, she was admitted to our hospital on June 2. The presence of systemic scleroderma, fever, hemolytic anemia, and thrombocytopenia suggested thrombotic microangiopathy (TMA) as a differential, but no crushed red blood cells were detected. MTX was discontinued on admission, and bone marrow puncture, biopsy, and random skin biopsy were performed. After admission, PSL 40 mg/day was started, but the improvement was poor. After random skin and bone marrow biopsy results were obtained, a diagnosis of intravascular large B-cell lymphoma with hemophagocytic syndrome was made. The patient was treated with chemotherapy because of the progression of symptoms even after discontinuation of MTX. Intravascular lymphoma is rare in patients with scleroderma, and we discuss its possible association with medically-induced immunodeficiency-associated lymphoproliferative disease.

P2-160

Consideration about how to use nintedanib for connective tissue disease-associated interstitial lung disease

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Conflict of interest: None

[Objective] For the patients with connective tissue disease-associated interstitial lung disease (CTD-ILD), early medical intervention would be desirable because pulmonary fibrosis often be irreversible. We analyze real-world single-center use of nintedanib for CTD-ILD patients, and discuss about the proper timing and medical indication of nintedanib. [Methods] We enrolled patients with CTD who received nintedanib for CTD-ILD from January 2020 to December 2021. A retrospective study and stratified analysis of patients who were administered nintedanib was conducted. [Results] %FVC tended to decrease in male (p=0.027), in the elderly group (>70 years, p=0.210), in the late group (p=0.03), in the severe %DLco group (< 40%, p=0.20). %FVC was not decreased more than 5% in the young group, in the early group who were started nintedanib within 10 months after confirmed a disease activity of ILD, and in the group whose score of pulmonary fibrosis was under 35%. According to our results, we had better consider starting nintedanib early especially for the patients who have the risks; over 70 years old, male, under 40% of %DLco, over 35% areas of pulmonary fibrosis. [Conclusions] It is important to diagnose ILD early and to start antifibrotic drugs with proper timing for cases in need.

P2-161

We report our experience with nintedanib in the treatment of interstitial lung disease associated with connective tissue disease in our department

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Conflict of interest: None

Methods: Sixty-nine patients who received NTB for ILD associated with collagen disease between August 2016 and April 2022 were included in the study, and the status of administration during the first 6 months after introduction was examined retrospectively. Results: The median age was 71 (58-77), 43 patients were female. 34 patients had systemic scleroderma (SSc) and 35 patients had other connective tissue diseases (non-SSc). When NTB started, the %FVC was 69.9% (60.8-78.1), KL-6 was 827 U/L (608-1251), and 42 patients were considered extensive disease. NTB starting dose was as follows: 300, 200, 150, and 100 mg/day in 41, 21, 2, and 2 patients, respectively. NTB-induced gastrointestinal symptoms and hepatotoxicity were observed in 31 and 14 patients, and the dose was reduced in 40 patients. NTB was discontinued due to gastrointestinal symptoms in 10 and due to hepatic impairment in 6 patients. Of the 50 continuing patients, 18 continued at 300 mg/day, 22 at 200, 4 at 150, and 6 at 100 mg/day, respectively. The frequency of NTB-induced gastrointestinal symptoms between patients with SSc and non-SSc did not differ. There was no difference in the frequency of gastrointestinal symptoms caused by NTBs in SSc patients with or without gastrointestinal lesions.

P2-163

Association for antiphospholipid antibodies with thrombosis in Japanese COVID-19 patients: a nested case-control study with propensity score matching

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Conflict of interest: None

[Objective] Thrombosis is a unique complication of coronavirus disease 2019 (COVID-19). We have reported a relatively high incidence of arterial thrombosis in Japanese COVID-19 patients. Although antiphospholipid antibodies (aPL) are frequently detected in COVID-19 patients, their clinical significance remains elusive. Therefore, we aimed to evaluate the associations of aPLs and the levels of β2GPI with thrombosis in COVID-19 patients. [Methods] We have experienced 34 thrombotic cases out of 594 patients admitted to our hospital. As non-thrombotic cases, 68 patients were selected based on the propensity score to make a 1 to 2 matched pair. Seven types of aPLs and β2GPI levels were measured using CLIA and ELISA, respectively. [Results] Of 102 patients, 39 (38%) were positive for one or more aPLs. The positive ratios of any aPLs were statistically indifferent regardless of the thrombosis; anti-CL IgG (8.8% vs 5.9%)/IgM (0% vs 5.9%), anti-β2GP1 IgG (21% vs 12%)/IgA (12% vs 16%)/IgM (0% vs 1.5%), and anti-PS/PT IgG (0% vs 2.9%)/IgM (12% vs 13%), respectively. No significant differences were observed in β2GPI levels in the two groups. [Conclusions] Although aPLs were frequently detected in Japanese COVID-19 patients, aPLs and β2GPI levels were irrelevant with thrombosis.

P2-164

A case of systemic lupus erythematosus with Shiga toxin-producing Escherichia coli infection differentiated from lupus enteritis by a fecal culture test

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Conflict of interest: None

[Case] A 38-year-old, female patient with systemic lupus erythematosus (SLE) and Sjögren's syndrome was admitted with right lower abdominal pain. She had no diarrhea or fever. She had experienced three relapses of lupus enteritis. CT revealed intestinal edema extending from the ileum to the ascending colon as in a previous episode. Initially, a SLE flare was suspected, but a fecal culture grew Shiga toxin-producing *Escherichia coli* (STEC). The patient was carefully followed-up with bowel rest, and her abdominal pain gradually improved. She was discharged on day 10. The source of STEC contamination could not be identified. [Clinical Significance] Lupus enteritis is a rare organ lesion associated with SLE, often involving small bowel inflammation, but there is no established diagnostic criteria. Lupus enteritis is empirically treated with high-dose glucocorticoids. On the other hand, an infection by STEC, which is implicated in foodborne disease, can resolve spontaneously. Foodborne diseases are difficult to diagnose without a fecal culture and may prompt unnecessary immunosuppressive therapy. When patients with an autoimmune disease present with colitis, infectious enteritis should be considered even in the absence of diarrhea, and a fecal culture should be performed.

P2-165

A case of Bordetella bronchiseptica pneumonia and bacteremia in a patient of dermatomyositis

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Conflict of interest: None

Case: A 79-year-old woman was diagnosed with anti Jo-1 antibody-positive dermatomyositis in X-19. She was taking 7 mg of prednisolone and 50 mg of azathioprine and her condition was stable. She was brought to our hospital with dyspnea in September X, and CT scan showed infiltrative shadows with air bronchogram, cardiac enlargement and bilateral pleural effusions. She was intubated and ventilated, and meropenem were administered for pneumonia. On the fifth day of hospitalization, *Bordetella bronchiseptica* was detected in two sets of blood cultures, so we diagnosed pneumonia and sepsis caused by *Bordetella bronchiseptica*. We changed meropenem to levofloxacin on the 8th day, and antibiotics was terminated on the 14th day. Her general condition improved, and she was transferred to the hospital on the 29th day. Discussion: *Bordetella bronchiseptica* is a gram-negative coccobacillus and is rarely pathogenic to humans. There have been reports of bacteremia in patients with acquired immunodeficiency syndrome, decompensated liver cirrhosis and so forth, but there are no reports of bacteremia during immunosuppressive therapy

for rheumatic disease. We often use immunosuppressive therapy for rheumatic disease, so we should be aware that *Bordetella bronchiseptica* can cause serious infections.

P2-166

The duration of viral shedding in patients infected with COVID-19 during remission induction treatment for connective tissue disease

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Conflict of interest: None

Objective: We studied the duration of viral shedding in patients infected with COVID-19 during remission induction therapy for connective tissue disease (CTD). Methods: Twelve patients with CTD admitted to our department between January 2021 and August 2022 who were infected with COVID-19 during induction remission therapy were included. The duration of the quarantine required was examined. Results: The median age was 73 (61-76), and 9 patients were female. Prednisolone was used in all patients, at a dose of 15.75 mg (10-45). Methylprednisolone pulse therapy, high-dose intravenous cyclophosphamide (IVCY), and rituximab were used in 6, 9, and 2 patients. IgG at the time of COVID-19 infection was 857 mg/dL (718-1218.5) and lymphocyte count was 736 /μL (403.2-980.5). The severity of COVID-19 was mild in 7 patients, moderate in 4, and severe in 1. Lemdesivir was were used in all patients. Sotrobimab, favipiravir, and dexamethasone were used in 4, 1, and 2 patients. One patient with severe disease died on day 5 of infection. The duration of the quarantine required in the 11 surviving patients was 14.5 days (10.8-25.3), which tended to be longer in patients treated with IVCY. Conclusion: IVCY and other immunosuppressive therapies may prolong the duration of viral shedding of COVID-19.

P2-167

HBV DNA monitoring in RA patients with resolved hepatitis B virus infection at our hospital

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Conflict of interest: None

[Objective] This study aimed to investigate HBV DNA monitoring in RA patients with resolved hepatitis B virus (HBV) infection at our hospital. [Methods] In September 2022, 438 patients receiving immunosuppressive drugs had been screened for HBV infection, and 74 patients were HBsAg negative and HBsAb or HBcAb positive. Excluding one vaccinated patient, 73 were included in this study. The mean age was 71.2 years, 24 males and 49 females. Medications used and mean HBV DNA monitoring intervals were examined. [Results] MTX was used in 53 cases, tacrolimus in 32 cases, biologic DMARDs in 22 cases, and JAK inhibitors in 4 cases, including those used in combination. Except for two patients, regular monitoring was performed with a mean interval of 7.4 weeks. [Conclusions] At our hospital, a pharmacist in the medical safety office has been checking the presence or absence of HBV testing and monitoring on the electronic medical record since this year, and has been sending requests for testing to the physicians in charge of cases in which no testing had been performed. Thereafter, monitoring was properly conducted according to the guidelines. Measures should be taken on the medical record to prevent physicians from forgetting to perform HBV-DNA testing regularly and to confirm the results.

P2-168

A case of polyarteritis nodosa (PAN) with relapse while suffering from COVID19

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Conflict of interest: None

[Case] A 28-year-old woman was diagnosed with PAN at age 5 with myalgia, erythema, and skin ulceration on her extremities and was treated with steroid pulse therapy. She relapsed at age 7. Her immunosuppressive therapy was discontinued after 1 year. She remained in remission for 20 years. At age 28, she had fever and sore throat on day X, and tested positive for SARS-CoV-2 PCR on day X+2. On X+7, although her sore throat improved, she began to have myalgia and painful subcutaneous nodules on her extremities. She was seen at our hospital on X+27. A skin biopsy of the subcutaneous nodule revealed severe inflammatory cell infiltration and fibrinoid necrosis in the middle artery, and an arteriography showed microaneurysms in the superior mesenteric artery and hepatic artery. She was treated with steroid pulse therapy starting at X+34. She was treated subsequently with methylprednisolone 32 mg/day and azathioprine 50 mg/day, and her symptoms were alleviated. [Conclusion] A patient with PAN who had remained in remission for 20 years without immunosuppressive therapy relapsed while suffering from COVID19. The association of COVID-19 with relapse of vasculitis has been reported in IgA vasculitis; further studies are needed on the association with relapse of PAN.

P2-169

An autopsy case of fungal optic neuropathy that was difficult to differentiate from temporal arteritis

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Conflict of interest: None

An 82-year-old man presented with left temporal pain that had persisted for more than 2 weeks and decreased vision in the left eye. Ophthalmologic examination revealed decreased visual acuity and upper horizontal visual field defect in the left eye, which was determined to be ischemic optic neuropathy. Based on new onset headache in an elderly patient, exacerbation and tenderness of the left shallow temporal artery, elevated inflammatory response, and ischemic optic neuropathy, the patient was determined to have temporal arteritis. Steroid pulse, PSL 0.6 mg/kg/day, and TCZ 162 mg/week subcutaneous injection were started, and the headache was relieved and vision in the left eye improved. However, the headache recurred, and the patient was treated again with steroid pulses. Biopsy of the temporal artery revealed no evidence of giant cell arteritis. The patient developed subarachnoid hemorrhage and died. Autopsy revealed filamentous fungi in the walls of cerebral arteries. The cause of death was determined to be subarachnoid hemorrhage due to rupture of an infected aneurysm that had spread from a fungal optic neuropathy. Fungal optic neuropathy is sometimes difficult to differentiate from temporal arteritis, and we report this case as an instructive case.

P2-170

Disseminated Mycobacterium chelonae infection with refractory nasal lesions

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Conflict of interest: None

[Case] A 79-year-old man. He was referred to our hospital with a chief complaint of refractory nasal septal ulcer and multiple skin ulcers. He had a history of sinusitis surgery about 30 years ago. He had been treated with steroid pulses for interstitial pneumonia and post-treatment prednisolone 6 months before the visit. 2 months before the visit, epistaxis appeared and a nasal septal ulcer was observed. A nasal biopsy showed severe necrosis of the nasal mucosa and an infiltrate of neutrophilic inflammatory cells, which raised suspicion of granulomatosis with polyangiitis. Nasal mucosa and skin rebiopsies showed acid-fast bacilli, and *Mycobacterium chelonae (M. chelonae)* was detected in culture. [Discussion] A systematic review of 8 cases of non-tuberculous mycobacterial with sinus lesions is available. In this report, all patients underwent endoscopic sinus surgery, and 4 cases were *M. chelonae*. Disseminated cutaneous *M. chelonae* has also been widely reported, with 92% of patients receiving steroids. Non-tuberculous mycobacterium tuberculosis should also be raised in the differential for

refractory nasal lesions that develop after sinus surgery or in patients receiving long-term steroid medication.

P2-171

The association between myalgia and the distribution of inflammatory cells and sensory nerve fibers in patients with myositis and fasciitis complicated with autoimmune diseases

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Conflict of interest: None

[Objective] We hypothesized that the difference in frequency of myalgia is related to the distribution of inflammatory cells and sensory nerves in the muscle and fascia in patients with inflammatory myopathy complicated with autoimmune diseases. [Methods] Among patients with suspected myositis or fasciitis who underwent en bloc biopsy, the immunostaining of substance P in the muscle and fascia was performed in 8 patients with myalgia and 8 patients without myalgia. The association between myalgia and the distribution of substance P-positive nerve fibers and inflammatory cells in the muscle and fascia was examined. [Results] In fascia, substance P-positive nerve fibers were present around small blood vessels in the subcutaneous adipose tissue adjacent to deep fascia and in the loose connective tissue between muscle and deep fascia, regardless of the presence or absence of myalgia. In the patients with myalgia, inflammatory cells and substance P-positive nerve fibers were adjacently present in the muscle and fascia. [Conclusions] The distribution of inflammatory cells and substance P-positive nerve fibers in fascia and muscle adjacently coincided in patients with myalgia, whereas the distribution in patients without myalgia was different.

P2-172

Current Status of Rheumatology Team Medical Care at Our Hospital

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Conflict of interest: None

[Objective] Toho Hospital Rheumatology Team was formed in September 2017, and we will examine the trajectory and future prospects. [Methods] Our Team consists of 16 occupations: doctors, nurses, pharmacists, physical therapists, occupational therapists, radiological technologists, registered dietitians, dentists, dental hygienists, doctor's clerk, nursing clerk, medical affairs department, system department, planning and public relations department, hospital-clinic cooperation section, and out-of-hospital dispensing pharmacist. The aim of team is to maximize their specialized knowledge and skills while enhancing and respecting their expertise and sharing information. As a specific team goal, we planned open seminars for patients. In daily medical care, we aim to provide medical care that is close to the patient by demonstrating each specialty. [Results] All occupations always thought about what was necessary for patient care, worked voluntarily, and came up with ideas. The contents are shared at the monthly conference. [Conclusions] In order to evaluate the five-year trajectory and connect it to future prospects, it is important to devise what each occupation can do to the maximum, set goals for each, and understand each other's occupations.

P2-173

A case in which a patient got pregnancy and a child after administration of sarilumab

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Conflict of interest: None

[Case] Female, 32 years old. She was diagnosed with juvenile idiopathic arthritis at age 12. Various treatments were performed, but the activity was still high. Several biological drugs became unusable due to side effect and secondary ineffectiveness. At age 28, she wished to get married and pregnancy, and visitted us. We changed biological treatment from infliximab to sarilumab. Her disease activity got into remission, and we reduced and discontinued methotrexate. She became pregnant at the age of 30, and sarilumab was temporarily discontinued. At 16 weeks of gestation, a temporary exacerbation of activity was observed, but the dose of PSL was increased to 5 mg/day, and the pregnancy continued without restarting sarilumab. A normal infant was delivered at 38 weeks of gestation.

P2-174

A case of difficult control of rheumatoid arthritis during pregnancy -Is it essential to withdraw biologics during pregnancy?-

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Conflict of interest: None

[Case] A 32-year-old woman with rheumatoid arthritis had worsening disease activity after withdrawal of SASP and ETN due to pregnancy. She resumed the use of biologic agents, but the high disease activity persisted. PSL 10 mg/day and intra-articular steroid injections were used to improve her joint symptoms. She had a vaginal delivery at 39 weeks and 3 days. The baby weighed 2341 g (-1.83 SD), and the placenta weighed 270 g (-3.0 SD). [Clinical Significance] We experienced a case of difficult management of RA during pregnancy. In this case, placental dysplasia was prominent, which may have affected the growth and birth weight of the fetus. It has been suggested that exposure to high concentrations of IFN-γ during pregnancy may lead to miscarriage, stillbirth, or premature delivery due to inhibition of syncytiotrophoblastic membrane formation, so it is very important to stabilize RA disease activity during early pregnancy, when the placenta is forming. It has been reported that worsening disease activity was observed in nearly 30% of pregnant women with RA who terminated biologic agents at the time of pregnancy, and the risk of preterm delivery increased. Depending on the disease course prior to conception, the option of not withdrawing biologic agents may be worth considering.

P2-175

A case of neonatal lupus with skin rash at birth

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Conflict of interest: None

[Maternal history] Mother was diagnosed with Sjögren's syndrome at age 20 years, and positive anti-SS-A and anti-SS-B antibodies. She was treated with loxoprofen sodium for joint pain and hydrocortisone acetate for erythema annulare. She became pregnant at age 31 and experienced no complications during the pregnancy, and Sjögren's syndrome. The baby was born by emergency Cesarean section at 38 weeks and 1 day of pregnancy. [Child history] The baby was born with an Apgar Score of 5 (heartbeat: 2, skin color: 0, others: 1). Physical examination revealed erythema up to 1 cm in size scattered. Blood tests showed liver damage, and positive for anti-SS-A and anti-SS-B antibodies. There was no evidence of blood cell loss or heart block. Hepatic enzymes peaked out at 4 days of age, and the skin rash began to appear at the same time. At a routine examination 2 months after birth, anti-SS-A and anti-SS-B antibodies were detected. No abnormalities were noted until the 2-year checkup. [Clinical Significance] Neonatal lupus rashes are generally seen at birth to by 3 months of age. The parents' acceptance of this case was good because we had explained, showing pictures. It is important to provide preconception care for the increased incidence of neonatal lupus, in the next pregnancy.

P2-176

A case of a patient with systemic lupus erythematosus whose lupus nephritis worsened due to pregnancy and further complications of TMA, and both patient and fetus were saved by emergency caesarean section, continuous hemodialysis, and plasmapheresis treatment

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Conflict of interest: None

Case 41-year-old female Clinical course Pregnancy was established by the second thawed embryo transfer. Because of high blood pressure at 13 weeks' gestation, methyldopa was started to be administrated. Furthermore, at 17 weeks, the increase in proteinuria and the thrombocytopenia were observed, and the symptoms were temporarily improved by increasing the dose of prednisolone and methyldopa. Though she has gradually increased blood pressure until 21st weeks gestation, she was hospitalized. Nevertheless, blood pressure was strictly managed in hospitalization, generalized edema and oliguria have worsened and first high dose glucocorticoid therapy was made at 23 weeks. but ineffective. The emergency caesarean section was quickly performed at 24 weeks, and the fetus was delivered safely. Pregnancy associated TMA was occurred and continuous hemodialysis and plasma exchange therapy were started. TMA was recovered, but lupus nephritis did not improve, so second high dose glucocorticoid therapy and first cyclophosphamide pulse therapy were made. Lupus nephritis was also improved. Lupus nephritis worsened and TMA was rarely observed. It is necessary to make quick decision to terminate the pregnancy. If symptoms were not improved, hemodialysis or plasma exchange should be performed.

P2-177

A case of ulcerative colitis-associated spondyloarthritis treated with golimumab until 27 weeks of gestation

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Conflict of interest: None

Objective: Safe drug delivery is critical to controlling immune disease during pregnancy. Certolizumab pegol is safe for use in pregnant women, and infliximab and adalimumab carry low fetal risks, and can be used until second trimester. The use of golimumab in pregnant women is rare, suggesting a need for case reports. We report a case involving outpatient pharmacist and physician collaboration in which golimumab was used until week 27 of pregnancy without harming the fetus. Case: A woman in her 30's with a history of mesalazine-induced pancreatitis and azathioprine-induced hepatitis developed ulcerative colitis two years ago. She was referred to rheumatology for arthritis and was diagnosed with spondyloarthritis. We made the collaborative decision to introduce golimumab with long dosing intervals due to work and lifestyle reasons. Clinical remission was achieved at six months, after which a pregnancy was confirmed. We considered switching to other bDMARDs, but the patient hoped to continue golimumab due to efficacy and side effect concerns. Despite a risk of exacerbating the disease, golimumab was stopped at 27 weeks of pregnancy. The patient gave birth by normal labor, and the infant displayed no side effects of vaccination. Discontinuation of golimumab did not worsen symptoms.

P3-001

Risk factors for cardiovascular disease among patients with systemic lupus erythematosus; an umbrella review

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Conflict of interest: None

[Objective] Cardiovascular disease (CVD) is one of the major causes of death in patients with systemic lupus erythematosus (SLE), and systematic reviews (SRs) have been conducted from various aspects. In this study, we aimed to synthesize previously published SRs to comprehensively evaluate CVD risk factors in SLE patients. [Methods] The study design was an umbrella review which was conducted in June 2022 using electric database including PubMed, Embase, Cochrane Library. The literature included was systematic reviews and meta-analyses examining CVD risk factors in SLE patients. [Results] 1159 articles were identified and, through full paper review, nine articles were included. We identified SLE-specific risk factors including disease duration, lupus nephritis, disease activity, organ damage index, neurological disorders, glucocorticoids, azathioprine, biologic agents, anti-phospholipid antibodies. After quantitative synthesis for lupus nephritis, which was the only one with an effect size in two SRs, the relative risk of CVD was 1.68 (95% confidence interval: 1.22, 2.30). [Conclusions] This study showed that lupus nephritis is a risk factor for CVD, however, other risk factors have not been studied enough, and more and better quality SRs are needed.

P3-002

The association of clinical manifestation and autoantibodies to arrhythmia in systemic sclerosis

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Conflict of interest: None

[Objective] Anti-centromere is reported as a risk factor for arrhythmia in the Systemic sclerosis (SSc) patients. Since the prevalence of arrhythmia in SSc has not been investigated in Asia, we evaluated the prevalence of arrhythmias and risk factors for arrhythmias in SSc. [Methods] We enrolled 468 SSc patients at our hospital from 2006 to 2021. The clinical data including electrocardiogram (ECG) and specific autoantibodies were collected. [Results] ECG was performed in 427 patients, and 22.7% (97/427) had arrhythmias (PAC, 39.7%; PVC, 44.1%; Pacemaker implant, 5.1%). Age, male sex, severity of skin lesion and the presence of pulmonary artery hypertension, dyspnea or palpitation were associated to arrhythmias. The prevalence of arrhythmias for each antibody was not significantly different (anti-topoisomerase I, 21.4%; anti-centromere, 22.4%; anti-RNA polymerase III, 25.7%; anti-RNP, 25.8%), and associations between specific autoantibodies and arrhythmia were not identified. [Conclusions] The present study identified several risk factors for arrhythmias in Japanese SSc patients, although no significant association was observed between arrhythmias and autoantibody profiles. These results might be due to regional differences, thus additional analysis will be needed.

P3-003

Analysis of polymyalgia rheumatoid arthritis patients who did not show joint echo findings at the first visit

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Conflict of interest: None

[Objective] Polymyalgia rheumatoid arthritis (PMR) is an inflammatory disease of unknown etiology that frequently occurs in the elderly. We previously reported that about 30% of PMR patients in our hospital had no joint ultrasound findings at the first visit. In this study, we analyzed the characteristics of these patients compared with patients who showed joint

echo findings at the first visit. [Methods] A total of 36 patients were included. Among them, we compared the physical findings, blood test findings, therapeutic drugs, and the time to improvement in 26 patients who showed joint echo findings at the first visit and 10 patients who did not. [Results] ESR was significantly reduced as a blood inflammatory marker compared to another group. Serum CRP tended to be low, although there was no significant difference. Serum sedimentation was significantly reduced as a blood inflammatory marker. Serum CRP tended to be low, although there was no significant difference. Also, in treatment, it tended to take a long time to reduce the steroid dose. [Conclusions] Among the PMR patients in our hospital, the group without joint echo findings at the first visit had a low inflammatory response in the blood, but tended to take a long time to stabilize after treatment.

P3-004

Treatment Experience of Polymyalgia Rheumatica in our Department

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Conflict of interest: None

[Objective] To investigate the treatment course of polymyalgia rheumatica (PMR) in our department. [Methods] Subjects were 71 patients (29 males, 42 females) diagnosed with PMR in our department between May 2011 and February 2022, and were retrospectively reviewed. [Results] The mean age at diagnosis of PMR was 77 years, CRP was 6.8 mg/dl, ESR was 75 mm/hr, and the RF positivity rate was 10%. The starting dose of steroids (PSL) was 7.9 mg. PSL could be discontinued in 47 patients. The time to discontinuation was 16 months, and half were able to discontinue within 2 years. Twenty-four patients were unsuccessful. Forty-two percent of patients who could discontinue were hesitant to taper their PSL. Among patients who could not discontinue, 66% were hesitant. During the course of the study, 9 patients (12.7%) developed malignacy, and the time from PMR diagnosis to cancer detection was 42 months. 9 patients were hesitant to taper PMR. Rheumatoid arthritis (RA) was diagnosed during the course of the study in 7 patients (9.9%), and the age at diagnosis was 69 years. Time to diagnosis was 24 months, and 6/7 patients were hesitant to taper their PSL. [Conclusions] In summary, we report the course of PMR treatment in our department, and patients who hesitated to taper PSL often had cancer or RA.

P3-005

Analysis of phenotypic and regulatory T cell function with aging in a mouse model of rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify age-related phenotypic and Treg cell differences in mice with GPI-induced arthritis (GIA). [Methods] 1) GIA was induced in young and old mice, and phenotypic differences were verified using the arthritis score. CD4-positive T cells sorted from each inguinal lymph node were analyzed by scRNA-seq, and extracted differentially expressed genes (DEGs). 2) GIA was induced in young and old mice, and the percentage of Treg cells and expression of functional molecules in inguinal lymph nodes were analyzed by flow cytometry. 3) GIA was induced in young and old mice after Treg depletion by administration of anti-CD25 antibody, and the arthritis scores were compared. The differences in arthritis pathological scores were evaluated. [Results] 1) The arthritis score was significantly higher in the aged mice on Day 16, and more DEGs were extracted in the Treg cluster than in the other clusters by scRNA-seq. 2) The proportion of Treg cells was significantly larger and CD25 expression was significantly lower in the aged group. 3) The arthritis score was significantly increased in the young group, and the inflammation scores and erosion scores were also significantly higher. [Conclusions] It was suggested that the functional decline of Treg cells is involved in old-onset arthritis.

P3-006

The lymphocyte specific tyrosine kinase inhibitor attenuates lung fibrosis via the suppression of TGF beta production in regulatory T cells

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Conflict of interest: None

[Objective] The significance of Lck inhibition in lung fibrosis has not yet been fully elucidated, even though lung fibrosis is commonly preceded by inflammation caused by infiltration of T cells. In this study, we examined the effect of Lck inhibition in an experimental mouse model of lung fibrosis. [Methods] In bleomycin induced pulmonary fibrosis model, A770041, a Lck specific inhibitor, was administrated daily by gavage. The expression of TGFβ on Tregs was examined by flow cytometry and quantitative polymerase chain reaction. The concentration of TGFβ in bronchoalveolar lavage fluid (BALF) and cell culture supernatant from Tregs was quantified by an enzyme linked immunosorbent assay. [Results] A770041 inhibited the phosphorylation of Lck in murine lymphocytes to the same degree as nintedanib. A770041 attenuated lung fibrosis in bleomycin treated mice and reduced the concentration of TGFβ in BALF. A flow cytometry analysis showed that A770041 reduced the number of Tregs producing TGFβ1 in the lung. In isolated Tregs, A770041 decreased the *Tgfb* mRNA level as well as the concentration of TGFβ in the supernatant. [Conclusions] Lck inhibition attenuated lung fibrosis by suppressing TGFβ production in Tregs and support the role of Tregs in the pathogenesis of lung fibrosis.

P3-007

Inhibition of STAT3 activation in the area postrema by baricitinib during collagen-induced arthritis

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Conflict of interest: None

[Objective] Baricitinib, a JAK inhibitor, drastically attenuates patients-reported outcomes associated with pain and fatigue, in patients with RA, which suggests that this agent can affect the brain. The brain-blood barrier (BBB) makes it difficult for baricitinib to reach the brain. However, it is possible that baricitinib can reach the AP where the BBB is weaker than brain regions. Here, to examine influence of baricitinib on the AP, we analyzed the brain of mouse models. [Methods] We created interleukin-6 intravenous administration (IL-6IV) model and collagen-induced arthritis (CIA) model, and performed oral administration of baricitinib or vehicle. We performed immunostainings for phospho-STAT3 (pSTAT3) using brain sections, and quantitatively analyzed immunoreactivity in the AP. In the experiments using CIA model, the sucrose preference test was also performed. [Results] IL-6IV and CIA induced the expression of pSTAT3 in the AP. Baricitinib significantly suppressed the pSTAT3 expression in both models. Sucrose preference during CIA was higher in baricitinib-treated mice. [Conclusions] Baricitinib could inhibited STAT3 activation in the AP. This agent might act on the brain via modulating STAT3 activity in the AP.

P3-008

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 pathogenesis of rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is unknown. Associations of cellular senescence (CSen) have been reported in idiopathic pulmonary fibrosis. We explored the involvement of cellular senescence in the mechanism of RA-ILD, using SKG/Jcl mice. [Methods] We induced ILD in SKG/Jcl mice (SKG-ILD) by administration of zymosan (Zym). To evaluate CSen in SLG-ILD, immunohistochemistry and RT-qPCR were used to detect a CSen marker, $p21^{WAF1/CIP1}$. The mixture of Dasatinib and Quercetin (D+Q) was administered as senolytics, and its effect on ILD was evaluated by histological analysis, RT-qPCR of fibrosis marker genes, and flow cytometric analysis of immune cells. [Results] p21 positive cells were found in SKG-ILD as early as 4 weeks after administration of Zym and increased along with fibrosis progression. *Cdkn1a*, encoding p21, was also significantly increased. Treatment with D+Q significantly decreased the expression of *Cdkn1a* and *Col1a1* and histological score of fibrosis, suggesting D+Q may alleviate lung fibrosis. [Conclusions] CSen increased in SKG-ILD and treatment with D+Q alleviated the ILD, indicating the involvement of CSen in the pathogenesis of ILD. As with SKG-ILD, CSen may be considered as a therapy for RA-ILD.

P3-009

Tissue macrophage is shifted to proinflammatory M1 type in model mouse of macrophage activated syndrome

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Conflict of interest: None

[Objective] To investigate activation state of tissue macrophages in mouse model of macrophage activation syndrome (MAS). [Methods] The model of MAS was developed in C57BL/6 mice by repeated injection of CpG synthetic oligodeoxynucleotide (ODN1829) which stimulates toll-like receptor 9-mediated signals. Blood and organ samples were collected on day 9 after 5 times of injection and analyzed by immunostaining and quantitative PCR. [Results] In ODN1829-injected mouse, pancytopenia, hepatosplenomegaly and liver dysfunction were prominent. By immunological staining, tissue macrophages expressed M1-type surface markers such as CD80. Quantitative PCR using RNA extracted from liver tissue showed increased expression of proinflammatory M1-type macrophage related gene products such as TNF-α, IL-6, and iNOS in ODN1826-treated mice. Furthermore, IFN-γ is supposed to be involved in macrophage activation by TLR9-mediated stimulation. In fact, serum IFN-γ and IFN-γ-induced chemokines levels were elevated and increased mRNA expression of IFN-γ in affected liver tissue was observed in ODN1826-treated mice. [Conclusions] In the liver tissue, the gene expression of IFN-γ is observed and macrophages were shifted towards proinflammatory M1 type, which explains one aspect of mechanisms of MAS.

P3-010

Complement factor C5a alone promotes NLRP3 inflammasome activation in myeloid cells

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Conflict of interest: None

[Objective] The anaphylatoxin C5a is contributes to immune cell recruitment into inflamed tissue and local inflammation. The role for C5a in rheumatic diseases has recently become clear. However, the association between inflammasome activation and C5a is unclear. [Methods] Human PBMCs were stimulated with C5a *in vitro* and measured for IL-1b secretion by ELISA. In addition, the expression of IL-1b in culture supernatants was also examined by western blotting analysis. Similarly, magnetic beads-isolated CD4 positive monocytes were stimulated with C5a *in vitro* and measured for IL-1b secretion by ELISA. Flow cytometry was performed to detect caspase-1 activation. [Results] C5a stimulation induced IL-1b production in C5a concentration dependent manner. Similarly, CD14 positive monocytes stimulated with C5a released IL-1b. FACS analysis showed the intracellular caspase-1 expression of C5a stimulated PBMCs was revealed in not CD3 positive T-cells, but CD14 positive monocytes. [Conclusions] C5a induced the production of IL-1b in human PBMCs. Furthermore, a major source of IL-1b was suggested to be CD14-positive monocytes. Because human PBMCs stimulated with C5a alone produce IL-1b, C5a seems to be associated with both the priming and activation process of the NLRP3 inflammasome activation.

P3-011

anti-OJ antibody positive interstitial pneumonia with mediastinum lymphadenopathy

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Conflict of interest: None

[Background] anti-aminoacyl-tRNA synthetases (ARS) syndrome is inflammatory myopathies characterized by anti-ARS antibodies. The number of cases is increasing after anti-ARS antibody ELISA test got available under the health insurance system in Japan. However, anti-OJ antibody cannot be detected with the ARS test because the specific antigen for anti-OJ antibody (anti-isoleucyl-tRNA synthetase) is not included in the ARS ELISA test. We here detected two cases of anti-OJ positive cases using Euroblot methods. [Results] Interstitial lung disease, lymphadenopathy, arthritis, obesity, diabetes mellitus and either the history of carcinoma of high tumor marker seems to be the shared symptoms with the two cases. [Discussion] The two cases showed close symptoms to the reported anti-OJ syndrome patiens, indicating they are also anti-OJ syndrome cases. Accumulatin of increased cases in the future would determine the clinical phenotype of anti-OJ syndrome.

P3-012

Increased levels of serum leucine-rich alpha 2 glycoprotein in inflammatory rheumatic diseases including vasculitis

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Conflict of interest: None

[Methods] A total of 247 patients who visited our department between September 18, 2020 and August 25, 2022 and had serum LRG measured were included in the analysis. Patient background, disease, and hematology data were collected and compared within cases. [Results] With regard to background diseases, polymyalgia rheumatica [PMR] (n=13), rheumatoid arthritis [RA] (n=38), vasculitis (n=43), adult-onset Still disease [AOSD] (n=10), inflammatory bowel disease [IBD] (n=12), bacterial infection (n=31), systemic lupus erythematosus [SLE] (n= 10), idiopathic inflammatory myositis [IIM] (n=7), spondyloarthritis [SpA] (n=7), other IMID (n=21), no rheumatic disease [non-IMID] (n=21), other diseases including malignant diseases [Others] (n=10). Overall, CRP averaged 0.51 mg/dL and LRG 20.5 μg/mL; for PMR, RA, vasculitis, AOSD, and IBD, the log-approximation curves for CRP and LRG tended to be higher than for bacterial infection. In contrast, they tended to be lower than those for bacterial infections in SLE, IIM, SpA, and IMID. The log-approximation curves for bacterial infections show LRGs of 37.1 and 42.9 μg/mL for CRP 5 mg/dL and 10 mg/dL, respectively. [Conclusions] If LRG is higher relative to CRP than bacterial infection, it is likely that inflammatory IMID such as PMR may be more likely.

P3-013

Collaboration for kidney biopsy to diagnose with rheumatoid disease

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Clinic

Conflict of interest: None

[Objective] kidney is one of the major targeted organs in some rheumatic diseases, thus some cases are necessary for the indication of the kidney biopsy. Although these indications were limited in some areas because of lacking in nephrologist, kidney biopsy was performed in our hospital for nephrologist and rheumatologist. [Purpose/Methods] The aim was to evaluate clinical aspect of 7 kidney biopsy cases. Results: Total 7 cases were 1 males and 7 females, and average age was 61.4±12.49 [46-76] years. The category of rheumatological disease were included various disease. [Results] The reasons for doing kidney biopsy were compromised with 6 urinalysis abnormality (including 1 nephrotic syndrome, 2 RPGN) and 1 cases of unknown kidney injury. After enforcing kidney biopsy, three cases were categorized non-collagen, and 4 case were differed from pre-test predictions, which changed treatment strategy. [Conclusions] Collaboration of several hospitals to enforce the kidney biopsy were meaningful.

P3-014

Research on evaluation of inflammation site using knee joint ultrasound for rheumatoid arthritis patients

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Conflict of interest: None

Objective: To determine the statistical results of the distribution of knee arthritis on ultrasonography in patients with rheumatoid arthritis. Methods: Subjects were patients who met the 2010 ACR/EULAR classification criteria. Eleven sites were examined: suprapatellar bursa, medial and lateral fossa, patellar tendon, medial aspect, medial lateral ligament, glenoid region, external aspect, glenoid tendon, lateral lateral ligament, and knee fossa, and synovial thickening and power Doppler signal were evaluated. Results: Twenty RA patients underwent ultrasound with 31 (15 right, 16 left) knees. The number of GS and PD signals above Grade 2 at each site of observation were as follows. Suprapatellar sac (GS/PD): 13 (42%)/3 (10%), medial fossa: 14 (45%)/5 (16%), lateral fossa: 21 (68%)/7 (23%), patellar tendon: 2 (6%)/2 (6%), medial aspect: 11 (35%)/5 (16%), medial collateral ligament: NA/2 (6%), the quadriceps: 3 (10%)/NA. NA, lateral aspect: 14 (45%)/7 (23%), orbicularis tendon: NA/7 (23%), lateral collateral ligament NA/3 (10%), glenoid fossa: NA/2 (8%). Conclusion: In RA patients, synovitis was observed mainly in the suprapatellar bursa, medial fossa, and lateral fossa. Patellar tendon tibial attachment inflammation and synovitis of the patellar tendon were also identified.

P3-015

Three cases of systemic sclerosis with poor findings of abnormal capillaries in the nailfold videocapillaroscopy

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Conflict of interest: None

[Background] In April 2016, we opened a Raynaud's outpatient clinic and have been providing connective tissue disease care with nailfold videocapillaroscopy (NVC) to make early diagnosis of SSc etc. In this report, we describe three cases of SSc with no characteristic findings on NVC, although skin stiffness was already present. [Cases] Of the 213 patients who visited our Raynaud's outpatient clinic between April 2016 and October 2022, 28 SSc patients were found to have skin stiffness at the time of examination. Among them, three cases were identified with normal or nonspecific findings with no SSc pattern (giant capillary, < 3 capillaries/mm). Unproportionally to the NVC findings, all three patients had skin induration greater than 6 points of mRSS. Two of them were complicated by interstitial pneumonia. In all 3 cases, these NVC examinations were performed within 2 years from the respective onset of Raynaud's symptoms. Two cases had anti-RNA polymerase III (one of them was co-positive for anti-Scl-70), and the other had anti-Th/To antibody. [Clinical Implications] Cases with SSc with established skin stiffening and organ damage may have NVC findings with non-SSc patterns. It is interesting in considering the sensitivity of NVC in diagnosis of SSc.

P3-016

Five cases of Rhupus

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Conflict of interest: None

[Conclusions] Case 1: 57 y.o. female, diagnosed RA, was treated by Golimumab had eruptions. She had CCP and ANA Ab., after injection, she had low-complimentemia and anti-ds-DNA. Case 2: 74 y.o. female was diagnosed RA from 18 y.o. and treated by Adalimumab. She had CCP and ANA Ab., after injection Anti-ds DNA became positive. Moreover, she had Jaccoud deformities. Case 3: 74 y.o. male, was suffered RA from 18 y.o., and Myocardial Infarction from 40 y.o., treated by Adalimumab. He had CCP, ANA, anti-Cardiolipin Ab IgG and pancytopenia. Case 4: 46 y.o. female was diagnosed RA because of arthritis, CCP, ANA, SS-A and fluorescence Dye test positive, treated with MTX. After 1 year, she had fever, eruption, low complimentemia and pancytopenia, then she was diagnosed SLE because of ANA, Sm, and ds-DNA, treated by steroids and hydroxychloroquine. Case 5: 66 y.o. female, CCP, ANA, SS-A and SS-B positive, had pain of both knee joints and left MCP arthritis. She was diagnosed RA and treated with MTX, afterwards she had ds-DNA Ab. Rhupus was combination words of RA and SLE. The differnce of arthritis between RA and SLE are RA has tenosynovitis, and SLE has non-erosive arthritis and Jaccoud deformities. They are associated by IFN-γ, characterized by pain during the stable state. We must analyse more cases.

P3-017

A case of chronic idiopathic intestinal pseudo-obstruction (CIPO) without typical SLE symptoms despite being positive for anti-PCNA antibodies

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Conflict of interest: None

Anti-PCNA antibody was reported by Miyachi et al. in 1978 as an SLE-specific antinuclear antibody that recognizes cell cycle-related molecules. We report a case with PCNA-type antinuclear antibodies but without the clinical features of SLE but with scleroderma-like CIPO. The patient was a 57-year-old woman who had a history of abdominal surgery. She was 44 years old with abdominal distension and was diagnosed with functional gastroenteropathy. She developed ileus at age 51 and was treated with medication, but her symptoms persisted. At the age of 52, she was diagnosed with adhesive hypoperistalsis of the small intestine, and underwent gastrojejunostomy and adhesion dissection, but diarrhea persisted after the operation. Raynaud's phenomenon appeared at the age of 53, and a blood test revealed positive PCNA-type antinuclear antibodies. She underwent an examination at the department of immunology at D Hospital, but was placed under observation because the pathology was not compatible with SLE. At the age of 54, she also developed biliary vomiting. She was referred to the department of gastroenterology at our hospital at the age of 56 because of recurrent ileus and fever. A scleroderma-like evaluation may be useful for evaluating disease conditions in patients with this antibody.

P3-018

A case of focal eosinophilic myositis with fever and swelling on the right buttock

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Conflict of interest: None

A 70-year-old man developed a slight fever and right buttock pain and swelling. MRI showed swelling of the right gluteus maximus muscle and high signal intensity on STIR image. The skin biopsy showed eosinophil infiltration in the striated muscle without neoplastic lesions. He had inadequate responses to antibiotics and glucocorticoids and therefore was admitted to our hospital. Blood tests revealed a high creatine kinase (CK) value at 5649 IU/L and elevated levels of C reactive protein (CRP). We reassessed the buttock biopsy specimen and identified inflammatory cell infiltration mainly composed of eosinophils surrounding muscle fibers, which led to the diagnosis of focal eosinophilic myositis. One week later, the swelling and pain of the gluteus maximus muscle disappeared and CK and CRP levels also normalized without treatment. Focal eosinophilic myositis is a disease in which inflammatory cell infiltration, mainly composed of eosinophils, occurs between the muscle fibers of the lower extremities, causing pain, swelling, and fever. Glucocorticoids are often effective, but self-limited cases have been reported. Our case, which is the first report of focal eosinophilic myositis in the gluteus maximus muscle, will be discussed with some literature review.

P3-019

PET-CT findings of 2 cases of possible VEXAS syndrome, with concurrent myelodysplastic syndrome and recurrent polychondritis

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Conflict of interest: None

[Clinical Implication] VEXAS syndrome is a novel disease concept proposed in 2020, but an appropriate clinical diagnosis has not been established. PET-CT has been reported to be useful in the diagnosis of various diseases, but the role of diagnosing VEXAS syndrome is unknown, and few reports have been published discussing the findings of VEXAS syndrome. We experienced two cases of suspected VEXAS syndrome, a recurrent polychondritis associated with myelodysplastic syndrome, in which bone marrow biopsies showed vacuoles. The PET-CT findings of the cases showed recurrent polychondritis-like findings of increased uptake in the nasal, auricular, limb adipose tissue, bronchi, and rib cartilage, as well as myelodysplastic syndrome-like findings of increased uptake in the bone marrow of the vertebral body, iliac bone, and sternum. The similarities between the two cases may help to investigate further the utility of PET-CT in patients with suspected VEXAS syndrome.

P3-020

COVID-19 vaccine-associated polyarthritis expressed as a mixture of synovitis, bursitis, and enthesitis; a case report

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Conflict of interest: None

[Case] Twelve days after the third dose of COVID-19 vaccination, a 73 year-old female began to feel pain in occipital region to bilateral upper arm and right frontal region to neck, difficulty of opening her mouth, and low-grade fever. She visited our hospital 1 months after her initial symptoms. Blood tests showed high levels of CRP 11.87 mg/dl and ESR 114 mm/h, but within the normal range of RF, ACPA, and ANCA. Large-vessel vasculitis was not observed in carotid artery echo and FDG-PET/CT. On the other hand, FDG-PET/CT showed PMR-like FDG uptakes in the interspinous process, sciatic tuberosity, periarticular shoulder, and periarticular hip. In addition, MSK-US showed synovitis in the right wrist, bursitis in the right shoulder, and enthesitis in the right elbow. Her symptoms gradually subsided after treatment with low-dose prednisolone and NSAIDs. [Discussion] In case reports of COVID-19 vaccine-associated arthritis, patients often complain of arthralgia and myalgia within 2-3 weeks after vaccination, which usually improve with NSAIDs, low-dose corticosteroids or anti-rheumatic drugs. Although our patient was consistent with previous reports, it's valuable because detailed imaging evaluation revealed mixed patterns of RA-like synovitis, PMR-like bursitis and SpA-like enthesitis.

P3-021

Bone scintigraphy helped definite diagnosis of pustulotic arthro-osteitis: A case report

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Conflict of interest: None

[Background] Arthro-osteitis is known to coexists in palmoplantar pustulosis (PPP) patients. We set out to highlight the effective usage of bone scintigraphy to detect the early stage of pustulotic arthro-osteitis (PAO). [Case] A 63-year-old male presented to the previous hospital with fever (above 39.0°C) and polyarthralgia, and admitted for further examination and treatment. Meropenem was administrated for 2 weeks concerning any bacterial infection. However, the treatment was ineffective and no evidence of bacterial infection was obtained from blood culture nor radiographic findings. The patient was transferred to our hospital as fever of unknown origin. There were no significant findings from CT, MRI and joint ultrasonography. On the other hand, he had a 20-year history of PPP and bone scintigraphy revealed an accumulation of ^{99m}Tc in sternocostoclavicular area, lower lumbar vertebrae and sacroiliac joint. Therefore, a diagnosis of PAO was made. Salazosulfapyridine was prescribed and the symptoms including fever was alleviated. After discharge from our hospital, guselkumab was initiated for the residue of PPP, back pain and elevation of CRP. [Discussion] Bone scintigraphy might effectively help the early diagnosis of PAO in the differential diagnosis of seronegative arthritis.

P3-022

A case of dialytic ectopic calcification with tendonitis and enthesitis

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Conflict of interest: None

[Introduction] We report a case of dialytic ectopic calcification with prominent soft tissue calcification of the extremities and the tendonitis and enthesitis. [Case] A man in his 50s visited our hospital with joint pain in his extremities. He started hemodialysis ten years ago for hypertensive nephropathy. Both RF and anti-CCP antibody were negative, and CRP was as high as 13.0 mg/dl. X-rays showed calcifications with a maximum length of 90 mm in the left deltoid muscle, calcifications with a maximum length of 55 mm in the right elbow flexor, and calcifications with a maximum length of 65 mm around the right ankle joint. Ultrasonography revealed swelling of the tendon and enthesis near the ectopic calcifications, power Doppler signal and inflammation in the finger flexor tendon, biceps brachii long head tendon, and ankle medial flexor tendon. In addition, bone formation was observed at the triceps tendon enthesis, supraspinatus tendon enthsis, quadriceps tendon enthesis, and Achilles tendon enthesis. [Conclusion] Ectopic calcification is thought to be caused by abnormal Ca

and P metabolism in dialysis patients, but the mechanism is not clear. In this case, the ectopic calcification of occurs due to exudation of plasma into the tendonitis and enthesitis site.

P3-023

Musculoskeletal ultrasonography aiding in the diagnosis of calcific tendinosis of the right flexor hallucis brevis

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Conflict of interest: None

[Case] A 40-year-old woman was referred to our outpatient clinic complaining of right front foot pain. She had a four-month history of irritation and callousness near the right hallux metatarsal phalangeal (MPT) joint, and had developed metatarsalgia with swelling and redness on a trip one month earlier. Before these symptoms, she would practice yoga and take walks daily. Non-steroidal anti-inflammatory drugs (NSAIDs) only partially alleviated the pain. There was no joint swelling on physical examination. X-ray and CT scan showed calcification near the right MTP and musculoskeletal ultrasonography (MSUS) showed calcification from the hallux sesamoid complex to the right flexor hallucis brevis tendon, with increased power doppler signals. Calcinosis tendinosis was suspected and peritendinous triamcinolone injections alleviated her symptoms. [Clinical Significance] Calcific tendinopathy is a frequent cause of arthralgia and though it rarely occurs in the lower extremities, there are some reports of flexor hallucis brevis tendinosis. MSUS is useful in evaluation of the affected anatomy, aspiration and injection of glucocorticoids. We report a case in which MSUS was useful in the evaluation and treatment of calcific tendinosis of the flexor hallucis brevis tendon.

P3-024

A study of aimed at construction of RA progression prediction algorithm and elucidation of RA onset mechanism using multilateral evaluation

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Conflict of interest: Yes

[Objective] To develop an algorithm to accurately predict the risk of progression to RA in patients with arthralgia. [Methods] This study retrospectively or prospectively included “patients with joint pain” (without clinical synovitis) who were less than 3 months old from the onset of symptoms. We will evaluate the following: conformity to clinically suspect arthralgia (CSA) definition, family history/life history (smoking/alcohol), autoantibody serostatus (AMPAs measurement), multiple serum biomarker concentrations (multiplex analysis), HLA typing, salivary microbiome (16SrRNA analysis), musculoskeletal ultrasound, hand/foot X-ray. We set the diagnosis of RA (introduction of DMARDs) at 12 months as the primary outcome and integrated analysis using machine learning on factors that predict progression to RA. [Results] We retrospectively collected information on the eligible patients and analyzed the factors that contribute to the progression of RA. A study system was established to prospectively enroll eligible patients (UMIN: 000047764, IRB approval number: 22051602). [Conclusions] We will increase the number of patients and proceed with the analysis. This research is ongoing as the “early RA research promotion program”, and we will report on the progress.

P3-025

Clinical Profile of Patients with RA with Elevated ACPA

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Conflict of interest: None

[Objective] To investigate the pathophysiology and treatment status of RA patients with elevated ACPA levels. [Methods] Age, disease duration, disease activity, progression of joint destruction, physical function, laboratory values, and therapeutic drugs were compared in 33 patients with high ACPA (>100 U/ml) and 25 patients with low ACPA (≦100 U/ml). [Results] In patients with high/low ACPA, age was 75.3±8.3/68.6±11.4 ye ars (P=0.014), disease duration was 15.0±10.2/12.7±10.7 years (P=0.42), SDAI was 4.1±4.3/2.9±2.5 (P=0.20), Stage 3&4 ratio was 60.6%/44.0% (P-0.21), HAQ-DI was 0.86±1.04/0.43±0.65 (P=0.077), ESR was 34.2±2 6.5/13.4±10.1 mm/h (P=0.00056), RF was 104.3±126.2/39.4±56.2 IU/ml (P=0.022), and MTX usage was 54.5/44.0% (P=0.426), b/tsDMARD usage was 9.1/20.0% (P=0.23). Patients with high ACPA had significantly higher age, ESR, and RF values, and greater physical dysfunction. However, there were no differences in duration of disease, disease activity, progression of joint destruction, or drug therapy. [Conclusions] High ACPA levels encountered in daily practice may reflect increased autoantibody production due to immune aging, and did not appear to be associated with resistance to treatment or progression of joint destruction.

P3-026

The association between laughter and frailty in patients with rheumatoid arthritis from the Fairy study

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Conflict of interest: None

[Background] In the improved treatment of RA, it is important for RA patients, who are prone to physical anxiety due to high disease activity and frailty, to be able to laugh and live their lives. The present study aimed to investigate the relationship between disease activity, laughter, and frailty in RA patients. [Methods] A total of 247 patients were included in a prospective cohort study on frailty in RA patients. The frequency of laughter was divided into four levels: “Everyday”, “1-5 times a week”, “1-3 times a month”, and “rarely”, and the kihon checklist (KCL), Locomo 25, and frequency of laughter were analyzed by analysis of variance. [Results] The frequency of laughter was “Everyday” (43%), “1-5 times a week” (40%), “1-3 times a month” (11%), and “Almost never” (6%). The DAS28-CRP of disease activity was 1.89/1.87/2.15/1.81 (P=0.487), KCL score was 3.5/4.6/7.3/8.1 (P<0.001), and locomotor 25 was 13/15/22/21 (P=0.001). On multivariate analysis, KCL score (OR: 0.81) and locomo 25 (OR: 0.97) were independently associated with laughter frequency. [Conculsion] We found that frailty was associated with laughter in RA patients with controlled disease activity. Interventions not only for disease activity but also for frailty may lead to a life of laughter.

P3-027

The prognosis of patients with difficult to treat RA -a study using the IORRA cohort-

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Conflict of interest: None

<Objective> To compare the proportions of achieving clinical remis-

sion and the incidence of clinical events in patients with difficult-to-treat (D2T)-RA and non-D2T RA. <Methods> Among the patients participated in the IORRA from 2018 to 2019, RA patients with moderately or highly disease activity were selected. Among them, RA patients who had used at least two bDMARDs or JAK inhibitors (D2T-RA group) and the others (non-D2T-RA group) were extracted using 1:3 matching method. Cox regression analysis was performed to determine the time to DAS28-ESR remission and unfavorable clinical events (death, hospitalization, infection, malignancy, or cardiovascular disease) for 3 years. <Results> After matching, there were 113 patients in the D2T-RA group and 324 in the non-D2T-RA group (95.9% female, age 60.6±12.6 years, disease duration 17.2±9.3 years, DAS28-ESR 3.9±0.5). The proportions of clinical remission for 3 years were 38.1% and 41.0% in the D2T-RA and non-D2T RA groups, respectively (adjusted HR: 1.28 [95%CI: 0.88-1.86], p=0.19). On the other hand, the 3-year incidence of clinical event was higher in the D2T-RA group (26.5% vs. 16.7%, adjusted HR 1.70 [95%CI 1.02-2.80], p=0.04). <Conclusion> Being D2T-RA was significantly associated with the incidence of unfavorable clinical events.

P3-028

Clinical characteristics of difficult-to-treat rheumatoid arthritis: A Real-World observational study of single center

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Conflict of interest: None

Objectives: Difficult-to-treat rheumatoid arthritis (D2T RA) is an emerging concept of refractory RA despite treatment according to the recommendations. We aimed to evaluate clinical characteristics of D2T RA in our center. Methods: A single-center observational study of patients with RA at Tonan Hospital was conducted in 2021. Clinical features including general background, autoantibodies, therapies, Steinblocker stage of RA as well as existence of D2T RA were retrospectively collected. Results: Among 538 patients with RA, 17 patients (3%) were identified to have D2T RA. 14 patients were female (82%). Anti-citrullinated peptide antibodies (ACPA) in 10 patients (58%), methotrexate use in 15 patients (88%), glucocorticoid use in 9 patients (53%). Median age and disease onset of D2T RA were younger than non-D2T RA (61 [58-66] (y. o) vs 70 [58-73] (y. o), p=0.01) (48 [46-52] (y. o) vs 51 [45-61] (y. o), p=0.02). The prevalence of Steinblocker stage III-IV was significantly higher in D2T RA than non-D2T RA (58% vs 31%, p=0.03). The most common reason for D2T RA was a mismatch in the wish for treatment between patient and rheumatologists (6 patients, 35%). Conclusion: Our study demonstrated clinical features of D2T RA in real-world. Personalized approach is needed to treat D2T RA.

P3-029

Analysis of D2TRA cases at our institution

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Conflict of interest: None

[Objective] To analyze D2TRA (Difficult to treat RA) cases at our institution, clarify the ratio of D2TRA and the factors that cause D2TRA, and consider measures to reduce D2TRA in the future. [Methods] Based on the definition of D2TRA proposed by EULAR in 2019, D2TRA cases were extracted from rheumatoid arthritis patients treated at our institution. The ratio of D2TRA and the factors of D2TRA were analyzed using statistical methods. We compared the results of previous reports on D2TRA with the results of our hospital, and analyzed the differences. [Results] Of 202 RA patients at our institution, 30 (15%) met the definition of D2TRA. This was a large number of results compared to past reports. The most common factors leading to D2TRA were multidrug resistance, side effects of drugs, and complication of infection. [Conclusions] It was suggested that many of the D2TRA cases in our hospital became D2TRA due to complications. In order to reduce the number of D2TRA cases in the future, it is considered important to perform more stringent management of complications and present more treatment options.

P3-030

Characteristics of difficult-to-treat RA (D2T-RA) patients at our hospital

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Conflict of interest: None

[Objective] To examine the background and treatment of D2T-RA patients in our hospital. [Methods] From the 2021 database of RA patients visiting our hospital, we extracted patients who used 2 or more b/tsDMARDs. Among these patients, we defined DAS28ESR ≧3.2 as D2TRA, and DAS28ESR <3.2 as non-D2TRA, and compared patient background and treatment status. [Results] There were 23 D2T-RA patients, average age 67.4 years, female 95.7%, average disease duration 22.3 years, RF positive rate 60.9%, anti-CCP antibody positive rate 91.3%, interstitial lung disease 8.7%, chronic kidney disease 30.4%, average DAS28 ESR 4.15, average HAQ 1.33, MTX usage rate 56.5%, MTX average dose 9.7 mg/w, PSL usage rate 17.4%, PSL average dose 5.0 mg/d, bDMARDs usage rate 56.5%, tsDMARDs usage rate 30.4%. The number of b/tsDMARDs used was 10 for the 2nd drug, 8 for the 3rd drug, 3 for the 4th drug, 1 for the 5th drug, and 1 for the 6th drug. Seven patients used tsDMARDs: four tofacitinib, two baricitinib, and one upadacitinib. Compared with non D2T-RA patients, they were older, had longer disease duration, had lower rates of MTX and bDMARDs, and higher rates of PSL and tsDMARDs. [Conclusions] D2T-RA patients in our hospital were elderly, had longer disease duration, and had a high use rate of tsDMARDs and PSL.

P3-031

A case of suspected Felty syndrome without joint symptoms based on leukopenia, positive anti-CCP antibody, and splenomegaly

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Conflict of interest: None

A 58-year-old woman referred to our department because of leukopenia (800/μL), neutrocytopenia (100/μL), splenomegaly and positive for anti-citrullinated peptide (CCP) antibody (106 U/mL), but no joint pain and negative for rheumatoid factor (RF). On examination, there were no swollen or tender joints and no findings suspect rheumatoid arthritis (RA) on X-ray examination. No drugs were administered to cause leukopenia, and bone marrow examination showed normal bone marrow. Based on the positive anti-CCP antibody and splenomegaly in addition to leukopenia, we diagnosed with Felty syndrome (FS) without joint symptoms. Although treatment with prednisolone (PSL) (40 mg/day), filgrastim (75 μg) and high-dose immunoglobulin was not effective, 9 consecutive days of filgrastim increased white blood cell count to 2600/μL and neutrophil count to 1300/μL. Currently, PSL is discontinued, but the white blood cell count remains at approximately 4000/μL. [Clinical Significance] This case was diagnosed with FS based on leukopenia, splenomegaly and positive for anti-CCP antibody, without arthritis. There are a few previous similar reported cases of FS without arthritis but positive for anti-CCP antibody or RF. We discussed with this case and previous cases of clinical features and treatment.

P3-032

Successful Peficitinib Monotherapy for the New-Onset Skin Manifestation of Rheumatoid Vasculitis After Long-Term Treatment with Tocilizumab

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Conflict of interest: None

[Background] Systemic rheumatoid vasculitis (SRV) is a severe extra-articular systemic disease manifestation of rheumatoid arthritis (RA) characterized by the development of a small to medium-sized vessel necrotizing vasculitis. the incidence of SRV has declined for decades. However, the mortality of SRV remains significant and has not still declined. A combination of glucocorticoid (GC), DMARDs, and cyclophosphamide (CYC) is known as standard treatment. [Case Presentation] A 85-year-old woman. She was diagnosed with rheumatoid arthritis at the age of 28. Since then, she has been treated with the following biological DMARDs such as infliximab and abatacept. She started tocilizumab at 76 years old. Three months ago, cutaneous ulcers emerged on both her legs and gradually enlarged. Topical medication was started, but the ulcers gradually exacerbated. A biopsy was taken from the area surrounding the skin ulcer of the left leg and skin manifestation associated with SRV was the most likely diagnosis. peficitinib was only started without GC or CYC. After that, her leg ulcers gradually ameliorated. After 6 months, they healed and diminished. [Conclusions] peficitinib has a potential treatment option for skin manifestation of SRV that developed while on bDMARDs.

P3-033

Felty Syndrome Successfully Treated with High-dose Prednisolone, Methotrexate and Abatacept

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Conflict of interest: None

[Case] A 62-year-old man developed rheumatoid arthritis (RA) 12 years ago and had been treated with salazosulfapyridine, which was discontinued 5 years ago because of remission. One month ago, he presented arthralgia in bilateral shoulders and fingers, fever, elevated levels of C-reactive protein, neutropenia and anemia. Then he was admitted to another hospital and eventually diagnosed as Felty syndrome (FS) because of high levels of RF and anti-CCP antibody, splenomegaly and excluding hematologic tumor by bone marrow biopsy. He transferred to our hospital and treated with 40 mg/day of prednisolone (PSL), tacrolimus and abatacept. As the neutropenia and anemia were not fully recovered, PSL was increased to 55 mg/day and thereafter methotrexate was administered instead of tacrolimus, which gradually improved the cytopenia. [Discussion] FS typically develops in RA patients with long time existing severer arthritis. However, our case is atypical because he developed FS after long time remission. Although his FS was resistant to initial treatment, it was successfully treated with the combination of high-dose PSL, methotrexate and abatacept. As there are few reports of FS treated with abatacept, we report this case as a rare case.

P3-034

A case of malignant rheumatoid arthritis complicated with systemic sclerosis and ITP appearing with pericardial effusion and pleural effusion

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Conflict of interest: None

[Case] A 79-years-old female, who had been diagnosed as rheumatoid arthritis and treated with PSL 1 mg and Tac 1 mg. Last April, she had developed ITP and treated with steroid and thrombopoietin receptor agonist. DAS28ESR (3.2) showed moderate activity, therefore, *Abatacept* subcutaneous injection was started. One week later, exertional dyspnea appeared and CT showed pericardial fluid and pleural effusion. Pericardial and pleural fluid drainage procedures performed, and antimicrobial treatment was also started considering the possibility of bacterial pericarditis. Bacterial culture test of pericardial fluid and pleural fluid, and TB-PCR tests were negative. Although joint and skin symptoms were poor, compared to last December, titer of rheumatoid factor significantly increased from 70 IU/ml to 340 IU/mL and IgG-RF (2.8 unit) was positive. The patient was diagnosed as malignant rheumatoid arthritis complicated with serositis. Treatment with PSL 30 mg /day (0.5 mg/kg) dramatically improved pericardial fluid and pleural effusion. [Discussion] We have experienced a case of malignant rheumatoid arthritis complicated with systemic sclerosis and ITP appearing with pericardial effusion and pleural effusion. We report this case with some literature discussion.

P3-035

A case of rheumatoid arthritis complicated by fasciitis

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Conflict of interest: None

[Case] 41-year-old woman [Chief complaint] thigh pain [Current medical history and progress] 14 years ago, she diagnosed rheumatoid arthritis (RA) with positive RF and CCP antibodies and was treated with methotrexate (MTX) 8 mg/week and tacrolimus 1 mg at another hospital. In April 20XX, her extra-articular symptoms such as pain in upper arms and thighs became more severe, and she was referred to our department in May. The patient was admitted to the hospital for a thorough examination, and a thigh MRI was performed, which led to a diagnosis of fasciitis. A muscle biopsy was performed to exclude infection, and an infiltrate of inflammatory cells, mainly lymphocytes and plasma cells, was observed in the fatty connective tissue. The patient was started on prednisolone 40 mg (1 mg/kg/day), and her symptoms improved promptly. Discussion: We have an experience of a case of myofasciitis with RA as an underlying disease, in which the patient's symptoms improved after the addition of steroids, suspecting an element of RA. There are few reports of myofasciitis complicated with rheumatoid arthritis, and we report this case as a valuable case study.

P3-036

A Case of paraneoplastic syndrome exhibited by relapse of rheumatoid arthritis

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Conflict of interest: None

Background. After resection of pulmonary adenocarcinoma, polyarthritis was improved. Case. A 72-year-old man with rheumatoid arthritis (RA) for 4 years had been treated solely with methotrexate (MTX). RA has been in low disease activity or remission. But when he was 71 years old, he had a painful and swollen joints of both hands, that were gotten progressively worse. His laboratory data showed that inflammatory marker levels were high (C-reactive protein: 2.51 mg/dL, matrix metalloproteinase-3: 214 ng/mL, rheumatoid factor: 91U/mL). Although amount of MTX was increased and prednisolone (PSL) was started to administer, there was no improvement. On the other hand, chest X-ray and computed tomography revealed a right mass lesion and ground-glass opacity clustering in the right lung. Adenocarcinoma was found by detailed examination. He underwent right upper lobectomy and lymphadenectomy immediately. After operation, his joint swelling and pain were found to be improving, and dose of MTX was reduced and oral PSL were not needed. Conclusion. We should take paraneoplastic syndrome into consideration when relapse of arthritis was found.

P3-037

A case of drug-induced hypersensitivity syndrome caused by IGU

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Conflict of interest: None

46-year-old female had been treated with tofacitinib and methotrexate for rheumatoid arthritis. Iguratimod (IGU) was added due to inadequate response. 1 month later, skin rash and slight fever appeared. Drug allergy was suspected, all drugs were discontinued. After 1 month later, the symptoms didn't improve, hepatosplenomegaly and multiple lymphadenopathy appeared. Since revealed increased EBV-DNA, those were thought to be due to EBV reactivation. Due to relapse of arthritis after drug discontinuation, short term steroid and not only arthritis but also the systemic condi-

tions were improved, and EBV-DNA became negative. IGU was administered again, severe facial edema, skin rash, and fever appeared 1 month later, and hepatosplenomegaly and multiple lymphadenopathy recurred. After 2 weeks discontinuation of IGU, those symptoms didn't improve, multiple pulmonary infiltrates appeared, and eosinophil count tend to increase, re-increase of EBV-DNA was observed. Drug hypersensitivity syndrome (DIHS) was suspected for the first time, and HHV-6 DNA was positive. High-dose steroid was symptoms rapidly improved. Although DIHS is caused by certain drugs, no case caused by IGU has been reported to our knowledge. We report a case of DIHS caused by IGU, including a review of the literature.

P3-038

Spontaneous regression of lymphoproliferative disorder associated with rheumatoid arthritis (RA-LPD) without withdrawal of methotrexate (MTX)

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Conflict of interest: None

[Case] 78y. o female The patient was diagnosed as RA 9 years ago based on polyarthritis at another hospital. MTX was started and she had been in remission state until 2 months before referred to our hospital, when she developed unintentional weight loss. Whole body CT scan and PET scan revealed multiple tumors in lung, liver, adrenal glands, kidneys and bones. Lung biopsy under CT guiding revealed atypical lymphocytes proliferation. She was diagnosed as MTX-LPD and referred to our hospital. Despite the MTX was continued during this course, her tumors almost disappeared on our initial examinations. The histopathology was re-evaluated at our hospital and diagnosis of diffuse large B cell lymphoma was made. [Clinical Importance] When lymphoma develop during treating RA with MTX, usually we think it is caused by MTX and stop the MTX with close monitoring. In this case we experienced spontaneous regression of lymphoma without withdrawal of MTX. This implies there are variety of pathogenesis in RA-LPD.

P3-039

A case of tacrolimus encephalopathy during treatment for rheumatoid arthritis

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Conflict of interest: None

Tacrolimus exerts an immunosuppressive effect by inhibiting the activation of calcineurin, which works in the activation stage of T cells, and suppressing the production of interleukin-2. We experienced a case of rheumatoid arthritis who developed encephalopathy during treatment with tacrolimus. 64-years-old woman had been treated with methotrexate and prednisolone for rheumatoid arthritis, but KL-6 increased, methotrexate was discontinued and tacrolimus therapy was started. Seven months after the start of treatment, she visited our hospital because of seizures and was admitted. Head MRI showed signal changes in the periventricular white matter, and leukoencephalopathy was diagnosed. Tacrolimus was discontinued, and administration of anticonvulsants was started. Afterwards, the symptoms improved. When using tacrolimus, attention should be paid to the appearance of central nervous system symptoms, and if symptoms appear, the dose should be reduced or discontinued, and treatment such as administration of anticonvulsants should be taken.

P3-040

Long-term effectiveness of tacrolimus on preventing flare after TNF inhibitor re-cessation in rheumatoid arthritis patients who had ever relapsed after a previous TNF inhibitor cessation

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Conflict of interest: None

[Objective] To evaluate the long-term effect of tacrolimus (TAC) to prevent flares after TNF inhibitor (TNFi) re-cessation in rheumatoid arthritis (RA) patients who had ever relapsed after a previous TNFi cessation. [Methods] Consecutive RA patients with a history of multiple TNFi cessations by Oct 2020, followed by both methotrexate (MTX) monotherapy (mono) and MTX+TAC combination (combi), were included. The retention rates of mono and combi without treatment intensification* after TNFi cessations were evaluated through Oct 2022. *Start oral glucocorticoids, biologics, Janus kinase inhibitors, immunosuppressive anti-rheumatic drugs, and investigational drugs for RA. [Results] 19 patients with 18 females, 14 were positive for anti-CCP and 16 for RF, were included. The median age was 61 years [range 18-71], and symptom duration was 1.3 years [0.4-17.8] at initial TNFi initiation. The initial TNFi treatment period was 1.9 years [1.0-6.1]. There were 22 lines of TNFi holidays with mono and 20 with combi with a mean TAC dose of 1.3 mg/day. The retention rates at 2 and 5 years were 18.2% and 4.5% for mono and 79.4% and 72.2% for combi. [Conclusion] For relapsed RA patients after a previous TNFi cessation, adding TAC on MTX maintenance therapy can reduce relapse after TNFi re-cessation.

P3-041

A case of cutaneous sarcoidosis-like reaction caused by administration of abatacept

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Conflict of interest: None

There are various side effects associated with biologics, but we report a case of a rare sarcoidosis-like reaction caused by abatacept (ABT). [Case] 75-year-old female [Course] In 2011, she developed rheumatoid arthritis. Abatacept (ABT) was started as her third biologic drug in 2015, and continued to be effective. Since around December 2022, the patient had been aware of skin hardening on both forearms. The soluble IL-2 receptor level was as high as 1043.0, and PET-CT showed diffuse high accumulation in the subcutaneous soft tissues of both forearms. A biopsy of the skin at the department revealed multiple alveolar epithelioid granulomas and Langhens-type multinucleated giant cells. The ACE level was 34.9 IU/dl. However, skin hardening improved after withdrawal from ABT, and after 8 weeks of withdrawal, skin hardening improved and disappeared on physical examination. [Discussion] Drug-induced sarcoidosis-like reactions are known, and TNF inhibitors are the causative agents. Since the symptoms improved, it is highly likely that ABT was the causative agent of the sarcoidosis-like reaction.

P3-042

A case of rheumatoid arthritis who developed encephalopathy 1 week after administration of certolizumab pegol and was also considered to have drug-related encephalopathy

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Conflict of interest: None

Case is a 26-year-old female who started certolizumab pegol (CZP) 400 mg with MTX for RF and ACPA-positive RA. One week after the CZP start, she developed hallucinations and delusions. CT and MRI of the head and CSF examination revealed no abnormality. Blood tests were positive for anti-SSA and anti-SSB antibodies but negative for other antibodies, and there was no evidence of low serum complement titer, abnormal thyroid hormones, or low vitamin levels. Infectious encephalopathy, autoimmune encephalopathy related to anti-SSA and anti-SSB antibodies, and drug-induced encephalopathy of CZP were the differentials, and high-dose steroids were started, but there was no improvement in symptoms. After a total of three plasma exchanges with concomitant IVCY according to CNS lupus, the patient's course was good and no sequelae were observed. We report a case in which CZP was thought to have had some effect on the encephalopathy in this patient, because the encephalopathy occurred early after CZP administration, steroid administration was at least not fast-act-

ing, and plasma exchange was very effective.

P3-043

A Case of Overlap Syndrome of Systemic Lupus Erythematosus and Rheumatoid Arthritis (Rhupus Syndrome) Effectively Treated with Abatacept

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Conflict of interest: None

[Introduction] Overlap of SLE and RA is known as rhupus syndrome. Evidence-based treatment has not been established. We report a case of overlap syndrome of rhupus effectively treated with Abatacept. [Case] 53-year-old woman presented with skin rash and arthralgia of upper extremities lasting one year. A diagnosis of rhupus was made based on polyarthritis, periungual erythema, and positive results of anti-nuclear antibody, anti-Sm antibody, anti-U1-RNP antibody, anti-SS-A antibody, RF and anti-CCP antibody, Anti-DNA antibody was negative, and complement level was normal. Although she was treated with glucocorticoid and hydroxychloroquine initially, we added belimumab and tacrolimus for persistent arthritis resulting good response. After tapering of glucocorticoid, arthritis flared gradually, so we changed belimumab to abatacept, and arthritis resolved completely without any other organ symptoms. [Conclusion] Rhupus was reported that represent 1-2% of SLE. Rhupus patients tend to have more severe arthritis like RA, but less prevalence of neuropsychiatric disorder, malar rash and nephritis. Neither diagnostic criteria nor treatment algorism have not been established. Abatacept was very effective in our rhupus case and may have potential ability in treatment of rhupus.

P3-044

Clinical evaluation of abatacept and golimumab in patients with rheumatoid arthritis in our department

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Conflict of interest: None

[Objective] To investigate the efficacy and adherence of abatacept (ABT) and golimumab (GLM) in RA patients. [Methods] ABT/GLM; 26 (5 males, mean 63.1 yo, mean disease duration 9.7 y)/ 25 (3 males, 66.1 yo, 11.1 y), MTX; 16 (5 mg) / 17 (5.5 mg), PSL; 19 (4.7 mg) /13 (1.9 mg). Bio-naïve: 6/11. The efficacy of ABT and GLM was evaluated by DAS28-ESR4 and SDAI for 468 weeks. [Results] 1) Mean DAS28 at the baseline (ABT/GLM): 5.87/5.8, CDAI, SDAI 28.64/27.48. Disease activity was significantly decreased in both groups. The ratio of LDA + remission increased significantly until 24 wks and maintained until 468 wks in both groups. No significant difference in both groups. 2) The adherence at 52 wks showed > 80% in both groups and that at 104 wks 69.2%, 156 wks 61.5%, 208 wks 46.2%, 260 wks 42.3%, 312 wks 34.6% in ABT, 56%, 40%, 36%, 32%, 28% in GLM. No significant difference in both groups. 3) HAQ-DI was significantly improved after 12 wks in ABT. 4) Both levels of CRP and MMP-3 were significantly reduced in GLM after 12 wks, while only CRP was reduced in ABT after 52 wks. 5) Drop-out reasons (ABT/GLM); inadequate response 5/8, cancer1/1, organizing pneumonia 0/1, pneumonia 3/1, EBV reactivation 1/1, remission1/0 and so on. [Conclusion] The efficacy and adherence of ABT and GLM were similar.

P3-045

A case of golimumab-associated lymphoproliferative disease

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Conflict of interest: None

[Case Report] She was diagnosed with rheumatoid arthritis at 75 years old and started MTX 4 mg/week and SASP 1000 mg/day. 77 years old, she was referred to our hospital. At age 83, RA control deteriorated and she was started golimumab (GLM) 50 mg/month with MTX 2 mg/week. At the age of 85 years, she was admitted to the hospital for a thorough examination due to Hb 7.1 g/dL. On the 10th day of hospitalization, the patient complained of abdominal pain, and abdominal CT showed no lymphadenopathy, but free air was observed, and emergency laparotomy was performed. The small intestine was perforated, and diffuse large B cell lymphoma (DLBCL) was found at the thickened perforation site. Because of the patient's advanced age and the pathological findings, lymphoproliferative disease was suspected, and chemotherapy was not given. During the follow-up, PSL 5 mg/day was added due to worsening arthritis, but there was no recurrence of DLBCL one year after the surgery. This case is also considered to be a GML-related lymphoproliferative disease because the tumor disappeared after discontinuation of GLM in DLBCL. In the literature, there is only one case of GLM-related LPD with EBV reactivation (DLBCL), and this case is also considered to be a very rare case of DLBCL caused by GLM monotherapy.

P3-046

Outcome of Golimumab in Patients with Rheumatoid Arthritis after Extended Dosing and Stopping

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Conflict of interest: None

[Objective] To investigated the continuation rate of Golimumab (GLM) in rheumatoid arthritis (RA) patients, and whether the efficacy could be achieved by re-administration after failed attempts to extend the dosing interval or stopping. [Methods] 106 RA patients who were introduced to GLM at our hospital from December 2011 to September 2021 were included. The study investigated treatment continuation rate (by age (<65 years/65 years or older) and dose (50 mg/100 mg)), secondary ineffectiveness (flare-up after remission), prolonged dosing interval (dosing interval >6 weeks), drug stopping, and resumption of treatment after interval extension and stopping. [Results] The continuation rates were 0.77 and 0.71 at 1 year and 0.62 and 0.53 at 5 years for patients under 65 years and over 65 years, respectively. The continuation rates for GLM 50 mg and 100 mg were 0.87 and 0.55 at 1 year and 0.73 and 0.33 at 5 years, respectively. Five patients who failed interval increase were achieved remission after re-treated. GLM was restarted in 3 patients who relapsed after stopping, and remission was again achieved. [Conclusions] The continuation rate was low in patients requiring 100 mg of GLM. Even when interval extension or stopping failed, GLM resumption was effective.

P3-047

A case of paradoxical reaction during adalimumab use

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Conflict of interest: None

Anti-TNFα inhibitors are used in the treatment of rheumatoid arthritis (RA) and psoriasis. However, there have been scattered reports of paradoxical reactions (PR) to anti-TNFα inhibitors. PR can cause or exacerbate inflammatory changes in the skin and other organs. We report a case of psoriasis-like skin rash due to PR during adalimumab (ADA) use. A 52-year-old woman with RA (stage I, class 1) was diagnosed and started methotrexate (MTX) in year X-7. She started concomitant use of ADA in year X-2. In year X-1, the interval of ADA administration was extended, and MTX 10 mg/2 weeks + ADA 40 mg/4 weeks was maintained. In year X, the interval of ADA administration was changed back to MTX 10 mg/2

weeks + ADA 40 mg/2 weeks, and a psoriasis-like skin rash appeared on the trunk and extremities. The drug use was continued, but the rash spontaneously disappeared after 4 months. Psoriasis-like skin rash due to PR with anti-TNFα inhibitors was first reported in 2003. Studies on the occurrence of PR are scarce, and no consensus has yet been reached on the pathogenesis of PR and its treatment. In this case, we experienced a patient with RA who had been treated with ADA for a prolonged period of time, and when the interval between ADA doses was shortened, PR appeared, causing a psoriasis-like skin rash.

P3-048

A rare case of refractory deep vein thrombosis in rheumatoid arthritis under anti-TNF-aipha inhibitor treatment

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Conflict of interest: None

The patient was 67 years old rheumatoid arthritis (RA) patient and received treatment with methotrexate, iguratimod and golimumab. Though her disease activity was well controlled, her both legs were gradually swollen in short duration. Her CRP level was elevated, but she did not have any arthritis, and blood test revealed high level of D-Dimer which increased to 20 μg/dL, thus deep vein thrombosis (DVT) was suspected. Ultrasonography and a computerized tomography scan indicated extensive thrombosis in the right femoral vein. The patient was admitted to our hospital and anticoagulant therapy was started. D-Dimer levels gradually decreased and heparin was switched to oral apixaban 20 mg. However, ultrasonography showed the increasing thrombosis. Thus, 2 mg of warfarin was started. Previous reports indicated that female over 65 years old, using cDMARDs as increasing factors of increasing risk of DVT in RA. In addition, 2020 EULAR PRESS RELEASE stated the use of bio-DMARDs including anti-TNF-alpha inhibitors as a reducing factor. Our case newly developed a refractory DVT under anti-TNF alpha inhibitor treatment. It is important to suspect the presence of thrombosis when pain in the lower extremities occurs and an increase in inflammatory reaction is observed.

P3-049

Golimumab dosage for patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To compare golimumab 100 mg and 50 mg efficacy in rheumatoid arthritis patients. [Methods] Fifty-three rheumatoid arthritis patients treated with golimumab at the Department of Rheumatology, Kinki University Hospital were included in the study. We divided the patients into two groups: golimumab 50 mg and golimumab 100 mg. We compared disease activity, persistence rates, and ultrasound synovitis at 24 and 52 weeks in these two groups. Disease activity was assessed by DAS28, and ultrasound was assessed by B-mode grayscale/power Doppler imaging at the hand, wrist, elbow, shoulder, and knee joints. [Results] There were no differences in patient characteristics such as age, number of previously used biologics, and disease activity in the golimumab 50 mg (n=17) and golimumab 100 mg (n=36) groups. Both groups showed no difference in disease activity and persistence rates of DAS28CRP and ESR at 24 and 52 weeks; golimumab 100 mg with MTX showed superior improvement in ultrasound gray scale compared to golimumab 50 mg with MTX. [Conclusions] We observed a predominant improvement in grayscale in the group using 100 mg golimumab with MTX.

P3-050

Efficacy and safety of filgotinib in our institution

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of filgotinib at our institution. [Methods] We retrospectively analyzed 36 cases of filgotinib use at our affiliated institution and examined whether there were differences in efficacy and safety according to the patient's background. [Results] Regarding previous use of Bio or JAK inhibitors, 9 cases were on their first drug, 7 cases on their second drug, and 20 cases on their third or later drugs. Of the 36 patients, 4 were discontinued due to adverse effects. The adverse effects included herpes zoster, hepatopathy, diarrhea, and pyogenic arthritis. 10 cases of ILD complications were included, but all patients did not have ILD exacerbations. All patients, patients with ILD, patients with Bio≧3 drugs, patients with Bio<3 drugs, and D2TRA patients had improved disease activity in ΔDAS28-ESR, ΔCDAI, and ΔHAQ between baseline and 12/24/52 weeks, and all showed a certain level of efficacy regardless of the conditions. [Conclusions] Filgotinib can be expected to be effective regardless of conditions such as ILD status, D2TRA, etc. Due to the small number of n, no statistical processing was performed, but the results suggest that filgotinib is effective in a wide range of patients.

P3-051

Clinical manifestations of filgotinib: Efficacy and safety

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Conflict of interest: None

[Objective] To assess short-term real-world outcomes of filgotinib (FIL). [Methods] The study included 41 patients was introduced by September 2022 because they had not responded well to multiple Bio or JAKi. Outcome measures for efficacy were CDAI, SDAI, morning stiffness time, and fatigue. For safety, they were actual neutrophils, total lymphocytes, hemoglobin, eGFR, CK, inorganic phosphorus, and AST/ALT. These were evaluated immediately before and at weeks 1 and 2 after starting FIL, then every 4 weeks up to 72 weeks. [Results] The patients' condition improved 1 week after starting FIL. Improvement and maintenance were observed during the treatment. No abnormal changes in laboratory values were observed. Notably, 12 patients with abnormal liver function test values and 3 patients with abnormal CK values due to the previous medications, showed improvement after starting FIL. [Discussion] FIL showed early efficacy. FIL appears to be effective in patients refractory to multiple Bio and JAKi. Efficacy was shown in 19 patients who selected FIL 100 mg for economic reasons; thus, FIL 100 mg may be a potential option. [Conclusion] FIL is potentially effective and safe, and may improve abnormal liver function and CK values caused by other medications.

P3-052

The clinical characteristics of effective and ineffective cases which were treated with Filgotinib

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Conflict of interest: None

[Objective] We compared the clinical characteristics of effective and ineffective cases which were treated with Filgotinib (FIL). [Methods] Fifty-four RA cases who introduced FIL from November 2021 to October 2022 at our hospital were evaluated. [Results] There were 45 cases who continued, and the mean follow-up period was 5.1 months. Reasons for discontinuation included adverse events, change of other drugs due to poor efficacy, difficulty in swallowing, and financial reasons. Adverse events included dizziness, ischemic enteritis, hyperCKemia, and bacterial bronchitis, none of which required hospitalization. Herpes zoster occurred in 2/54 cases. Effective cases were 18/25 in the 100 mg group and 26/29 in the 200 mg group. In the 100 mg group, 5 cases were changed to 200 mg,

and 2 cases were difficult to increase the dose due to chronic renal failure and changed to other drugs. On the other hand, 3 cases in the 200 mg group had a poor response and switched to the other drug. They had the D2TRA background factors. [Conclusions] The average age was 75 years in the 200 mg group, but they could continued safety. In addition, 5 cases who reduced the dose to 100 mg due to remission are doing well.

P3-053

Clinical efficacy of short-term filgotinib in rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the treatment results of FIL for RA. [Methods] Patients were selected from a multicenter collaborative study, TBCR. 45 RA patients who used FIL after November 2020 were included. We retrospectively investigated patient background, changes in disease activity, and continuation rate. [Results] The patient backgrounds were 63.7 years old, 43 females (95.5%), 14 years of disease duration, and 21 cases (46.6%) of MTX concomitant use. 10 cases (22.2%) had no history of administration of bDMARDs or JAK inhibitors. FIL was used at 100 mg in 9 cases (20.0%). Overall changes in DAS-28CRP/CDAI at the baseline: 3.9/17.4, 1 month: 2.5/7.5, 3 months: 2.3/6.8, 6 months: 2.3/6.8. After 1 month, it decreased significantly from the baseline. DAS-28CRP/CDAI in the FIL 100 mg administration group and the MTX non-combination group also decreased with a significant difference after one month from the baseline. (FIL 100 mg group: 3.3/11.7 at baseline, 2.6/7.0 at 1 month; MTX non-combination group: 4.2/19.8 at baseline, 2.8/8.4 at 1 month) The continuation rate was 86.6% at 6 months. [Conclusion] FIL was found to be effective early. In addition, it was suggested that MTX non-concomitant and 100 mg administration may be effectively treated.

P3-054

A Review of Filgotinib Use at Our Institution

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Conflict of interest: None

Objective We retrospectively studied the treatment course of patients treated with filgortinib (FIL) to determine the clinical characteristics and suitable patient profile for its use. **Methods** Twenty-five RA patients (3 males and 22 females) using FIL in our clinic were included. Mean age was 72.1 years, mean disease duration was 10.1 years, 19 patients used MTX, 16 patients used PSL, 9 patients had coexisting ILD, 11 patients had previous herpes zoster. Clinical course at 24 weeks of use was investigated. **Results** The LDA rate was 72.8% at 2 weeks and 90.4% at 24 weeks, and the HAQ remission rate was 48.4% at 24 weeks. A greater proportion of patients had early improvement in large joints. The percentage of patients who were able to reduce concomitant medications was 78% at 24 weeks. There was no ILD exacerbation. 92% of patients continued treatment after 24 weeks. There were no cases of cardiovascular, thrombosis, malignancy, or infection including herpes zoster. **Conclusion** FIL was effective from the early stage, especially in large joints. Although the short observation time should be taken into consideration, the patient progressed without serious adverse events. The use of FIL may be considered for elderly RA patients with concerns about ADL decline due to large joint inflammation.

P3-055

Short-term study of the efficacy of filgotinib in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: To evaluate the efficacy of filgotinib (FIL) in t in patients with rheumatoid arthritis (RA). Methods: In 11 RA patients (11 female patients) treated with FIL, we evaluate the changes in DAS28CRP, DAS28ESR, SDAI, and MMP-3 at 3 months after the start of treatment, and adverse events, outcome at the last observation. Results: The mean age at initiation of FIL was 69.7 years old, disease duration was 18.0 years, and follow-up was 6.4 months. FIL was started after mean 1.25 drugs. Starting dose of FIL was 100 mg in 3 patients, 200 mg in 4 patients, and the dose was increased from 100 mg to 200 mg in 4 patients. DAS28CRP improved from 3.59 to 2.82, DAS28ESR improved from 4.14 to 3.14, SDAI improved 15.2 to 12.6, and MMP-3 improved from 154.9 to 60.8, significantly. All four patients started on 200 mg showed low disease activity or less on DAS28CRP after 3 months, but only one of five of the seven patients started on 100 mg, excluding two patients with chronic renal failure. At the last observation, 10 patients continued on the drug, and one patient had a decline in renal function and was switched to another JAK inhibitor. Conclusions: It was thought that starting treatment at 200 mg should be considered in patients with high disease activity at the time of initiation of treatment.

P3-056

Effectiveness and safety of filgotinib in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the effectiveness and safety of filgotinib (FIL) in patients with rheumatoid arthritis (RA) during 12 weeks. [Methods] RA patients who were treated with FIL between November 2021 and July 2022 were included. DAS28-CRP, CDAI, SDAI, and J-HAQ were evaluated at 0, 2, 4, 8, and 12 weeks. [Results] Nine patients were included: 7 women (77.8%), median [IQR] age 74 [61, 78] years, disease duration 2.3 [1.4, 7.9] years, and Charlson comorbidity score (CCI) 1 [1, 2] points. Two patients discontinued FIL after 2 and 8 weeks due to elevated liver enzymes and abdominal pain, respectively. Among 7 patients who were treated with FIL during 12 weeks, no significant improvement in DAS28-CRP ($p=0.06$) or J-HAQ ($p=0.36$), but in CDAI and SDAI ($p<0.05$, $p<0.05$). There were no significant differences in change in DAS28-CRP, CDAI, and SDAI between patients with and without MTX or prior use of biologic agents. [Discussion] The difference in therapeutic effects between DAS28-CRP and CDAI or SDAI may be due to differences in the presence or absence of physician evaluation. [Conclusions] FIL significantly improved CDAI and SDAI. Adverse events were observed in two patients received with FIL, therefore require careful monitoring during treatment.

P3-057

The efficacy of upadacitinib in rheumatoid arthritis patients with treatment failure of many biologics

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Conflict of interest: None

[Objective] The prognosis of rheumatoid arthritis (RA) has changed greatly with the advent of biologic agents. We report two patients with rheumatoid arthritis (RA) who successfully switched to upadacitinib (Upa). [Case 1] A 67-year-old man with stage IV and class 2 has a RA

history of 18.5 years. He was treated with etanercept (ETN), tocilizumab (TCZ), and sarilumab, but was switched to Upa due to worsening disease activity. RA disease activity was 5.55 for DAS28-ESR and 32.5 for CDAI, indicating high disease activity. He was treated with Upa 15 mg/day under the concomitant use of DMARDs and steroids. After 4 weeks of treatment with Upa, DAS28-ESR improved to 4.91 and CDAI improved to 18. After 52 weeks, DAS28-ESR improved to 3.02 and CDAI improved to 10.1, showing improvement to low disease activity. [Case 2] A 67-year-old woman with stage IV and class 2 with a RA history of 37 years. She had been treated with infliximab, TCZ, ETN, and ETN-BS, but was switched to UpA as disease activity worsened. RA disease activity was DAS28-ESR of 5.68 and CDAI of 19.1. [Conclusions] The therapeutic effect of Upa in patients with insufficient bioeffects has been reported, and favorable long-term therapeutic effects were also obtained in patients with multidrug failure.

P3-058

A case report showing efficacy of baricitinib for intractable skin ulcers

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Conflict of interest: None

[Introduction] JAK inhibitors are excellent in fast-acting and anti-inflammatory effects, according to my experience and previous reports. By suppressing various cytokines, it has autoimmune suppression, anti-allergic, and anti-inflammatory effects, and is expected to be applied to various diseases. [Case] Female in her 60s. He has been visiting a dermatologist since March of X-5. She had repeated skin ulcers and was on and off steroids. In December of X-1, she was referred to our department because she was RF positive. Blood test findings showed mild anemia, thrombocytosis, and elevated CRP. Vasculitis could not be proven pathologically, but baricitinib was administered assuming rheumatoid vasculitis. CRP decreased after administration, and edema and skin ulcer tended to improve. After 1 month, the ulcer was partially epithelialized, and after 5 months, it was completely epithelialized. [Discussion] At present, six types of JAK inhibitors are available, and their indications are expanding not only for rheumatoid arthritis, but also for ulcerative colitis, atopic dermatitis, and alopecia areata. Although it is not indicated for intractable skin ulcer lesions, it has been reported to be effective for similar diseases, and it is expected as a therapeutic strategy.

P3-059

A case of rheumatoid arthritis in which osteoarticular destruction was repaired by JAK inhibitor

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Conflict of interest: None

[Objective] To report a case of rheumatoid arthritis (RA) in which osteoarthritis was repaired by JAK inhibitor treatment. [Case] A 50-year-old male, around 42 years old, visited his local doctor because of morning stiffness, RF and anti-CCP antibodies were positive, and he was diagnosed as RA based on his clinical symptoms. He was started on salazosulfapyridine (SASP) 250 mg/day, then increased to 500 mg/day, then methotrexate (MTX) 6 mg/week, and then MTX 8 mg/week. He was referred to our department due to poor disease activity control of RA. The patient had CRP 5.20 mg/dl, ESR 63 mm, RF 93 units/ml, MMP3 234.5 ng/ml, 24 tender joints, 24 swollen joints, and VAS 88 mm. Baricitinib (BAR) was added to the treatment regimen. One week after BAR administration, the effect appeared and the arthritis symptoms improved markedly. Currently, 2 years and 9 months after BAR administration, the patient continues to be in clinical remission, and prescribed BAR 4 mg/day alone. Periodic x-photos showed that narrowing of the joint space in both wrist joints and bone erosions in the carpal bones were repaired, which were present before BAR administration. [Clinical Significance] As in the case of biologics, there are RA patients in whom osteoarticular destruction was repaired by JAK inhibitors.

P3-060

A case of bilateral adrenal masses during use of tofacitinib for rheumatoid arthritis

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Conflict of interest: None

[Case] 63-year-old female [Chief complaint] fever, fatigue [Current medical history] She developed rheumatoid arthritis 16 years ago. She was treated with methotrexate, abatacept, and tocilizumab but stopped due to inadequate response or adverse events; and finally started tofacitinib (TOF) two years ago in February and was in remission. In mid-September, fever began appearing at night, and she became aware of easy fatigability. In late September, pancytopenia and high serum LDH were observed. She was admitted to our department for further examination and stopped TOF due to consideration of the possibility of other iatrogenic immunodeficiency-associated lymphoproliferative disorders (OIIA-LPD). Contrast-enhanced computed tomography revealed bilateral adrenal masses, and the pathological diagnosis of B-cell malignant lymphoma was made. Due to her fever, pancytopenia, and other abnormal findings becoming milder after stopped TOF, the hematologist determined that OIIA-LPD due to TOF was the most likely cause, and the patient was placed under strict observation. [Discussion] Based on the results of ORAL Surveillance study, the risk of developing malignancy during TOF use has recently become a concern. We report here this case based on the literature review, including similar cases.

P3-061

Three cases of fibromyalgia-like pain during treatment for rheumatoid arthritis that were unresponsive to biologics but effectively managed using JAK inhibitors

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Conflict of interest: None

During the treatment of rheumatoid arthritis (RA), joint swelling and inflammation are not observed in some cases, but joint and muscle tenderness are pronounced; such cases are called secondary fibromyalgia. I report three cases in which JAK inhibitors were effective in pain management, while bDMARDs were ineffective. Case 1: A 38-year-old woman developed myasthenia gravis (MG) in X-16. She developed RA in X-14. Several csDMARDs, including methotrexate (MTX), were inadequately effective. Six bDMARDs were administered, and the inflammation was resolved, but joint and muscle pain persisted. Peficitinib 150 mg/day was started in December X, after which the pain disappeared entirely. Case 2: A 56-year-old man had an 8-year history of depression. In X-3, he developed RA and was prescribed MTX. In X-1, an antiTNF inhibitor was added, but joint and muscle pain persisted. Tofacitinib (TOF) 10 mg/day was started in July X, after which the pain improved markedly. Case 3: A 58-year-old woman developed RA in X-6. MTX was insufficiently effective, and four bDMARDs had been used since X-2. Although joint swelling and inflammation had resolved, joint and muscle pain persisted. After adding Upadacitinib 15 mg/day to MTX in January X, the pain improved, and MTX was discontinued.

P3-062

A case of refractory RA-ILD that showed improvement with JAK inhibitor

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Conflict of interest: None

A 74-year-old man was diagnosed as seronegative rheumatoid arthritis

(RA) complicated with interstitial pneumonia (ILD) in X-5, and was treated with PSL, MTX and IGU. MTX was discontinued, and he was switched to TAC, which was discontinued due to side effects, and PSL dose was increased to 30 mg/day. During the PSL tapering, his joint symptoms worsened, and ABT was added in August. Although he was relatively well controlled, in May of X-1, he was found to have a worsening of ILD, and IVCY was performed a total of 7 times, but ILD did not improve. Subsequently, he was switched to upatatinib and marked improvement of ILD was observed. Since the mortality rate of RA patients with ILD is be three times higher than that of patients without ILD, disease control of ILD is an important issue. JAK/STAT play an important role in cytokine activation via IL-6, IL-11, and IL-13. JAK1 is overexpressed in inflammatory cells and epithelial cells in lung tissue, and JAK2 is overexpressed in fibroblasts and in the inner and mesangial layers of pulmonary arteries. It is suggested that JAK inhibitors may be effective not only in controlling RA joint symptoms, but also in RA-ILD, which mainly consists of pulmonary frosted-glass lesions that are considered to be mainly inflammatory.

P3-063

Evaluation with routine assessment of patient index data 3 (RAPID3) in patients with rheumatoid arthritis treated Janus kinases (JAK) inhibitors

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Conflict of interest: None

[Objective] We investigate RAPID3, one of patients reported outcome (PRO), in patients with rheumatoid arthritis treated JAK inhibitors in daily clinical practice. [Methods] We conducted a retrospective survey of the medical records of 71 patients with rheumatoid arthritis who started JAK inhibitors from August 2019, and examined RAPID3, fatigue, and treatment satisfaction at the baseline, 4, 12, and 24 weeks. [Results] 71 patients (67 female) were evaluated, JAK inhibitors included 2 tofacitinib, 20 baricitinib, 4 peficitinib, 27 upadacitinib, and 18 filgotinib. RAPID3 was significantly decreased by 12.67±0.62, 10.03±0.66, 8.95±0.78, 9.04±0.92 at the baseline, 4, 12 and 24 weeks, respectively ($p<0.001$ for each; Wilcoxon's signed rank test). RAPID3 low disease activity or clinical remission was 12.7%, 31.3%, 32.2%, and 35.0%, respectively. Fatigue and treatment satisfaction were significantly improved from the baseline. There was also a positive correlation between 4 weeks RAPID3 and fatigue, and a negative correlation with treatment satisfaction ($\rho=0.846$, $p<0.001$, $\rho=-0.551$, $p=0.002$; Spearman's rank correlation coefficient). [Conclusions] JAK inhibitors can be expected to improve PRO in patients with rheumatoid arthritis from the early stage of treatment.

P3-064

Abatacept, tofacitinib and upadacitinib treatment in patients with rheumatoid arthritis in clinical practice: efficacy of the treatment

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Conflict of interest: None

[Objective] To elucidate the efficacy of treatment with abatacept (ABT), tofacitinib (TOF) and upadacitinib (UPD). [Methods] All rheumatoid arthritis (RA) patients with moderate or active were treated with ABT, TOF, or UPD during the year 2012-2022. We compare the efficacy among patients with RA who treated with ABT, TOF and UPD at 4, 8, 12 weeks after administration of the treatment. [Results] Out of the 80 patients, 29 were treated with ABT, 28 were TOF, 23 were UPD. There was no difference in the demographic characteristics, disease duration, proportion of anti-CCP antibody or rheumatoid factor, and disease activity (DAS28-CRP) before treatment in the 3 groups. DAS28-CRP at 4 weeks after treatment was significantly improved in TOF and UPD treatment groups compared with ABT. There was no difference of DAS28-CRP at 4 weeks after treatment between TOF and UPD groups. DAS28-CRP was significantly improved in RA patients with UPD compared with TOF at 8 weeks after treatment. Among the 23 patients treated with UPD, 7 patients were switched from TOF to UPD. DAS28-CRP was improved in 6 of 7 patients who treated with UPD. [Conclusions] The efficacy of UPD at 8 weeks after administration was superior in comparison with ABT and TOF in patients with RA.

P3-065

Changes in disease activity by taking alternative-day regimen of JAK inhibitors for rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate its effectiveness of alternative-day regimen of JAK inhibitors (JAKi) for Rheumatoid arthritis (RA) [Methods] In patients with RA who were treated with JAKi every other day, we investigated the age, sex, duration of disease, prior treatment, concomitant use of steroids or MTX, the duration of remission before the start of every other day, and changes in SDAI. [Results] 1 tofacitinib, 5 baricitinib, and 4 upadacitinib for a total of 10 patients. 4 males and 6 females. The disease duration is 2-8 years. As for previous treatment, 8 cases received the same JAKi every day, 1 case changed from another JAKi alternative day, and 1 case changed from tacrolimus. 4 cases of concomitant use of MTX, no case of concomitant use of steroids. The remission period before alternative-day regimen was 6 months or more in 7 cases. In 8 cases, SDAI was unchanged. In 1 case, SDAI improved from 9 to 0.1 and remained in remission. In 1 case, SDAI worsened from 23 to 26 and was switched to daily oral administration. 6 of the 7 cases who had a remission period of 6 months or more before the start of alternative-day regimen were able to maintain remission. [Conclusions] Alternative-day regimen of JAKi for RA may be a useful option if the patient is in sustained remission.

P3-066

Comparison of anti-inflammatory effects of JAK inhibitors in IL-6 and TNF alpha-stimulated fibroblast-like synoviocytes derived from patients with rheumatoid arthritis

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Conflict of interest: None

[Object] In this study, we investigated the anti-inflammatory effects of each JAK inhibitor in IL-6 and TNFα-stimulated fibroblast-like synoviocytes derived from patients with rheumatoid arthritis (RA-FLSs) to clarify the effect of JAK inhibitors targeting the JAK-STAT pathway involved in the pathogenesis of RA. [Methods] RA-FLS were stimulated with estimated blood concentrations of JAK inhibitors (Tofacitinib (TOF) 0.3 μM, Baricitinib (BAR) 0.3 μM, Peficitinib (PEF) 1 μM, Upadacitinib (UPA) 0.3 μM, Filgotinib (FIL) 0.01 μM), followed by IL -6 (100 ng/ml) and sIL-6R (100 ng/ml) or TNFα (10 ng/ml) for 24 hr. The relative mRNA expression levels of ICAM1, VCAM1, VEGF, MCP1 and MMP1 were assessed by qRT-PCR. [Results] In IL-6 stimulation, ICAM1 expression was significantly lower in all other drugs relative to FIL; VCAM1 expression was significantly lower in PEF and UPA relative to FIL; VEGF, MCP1 and MMP1 expression was significantly lower in BAR, PEF and UPA relative to FIL. On the other hand, all targets showed no significant differences between groups in TNFα stimulation. [Conclusions] JAK inhibitors suppress synovial inflammation induced by IL-6. However, there may be differences in the anti-inflammatory effects between JAK inhibitors depending on the suppression of molecules.

P3-067

Analysis of JAK inhibitors effect for normal human articular chondrocytes from the knee joint

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Conflict of interest: None

[Object] In this study, we investigated the effects of each JAK inhibitor under IL-6 stimulation in Normal human articular chondrocytes from the knee joint (NHAC-kn) cells. [Methods] NHAC-kn were cultured with by IL -6 (100 ng/ml) and sIL-6R (100 ng/ml) and estimated blood concentrations of JAK inhibitors (Tofacitinib (TOF) 0.3 μM, Baricitinib (BAR) 0.3 μM, Peficitinib (PEF) 1 μM, Upadacitinib (UPA) 0.3 μM, Filgotinib (FIL) 0.01 μM), followed stimulation for 24 hrs. The relative mRNA expression levels of MMP1, MMP3, RUNX2 and ACAN were assessed by qRT-PCR. [Results] MMP3 expression was significantly lower in all other drugs relative to IL-6 stimulate control group (TOF; p=0.02, BAR; p=0.0005, PEF; p=0.02, UPA; p=0.03). On the other hand, any other targets showed no significant differences between IL-6 stimulate control group. [Conclusions] JAK inhibitors suppressMMP-3 induced by IL-6 in chondrocytes.

P3-068

Usage of Rheumatoid Arthritis Patients Initiated on JAK Inhibitors at our Hospital

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Conflict of interest: None

[Objective] To investigate the continuation and discontinuation of the 1st JAK inhibitor (JAK-i) in patients with rheumatoid arthritis (RA). [Methods] Sixty-eight RA patients (62 female and 6 male) who started JAK-i between October 2014 and November 2021 at our hospital were surveyed to determine whether JAK-i was continued or discontinued. Patients who discontinued JAK-i were grouped by cause as follows: ineffective, adverse events (AE), transfers to other physicians, and others. [Results] The 68 cases included 19 tofacitinib (TOF), 25 baricitinib (BARI), 3 peficitinib (PEFI), 13 upadacitinib (UPA), and 8 filgotinib (FIL), for a total of 48 continuing cases and 20 discontinued cases. The latter 20 cases included 9TOF, 8BARI, 3PEFI, 0UPA, and 0FIL cases. By reason for discontinuation, ineffective: 4TOF, 4BARI, 1PEFI, 0UPA, 0FIL, AE: 3TOF, 1BARI, 0PEFI, 0UPA, 0FIL, transfers: 2TOF, 3BARI, 2PEFI, 0UPA, 0FIL, other: 1TOF, 0BARI, 0PEFI, 0FIL cases. Ineffective was the most common reason for discontinuation, and 9 cases who selected other JAK-i after discontinuation of the 1st JAK-i were as follows; TOF→BARI: 4, BARI→PEFI: 2, BARI→UPA: 2, PEFI→FIL: 1 cases respectively. [Conclusions] With more RA treatment options available, further analysis is needed to use each drugs more appropriately.

P3-069

Impact of hip replacement on disease activity in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Hip destruction due to RA progression significantly affects pain and gait disturbance, but the hip is often not included in disease activity assessments Consider disease activity in RA patients who have undergone THA. [Methods] Subjects were RA patients who underwent initial THA at our department from September 2010 to December 2020, who could be followed up to 1 year postoperatively, and disease activity was evaluated before and after surgery in 7 cases and 8 hips. The mean age was 67.5±11.1 years, 1 male and 7 females, mean duration of RA was 16.6±12.8 years, and Larsen grade was grade 3 in all patients. RA disease activity was assessed by DAS28-ESR, DAS28-CRP, SDAI, and CDAI. [Results] Preoperative RA disease activity was 4.25 for mean DAS28-ESR, 3.38 for mean DAS28-CRP, 17.69 for mean SDAI, and 15.25 for mean CDAI; postoperative RA disease activity at 1 year was 3.42 for mean DAS28-ESR, 2.32 for mean DAS28-CRP, 7.19 for mean SDAI, and 7.19 for mean CDAI. 68, and the mean CDAI was 7.19. Disease activity decreased with THA. [Discussion] This study also showed improvement in disease activity in the short term, but continued treatment of RA is necessary in the future.

P3-070

A case of Cup Migration after total hip replacement in a patient with femoral neck fracture with history of rheumatoid arthritis, revision using the Impaction Bone Graft technique

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Conflict of interest: None

[Objective] In patients with rheumatoid arthritis, hip joint destruction may lead to protrusio acetabuli due to bone fragility and operative reconstruction may be difficult. We used the Impaction Bone Graft (IBG) technique to perform revision surgery to correct delayed cup migration after hip arthroplasty for femoral neck fracture in a relatively young patient with rheumatoid arthritis. We report that with some discussion of the literature. [Methods] The patient was a 64-year-old woman who had developed rheumatoid arthritis at the age of 54 and had been treated for it. Around 2 years after the initial surgery, Cup Migration gradually progressed and pain appeared, so revision surgery was performed using the IBG technique with metal mesh and allogeneic bone. [Results] A 14-week postoperative X-ray showed a tendency toward bony union. Five years after the revision surgery, the implants are stable. There have been no complications. [Conclusions] To augment large bone defects in total hip arthroplasty, the IBG technique using allogeneic bone has the advantage of augmenting large bone defects and providing more permanent bony fixation. The IBG technique was effective in this case as well. However, there is a possibility of re-failure in the future, and long-term follow-up should continue.

P3-071

Evaluation of disease activity and nutritional status of rheumatoid arthritis patients undergoing total knee arthroplasty

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Conflict of interest: None

[Objective] The purpose of this study was to investigate changes in disease activity and nutritional status before and after total knee arthroplasty (TKA) in patients with rheumatoid arthritis (RA). [Methods] Forty-four patients with RA knee arthritis who had undergone TKA and could be followed up for at least one year were included in the study. DAS28 (4)-CRP (DAS28) as disease activity before and one year after surgery, Prognostic Nutrional Index (PNI) as evaluation of nutritional status, and changes in drugs used were investigated. The correlation between pre- and postoperative changes in DAS and PNI was evaluated using pearson's correlation coefficient. [Results] DAS28 significantly improved from 3.3±1.2 preoperatively to 2.5±1.1 postoperatively ($p<0.01$), and PNI significantly improved from 47.3±5.2 to 48.5±5.2 ($p<0.01$). There was no change in drug status. There was a weak significant negative correlation between pre- and postoperative DAS change and PNI change ($r=-0.326$, $p<001$). [Conclusions] Improvement in disease activity before and after TKA was significantly correlated with improvement in nutritional status, suggesting that local surgical intervention may affect not only disease activity but also nutritional status.

P3-072

Postoperative range of motion of TKA for rheumatoid knee with flexion contracture

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Conflict of interest: None

[Objective] RA is considered to have weak soft tissues, and it is said that when performing knee joint replacement surgery, it is better to place the implant slightly tighter in extension than OA. In this study, we investigated the effect of surgery on the ROM and postoperative clinical outcomes of RA patients with flexion contracture by performing the surgery under anesthesia in a slightly loose hyperextended position. [Methods] The study included 10 knees in 9 patients who underwent knee replacement surgery for rheumatoid knees with flexion contracture of more than 30. The mean age was 71.5 years. Mean preoperative knee joint ROM was 34.1 of extension with flexion contracture and 111.8 of flexion. The knee extension angle under anesthesia immediately after surgery was 1.2 of hyperextension. Knee joint ROM was investigated at 6 months postoperatively. [Results] At 6 months postoperatively, the knee extension angle was significantly better than the preoperative flexion contracture angle of 34.1, although an average of 8.6 of flexion contracture remained. The knee flexion angle averaged 122.7. [Conclusions] If the rheumatoid knee also has preoperative flexion contracture, the flexion contracture will remain even if TKA is performed in a slightly loose extension position under anesthesia.

P3-073

Spinopelvic Alignment Before and After Total Knee Arthroplasty for Rheumatoid Patients

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Conflict of interest: None

[Objective] To investigate the change of spinopelvic alignment and sagittal global balance after removal of knee flexion contracture by total knee arthroplasty (TKA). [Methods] Sagittal spinopelvic alignments were investigated in 15 rheumatoid subjects using radiographs of the whole spine. Parameters measured in this study were sagittal vertical axis (SVA), lumber lordosis (LL), sacral slope (SS), pelvic tilt (PT), pelvic incidence (PI), and C1C2, C2-C7 angle (C1C2, C2C7). The association of pre and postoperative spinopelvic alignment and knee extension was investigated. [Results] Most subjects exhibited anteriorly shifted global imbalance associated with decrease of LL and retroversion of pelvis. Although knee flexion contractures were eliminated postoperatively, global imbalance was not improved in most subjects. SVAs were decreased in 6 subjects associated with slight increase of LL. However, more anteriorly shifted SVAs were confirmed in the rest of 9 subjects. There were no significant differences in other values of spinopelvic parameters and clinical factors between subjects with and without improvement of SVA. [Conclusions] The sagittal global imbalance was not restored by the removal of knee flexion contracture after TKAs.

P3-074

Two cases of rheumatoid arthritis with two-stage total knee arthroplasty for severe knee flexion contracture

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Conflict of interest: None

[Objective] We report two cases of bilateral severe knee flexion contractures due to rheumatoid arthritis (RA) in which bilateral two-stage total knee arthroplasty (TKA) was performed and flexion contractures improved. [Case 1] The patient was a 57-year-old woman who had RA for 9 years. Her preoperative range of motion (ROM) of the knee joints was 80/80 degrees of flexion and -60/-70 degrees of extension. After posterior release of the knee, the ROM improved to -20 degrees of extension bilaterally. TKA was then performed, and at the time of the final investigation, the ROM had improved to 0/0 degrees of extension. [Case 2] The patient was a 67-year-old man who had RA for 10 years. His preoperative ROM of the knee joints was 130/130 degrees of flexion and -90/-90 degrees of extension. After posterior release of the knee, the ROM improved to -20 degrees of extension bilaterally. TKA was then performed, and at the time of the final investigation, the ROM had improved to 0/0 degrees of extension. [Conclusions] The most common cause of severe flexion contracture of the knee is RA, which has a long duration of disease. When flexion contracture is severe, as was the case in our own case, it is suggested that a two-stage surgery with soft tissue release and TKA can provide good results.

P3-075

Early periprosthetic distal femoral insufficiency fracture after total knee arthroplasty in rheumatoid arthritis patient: a report of two cases

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Conflict of interest: None

[Objective] We report two cases of early periprosthetic distal femoral insufficiency fracture after TKA in RA patient. [Case 1] A 78-year-old female suffered from RA around the age of 50 but had never received any treatments. She had high disease activity and showed marked ROM limitation. After five months of medication and rehabilitation, she underwent right TKA. She was immediately able to walk and improved ROM, but an X-ray on postoperative day 14 revealed an insufficiency fracture of her right supracondylar femur. [Case 2] A 52-year-old female suffered from RA at the age of 31 and was referred due to exacerbation of bilateral knee pain. She had moderate disease activity and significant ROM limitation. Six months after left TKA, she underwent right TKA. She was able to walk and improved ROM. An insufficiency fracture of her right supracondylar femur was revealed on X-ray one month after discharge. [Clinical Significance] Both cases were lean, had inadequate osteoporosis treatment, poor preoperative ROM, and long-term RA with poor disease control. Such patients are at high risk of intra- and post-operative fractures and tend to endure pain. Therefore, even if the postoperative course is good, careful attention should be paid to the occurrence of insufficiency fractures.

P3-076

A case of TKA after HTO, which subsequently led to the diagnosis of rheumatoid arthritis

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Conflict of interest: None

[Objective] RApatients are often complicated with knee osteoarthritis. We report a case in which a TKA was performed after a HTO, but the pain did not improve, and a subsequent close examination led to the diagnosis of RA. [Case] She is a 60-year-old female. Height 157 cm, weight 69 kg. She was referred to another hospital with a diagnosis of right knee meniscus injury and locking. In December of the same year, she underwent a specoscopic meniscectomy and HTO. However, since range of motion limitation remained, TKA was performed in March 2022. Since she had been suffering from fever, mildly elevated inflammatory response, and fatigue before the surgery, she underwent a close examination for RA, leading to the diagnosis of RA. MTX was started in June of the same year, and her knee joint pain has been relieved. [Consideration] We have an experience of a patient with OA from the time of initial examination, and despite the finding of synovitis at the time of speciologic surgery, it took a long

time to reach the diagnosis of RA. It is necessary to keep in mind the possibility of RA in patients who present to our hospital with joint pain as a main complaint.

P3-077

Revision surgery using a retrograde intramedullary nail with allogeneic bone graft for a loosed total ankle arthroplasty with medial malleolus fracture; a case report

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Conflict of interest: None

[Objective] Various techniques have been reported for salvage surgery for periprosthetic ankle fractures of total ankle arthroplasty (TAA). We report a revision surgery using a retrograde intramedullary nail with allogeneic bone grafts for a patient with rheumatoid arthritis (RA) which have her right loosed TAA with medial malleolus fracture. [Methods] The patient is a 76-year-old woman with 15 years of RA duration. She had a right loosed TAA performed 6 years ago. Before one month, she had suffered a right ankle medial malleolus fracture. We considered applying a combined TAA with artificial talus as a salvage procedure, but she had severe dementia with Lewy bodies (DLB). Therefore, ankle joint fusion using a retrograde intramedullary nail in combination with allogeneic bone was performed. [Results] The JSSF RA foot ankle scale improved from 37 points preoperatively to 75 points at the last observation. She started full-weight-bearing walking 3 weeks after her surgery and was able to walk without any assisted aid at the last observation. [Conclusions] Retrograde intramedullary nails structurally require fixation of the talocrural joint with the talocalcaneal joint. We need careful concerns and long-term follow-up for it.

P3-078

A case of pain due to subsidence of the talus component of an total ankle arthroplasty treated by resection of the residual protruding talus bone

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Conflict of interest: None

While the effectiveness of total ankle arthroplasty (TAA) for rheumatoid arthritis has been reported, loosening of the component and subsidence of the talus component have also been reported. We report a case of an ankle joint pain caused by the subsidence of the talus component after a total ankle arthroplasty, which was relieved by resection of the protruding anterior talus bone caused by the subsidence. The patient, a 78-year-old woman, developed RA at the age of 40. A biologics was introduced at 67 year-old. At the age of 72, she underwent TAA. Postoperatively, the talus component subsided. Denosumab was started. Sinking stopped, but ankle joint pain remained. Under fluoroscopic study, we found that the remaining bone on the anterior talus impinged during dorsiflexion of the ankle joint, causing pain. 78 years old, we underwent resection of the protruding bone of anterior talus and forefoot surgery. Postoperatively, her ankle joint pain was relieved and her walking ability increased. Although the removal of the TAA and arthrodesis with autologous iliac bone graft were considered, the above method was selected in consideration of the invasiveness and prolonged postoperative rehabilitation. Although the pain did not disappear completely, ADL was improved.

P3-079

Proximal humeral plate for arthrodesis of ankle severe inversion deformity in a patient with rheumatoid arthritis: A case report

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Conflict of interest: None

The aim of this presentation is to highlight the benefits of applying proximal humerus locking plates in the fixation of ankle joint. A 60-year-old woman had been diagnosed with rheumatoid arthritis at 54 years old. She presented with pain on the right ankle without trauma. Six weeks after onset, conventional X-ray showed fractures of the left distal tibia and distal fibula that required surgery to repair. She underwent fracture fixation with screw for Medial malleolus, locking plate for posterior malleolus and locking plate for lateral malleolus of left ankle. However, the patient returned twelve weeks after surgical treatment complaining of persistent pain. Repeat X-ray showed progressive collapse of medial distal tibia, and 1 year after surgery, her ankle had severe inversion deformity because non-union of fracture site. Therefore, ankle arthrodesis using proximal humeral plate (zimmer-biomet NCB plate) medial plating was subsequently performed. Pain relief and union at the ankle joint were observed twelve weeks after the arthrodesis surgery. Proximal humerus locking plates may be useful of ankle arthrodesis for severe ankle deformity.

P3-080

A case of ankle joint tuberculosis during RA treatment, resulting in lower limb amputation

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Conflict of interest: None

[Background] Osteoarticular TB is a rare disease, accounting for only 0.3% of all TB patients. We report a case of ankle joint TB that developed during treatment of rheumatoid arthritis (RA) and required amputation of the lower limb. [Case Report] A 68-year-old man developed MTX-LPD while being treated with MTX for RA, and he stopped taking MTX. Chest CT was performed for follow-up of MTX-LPD, and miliary shadows were observed in both lung fields, and after biopsy, a diagnosis of pulmonary tuberculosis was made. Subsequently, swelling and pain in the right ankle joint appeared, which was thought to be an exacerbation of RA, and SAR administration was started. However, the pain did not improve, Synovectomy resulted in a diagnosis of tuberculosis of the ankle joint. The patient was treated with multiple anti-tuberculosis drugs for about 10 months, Two synovectomies were performed, tuberculosis was not improvement. Lower limb amputation was selected as the curative treatment. [Summary] We have experienced a case of ankle joint tuberculosis that developed during RA treatment. Tuberculous arthritis is rare, and its diagnosis is often delayed. It is important to always tuberculous arthritis in mind as a differential diagnosis in patients with arthritis.

P3-081

Outcome of Lateral Phalangeal Joint Sparing Surgery in Forefoot Surgery for Rheumatoid Arthritis

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Conflict of interest: None

[Objective] In rheumatoid arthritis, destruction and deformation of the MTP joint in the forefoot progresses from an early stage. We have performed joint-sparing surgery since July 2016 in such cases, and we report here the results of this study comparing the outcomes with those of patients who underwent lateral phalangeal resection arthroplasty. [Methods] Hallux valgus angle, first and second intermetatarsal angle, first and fifth intermetatarsal angle by simple x-ray, score by SAFE-Q, and postoperative complications were evaluated before and after surgery. [Results] In

the simple radiographic evaluation, the all angle was no significant difference in the degree of improvement between the two groups. Preoperative and postoperative SAFE-Q scores between the two groups were not significantly different for all items. As for postoperative complications, there was a significant difference in the incidence of dislocation. [Conclusions] Indicating that at this stage there are no significant differences in treatment outcomes for forefoot deformity depending on the surgical technique. We believe that this is largely due to the small sample size and subjective evaluation. We will continue to perform joint-sparing surgeries and monitor the progress of these surgeries over the long term.

P3-082

Scarf osteotomy as a salvage of non-preserving arthroplasty in patients with rheumatoid arthritis patients

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Conflict of interest: None

[Objective] Although arthrodesis of 1st MTP joint had been considered to be a definitive salvage procedure after HV surgery, in this case series (5 cases) with RA patients, scarf osteotomy was undergone as a salvage procedure after resection or silicon implant arthroplasty to preserve the mobility of 1st MTP joint. [Methods] 5 rheumatoid forefoot deformities that showed recurrence after resection or silicone implant arthroplasty in 1st MTP joint. All feet were treated with scarf osteotomy. Radiographic evaluation, ROM of 1st MTP joint, clinical evaluations [JSSF and SAFE-Q] were investigated at the time of pre-operation and final follow-up. [Results] All cases achieved significant correction after scarf osteotomy, even though 1st MTP joint had been resected. HVA and M1M5A were significantly improved at the final follow-up. Dorsiflexion of 1st MTP joint was significantly improved at the final follow-up. In clinical evaluations, JSSF-scale and SAFE-Q score were improved at the final follow-up. [Conclusions] We believe that scarf osteotomy has a possibility to be one of definitive procedure salvage after resection or silicone implant arthroplasty in RA patients, because it can good realign 1st MTP joint, preserve ROM of 1st MTP joint and get good patients satisfaction.

P3-083

A case report; A rheumatoid arthritis patient performed metatarsal osteotomy for severe hallux valgus. We worried about non union. However her bone united one year after osteotomy

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Conflict of interest: None

[Objective] Many patients with rheumatoid arthritis use many anti-inflammation drugs. For their poor bone quality, we often experience delayed bone union after surgery. We report a case; a patient observed bone union 1 year after the operation of hallux valgus, despite the risk of non-union. [Methods] The patient is a 64-year-old woman. The duration of rheumatoid arthritis was 44 years. MTX cannot be used due to her interstitial pneumonia, she is treated with PSL, SASP, TAC, and IGU. She currently maintains low disease activity. In September 2021, we performed metatarsal osteotomy for a severe hallux valgus patient. Postoperative callus formation and symptom were followed at outpatient clinic. [Results] Six months after the operation, the callus formation was poor. We worried about non-union. However, callus became clear one year after the osteotomy. Her symptom also got improved. [Conclusions] Generally, the metatarsal osteotomy is indicated for moderate hallux valgus. We would like to argue on the application of the methods and callus formation, including a review of the literatures.

P3-084

Examination of the prevalence of axial spondyloarthritis by CT evaluation of sacroiliac joints in psoriasis patients

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Conflict of interest: None

[Objective] To evaluate the sacroiliac joints (SIJ) of psoriasis patients by CT and examine the rate of patients with erosion and fusion of SIJ and patient background. [Methods] We evaluated the SIJ of patients with psoriasis in the past two years and underwent abdominal CT. SIJ changes were defined as erosion or fusion (Yahara et al.'s classification criteria Type 4C). Sex, age, comorbidities such as diabetes, disease duration, PsA (psoriatic arthritis), and the use of biologics were compared by SIJ changes. A t-test and a chi-square test were used, and the significance level was set at 0.05. [Results] There were 58 psoriasis patients (44 men, mean age 60.5 years, mean disease duration 10.3 years). Of these, 20 (34.5%) had SIJ changes (erosion; 17, fusion; 4, duplication; 1). When patients were compared according to SIJ changes, there was no difference in sex, age, age of onset, use of biologics, PsA and the comorbidities. Eight of the 20 were undiagnosed with PsA and were not using biologics. [Conclusions] In this study, 34.5% of patients with psoriasis had SIJ changes. SIJ changes occurred irrespective of the patient background such as age and gender, PsA, and use of biologics. Patients with psoriasis without PsA may also have asymptomatic axial spondyloarthritis.

P3-085

Examination of sacroiliac joint fusion range in DISH (Diffuse Idiopathic Skeletal Hyperostosis) patients and comparison with AS (Ankylosing Spondylitis) patients

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Conflict of interest: None

[Objective] To compare the range of sacroiliac joint (SIJ) fusion in patients with DISH with those in patients with AS by CT. [Methods] Among patients who visited our ER underwent thoracoabdominal CT, those who have SIJ fusion (Yahara criterior Type4c) and thoracic spine findings meeting the diagnostic criteria for early DISH by Kuperus et al. were selected. The most proximal position of the SIJ was ranked as 0, and the most distal position as 1, and the range of fusion between 0 and 1 was measured. Similar measurements were made in the fused SIJ of patients diagnosed with AS. A t-test was used with a risk rate of 0.05. [Results] 35 patients (34 males, 21 bilateral fusions, mean age 73.4 years) had 56 joints with SIJ of Type4c in early DISH or DISH. The range of fusion was 0.052-0.45 on average, and the mean of the most anterior L-shaped ear was 0.61. In most DISH patients, the SIJ fusion started most proximally and was near the corner of the L-shaped ear. On the other hand, 6 AS patients (all male, average age 56.0 years) had 12 joints with an average range of fusion ranging from 0.01 to 0.98. The position of the fusion end was significantly different between DISH and AS ($p<0.001$). [Conclusions] The range of SIJ fusion could be a point of differentiation between DISH and AS.

P3-086

Spinal and sacroiliac radiographic changes in SAPHO syndrome

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Conflict of interest: None

[Objective] To investigate radiographic changes of spine and scroiliac joints in SAPHO syndrome. [Methods] 16 patients diagnosed or treated with SAPHO at our hospital from January 2004 to July 2022 who were evaluated with spine and scroiliac joints using CT were included. The CT findings of hyperostosis and/or osteolysis of the spine and sacroiliac joints

were considered to be radiographic changes. [Results] The mean age at the time of CT was 56 years, and the mean disease duration was 6.4 years. 56% of patients had palmoplantar pustulosis. 6 patitents had spinal radiographic changes. All 6 patients had radiographic in multiple vertebrae, and 3 of the 6 patients had discontinuous radiographic changes. One patient showed lesions only in the cervical spine, one in the thoracic spine, one in the lumbar spine, one in the thoracic and lumbar spines, and two patients in the cervical, thoracic, and lumbar spines. 3 patitents had radiographic changes at scroiliac joints. Radiographic changes at scroiliac joints were predominantly iliolateral and symmetrical. [Conclusions] 38% of SAPHO patients had hyperostosis and osteolysis at the spine, and 19% had hyperostosis and osteolysis at sacroiliac joints.

P3-087

Process up to the diagnosis of ankylosing spondylitis

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Conflict of interest: None

[Objective] To investigate the process of being diagnosed with ankylosing spondylitis (AS). [Methods] 46 patients diagnosed with AS at our hospital from January 2004 to July 2022 were included. We investigated the duration from onset to diagnosis, the department that diagnosed AS, the department that first suspected AS, and the symptoms and laboratory findings that gave reason for suspicion. [Results] The mean duration from onset to diagnosis was 8.2 years. The departments diagnosed with AS were orthopedics in 85%, general medicine in 13%, and pediatrics in 2%. The departments first suspected with AS were orthopedics in 74%, general medicine in 11%, ophthalmology in 9%, and surgery, internal medicine, and radiology in 2% each. Symptoms that gave reason to suspect AS were axial joint symptoms in 72%, peripheral joint symptom or enthesitis in 48%, and extra-articular symptoms in 15%. Findings that gave reason to suspect AS were abnormal x-ray or CT in 41%, elevated inflammatory response in 26%, abnormal MRI in 20%, HLA-B27 positivity in 9%, and abnormal bone scintigram in 4%. [Conclusions] Symptoms that gave reason to suspect AS included not only axial joint symptoms, but also peripheral joint symptom or enthesitis and extra-articular symptoms.

P3-088

Disease misdiagnosed prior to diagnosis of ankylosing spondylitis

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Conflict of interest: None

[Background] Ankylosing spondylitis (AS) is a rare disease in Japan, so AS is recognized as another disease, resulting in delayed diagnosis. [Objective] To investigate diseases recognized prior to the diagnosis of AS. [Methods] Of 82 patients diagnosed or treated with AS at our hospital from January 2004 to July 2022, 38 patients (46.3%) who were recognized as having another disease prior to the diagnosis of AS. [Results] 36 patients were recognized as having musculoskeletal diseases prior to the diagnosis of AS. 13 patients were recognized as hip degenerative diseases, 10 patients were recognized as rheumatic diseases, and 10 patients were recognized as spinal diseases. Of the patients recognized as hip degenerative diseases and rheumatic diseases, 61.5% and 80% respectively, presented with axial symptoms. Of the patients recognized as spinal diseases, 60% presented with peripheral symptoms. [Conclusions] Many cases were recognized as another musculoskeletal diseases prior the diagnosis of AS. Rheumatologist should consider AS especially in young male with axial and peripheral symptoms.

P3-089

Relationship between Ankylosis and Physical Function Assessment in Ankylosing Spondylitis

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Conflict of interest: None

[Background] Ankylosing spondylitis (AS) causes physical dysfunction such as limitation of movement depending on the progression of the disease. The aim of this study was to investigate the relationship between the degree of ankylosis and physical function and frailty in patients with AS. [Methods] 16 patients with AS who attended our hospital underwent hole spine CT and physical function assessment. The area and number of ankylosis in each spine were evaluated. Patients' objective assessment was physical function measurement, and their subjective assessment was investigated using a self-administered questionnaire. Spearman's rank correlation coefficient was used to analyze the correlation between the degree of ankylosis and each evaluation item. [Results] Patients' objective assessment, BASMI, showed a significant correlation with the number of total/cervical/thoracic/lumbar spine ankylosis (r=0.828/0.801/0.798/0.582). The BASFI and Locomo 25 were significantly correlated with the number of total spine/cervical/thoracic vertebral ankylosis (r=0.750/0.806/0.676) and total spine/cervical spine ankylosis (r=0.522/0.655), respectively. [Conclusion] The BASFI and Locomo 25, which assess physical function, were significantly correlated with the number of ankylosis in AS patients.

P3-090

Examination of the clinical significance of Leucine alpha glycoprotein measurement in spondyloarthritis

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Conflict of interest: None

Leucine-α-glycoprotein (LRG) in spondyloarthritis is produced from the liver and is also produced locally inflammatory. It has been approved as an indicator of disease activity in ulcerative colitis, and its association with psoriasis skin lesions has also been reported. Peripheral spondyloarthritis (psoriatic arthritis, arthritis associated with inflammatory bowel disease, etc.), axial spondyloarthritis Paloplantar pustular arthritis The clinical significance of LRG measurement in was examined. Methods: Blood LRG was measured in 30 cases of spondyloarthritis. Patients with axial spondyloarthritis, peripheral spondyloarthritis, and pustulotic arthro-osteitis were measured LRG in serum and examined clinical findings, and their association with laboratory findings was examined. LRG and blood tests and MRI XP findings were also examined. Results: Axial spondylitis had a significantly higher LRG value than peripheral spondylitis. (Axiality SpA, 33.75±8.1, ng/ml peripheral SpA 18.2±3.2, P<0.95), also. It also recovers to normal values with treatment. LRG does not correlate positively with CRP values and may reflect a different pathology from IL6-mediated inflammation, and may be a useful test for diagnosing the presence of axial lesions of spondyloarthritis.

P3-091

Analysis of clinical features for early diagnosis of psoriatic arthritis preceded by arthritis

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Conflict of interest: None

[Objective] The diagnosis of PsA preceded by arthritis is difficult. We analyzed the clinical features that contribute to the early diagnosis of arthritis-preceding PsA. [Methods] Among 1565 patients with psoriasis, we described the epidemiology and laboratory findings of patients classified

according to CASPAR criteria who had psoriasis preceding arthritis, and determined the sensitivity of symptoms and radiological findings at the time of initial examination and at the time of definitive diagnosis, and extracted factors contributing to early diagnosis. [Results] The sensitivity of the CASPAR classification criteria for PsA proceed by arthritis was low (28.6%). The sensitivity of periarticular bone proliferation, diaphyseal periostitis, lysis of the tufts, non-typical bone erosions of PsA (those are not found in rheumatoid arthritis), and calcification of the joint capsules was moderate. [Conclusions] Early diagnosis of arthritis-preceding PsA requires comprehensive interpretation based on radiographic findings and clinical features. It is necessary to further analyze the specificity of the factors and establish a method for early diagnosis.

P3-092

Comorbidities and treatment response in patients with Psoriatic arthritis

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Conflict of interest: None

[Objective] Patients with psoriatic arthritis (PsA) are also known to have a high prevalence of lifestyle-related diseases such as obesity and hypertension. But there are few reports on the effects of these comorbidities on the treatment of PsA. We investigated the therapeutic response of PsA in different comorbidities in clinical practice. [Methods] We examined the achievement rates of 0 M, 6 M, and 12 M for MDA, PASI, DASCRP, and ASDASCRP by the presence or absence of complications (Obesity, HT, diabetes (DM), dyslipidemia (DL), and hyperuricemia (HU)) In addition, the bio continuation rate by comorbidity was also examined. [Results] Patients were 61 years of age, 4 years of PsA history, 55% men. Treatment was TNFi 60% and IL17i 40%. Comorbidities were 53%/37%/10% for BMI 23/25/30 and 46%/19%/35%/23% for HT/DM/DL/HU. DM (+) had a significantly lower achievement rate of MDA and DASCRP-CR/LDA at 6 M, than DM (-). PASI and ASDAS and activity assessments at each 12 M were low. There was no difference in treatment response with obesity, HT, DL and HU. The retention rate differed only with or without DM, and DM (+) was lower than DM (-). [Conclusions] We found that the treatment response of biologics at 6 M differs depending on the presence or absence of DM complications in PsA patients.

P3-093

Treatment result of Inflammatory back pain in our department

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Conflict of interest: None

[Purpose] Inflammatory low back pain is one of the symptoms of spondyloarthritis (SpA) and is often observed in axial spondyloarthritis (Axial SpA). We report the treatment results of patients with inflammatory low back pain in our department. [Subjects] Of the 28 spondyloarthritis patients (18 males and 10 females, average age 52.3 years old) being treated at our department, 25 had axial pain. Radiographic axial SpA: r-ax SpA All 9 cases, Non radiographic Axial SpA (nr-axSpA) 8 cases out of 9, Psoriatic arthritis (PsA) in 8 out of 9 cases and SpA associated with IBD in 0 out of 2 cases). RESULTS: For r-axial SpA, 8 cases of Nsaids and 5 cases of acetaminophen had pain improvement (VAS<2) within 6 months, and pain relief was good. In 6 cases of nr - ax SpA, pain relief was observed with NSAIDs, methotrexate (MTX) in 2 cases, and biologic agents (bDMARDs) in 1 case. All patients with PsA were treated with MTX, and analgesia was achieved with bDMARDs in 2 patients and JAK inhibitor (JAKi) in 1 patient. [Conclusion] In patients with r-ax SpA, Nsaids often reduced symptom during follow-up. In nr-ax SpA, active inflammation was often present, and MTX and bDMARDs were used in some cases. MTX was effective against PsA, but bDMARDs and JAKi were also effective when insufficient.

P3-094

Efficacy of granulocyte and monocyte adsorption apheresis (GMA/GCAP) in the treatment of psoriatic arthritis in our department

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Conflict of interest: None

[Objective] In addition to biologics, JAK inhibitor is an option for the treatment of psoriatic arthritis (PsA). However, there are many cases in which disease control is difficult. Granulocyte and monocyte adsorption apheresis (GMA/GCAP) is an extracorporeal therapy that aims to control cellular functions and improve disease activity by removing granulocytes and monocytes. In this study, we evaluated the efficacy of GMA/GCAP in 21 patients with PsA who had an inadequate response to drug therapy. [Methods] Between February 2021 and December 2021, 21 patients with PsA, including some with axial lesions, who had an inadequate response to pharmacological treatment. The efficacy of GMA/GCAP was evaluated using composite measure such as DASPA and BASDAI and ASDAS, and sPGA for skin symptoms. [Results] Comparison of disease activity before and after 2 courses of treatment in 21 patients showed significant improvement in sPGA, DAPSA, BASDAI, ASDAS ($p<0.01$). [Conclusions] Despite the limitation of 21 patients at one institution and a short term of 10 weeks, GMA/GCAP is a useful treatment for PsA patients who have inadequate response to various biologics and JAK inhibitors, not only for cutaneous and peripheral joint symptoms but also for PsA patients with axial lesions.

P3-095

Investigation on Sarcopenia and Osteoporosis in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To investigate sarcopenia and osteoporosis in RA patients [Methods] From March to October 2022, RA patients (30 cases, all female, average age 71.9±8.4) were measured for limb skeletal muscle mass by BIA method, and the skeletal muscle mass index (SMI) was calculated. According to the AWGS criteria, we classified them into the sarcopenia group (S group) and non-sarcopenia group (NS group), and investigated bone mineral density (BMD) of lumbar and femur (YAM values) BMD was measured by DXA method. The relationship between SMI and BMD was investigated (Spearman's rank correlation). [Results] In the S: NS group, 21: 9 cases, 57.1: 33.3% in the complication rate of osteoporosis, mean YAM values 78.7±9.3: 89.2%±15.9 in lumber, 69%±10.0: 75.0%±10.9 in femoral neck, 71%±11.2: 79.8%±12.1 in total femur. Significant differences were identified in BMI and PSL usage. SMI tended to be weakly positively correlated with lumbar BMD ($r=0.36$, $p=0.059$). [Conclusions] The prevalence of sarcopenia in RA patients was 70%, and the complication rate of sarcopenia and osteoporosis was 40%, suggesting that screening for sarcopenia and osteoporosis is important in RA patients. In addition, it was suggested that patients with low BMI and PSL administration may be at risk of sarcopenia.

P3-096

The microdensitometry method is useful for diagnosing osteoporosis in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Osteoporosis is one of the major complications in patients with RA. However, the treatment rate is low because few medical institutions have device using DXA. We have performed bone mineral density (BMD) measurement by the second metacarpal bone microdensitometry (MD) method. [Methods] BMD measurement using the MD method was performed on RA patients, and YAM values were evaluated according to age, disease activity, and physical function. [Results] The average YAM of 91 RA patients (mean age 74.4 years, 75 females, 16 males) by the MD method was 71.7%. The mean YAM was 76.5% in the 60s, 69.1% in the 70s (p=0.027, vs 60s), and 63.2% for those over 80 (p=0.0004, vs 60s). The mean YAM was 75.4% in the SDAI remission group and 69.6% (p=0.030) in the non-remission group. The mean YAM was 74.7% in the HAQ remission group and 69.2% (p=0.038) in the non-remission group. Medication was administered to 54 (59.3%) of 91 patients who underwent BMD measurements. [Conclusions] YAM values obtained by the MD method were lower in older patients and those with higher disease activity and higher functional disability. This result agrees with previous reports on the DXA method. Osteoporosis in patients with RA can be detected with the MD method at facilities that do not have DXA equipment.

P3-097

Characterizing the risk of Fragility Vertebral Fracture in Patients with Rheumatic Diseases

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Conflict of interest: None

[Objective] To investigate the risk factors for vertebral fractures (VF) in patients with rheumatic diseases. [Methods] We analyzed the age, the parts of fractures, glucocorticoid (GC) doses, the YAM values in the bone mineral density (BMD) tests, and treatment for osteoporosis in patients with a history of VF. [Results] A total of 32 patients (29 females, 3 males), including 13 RA, 7 SLE, 5 MPA, and 7 other autoimmune diseases, were eligible for this study. The average age was 73 (female) and 71 (male). Twenty-seven lumbar and 10 thoracic VF were analyzed. The PSL doses were 6.7±5.7 mg/day (female) and 5-25 mg/day (male), and 5 patients (16%) experienced VF without GC use. The BMD tests revealed 59.5±6.0% (femoral YAM) and 78±19.6% (lumbar YAM). Bisphosphonate (Bis) for 20 patients, denosumab (Dmab) for 2, and PTH analog (PTH) for 2 were used when VF occurred. After VF, the treatments were changed to Bis for 3, Dmab for 4, PTH for 17, and romosozumab for 9 patients. Two elderly female patients experienced VF despite using PTH. They used 5 mg/day or less PSL with a history of Bis. Lumbar VF occurred on 2 months and 6 months of PTH use. [Conclusions] Our results suggested the importance of timely osteoporosis evaluations due to the risk of VF even using osteoporosis medications.

P3-098

Therapeutic intervention for steroid osteoporosis in our Department of Collagen Disease and Rheumatology and its current status

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Conflict of interest: None

[Objective] Corticosteroids are frequently used in collagen diseases. On the other hand, there are many side effects, and steroid-induced osteoporosis (GIO) is one of the most important side effects. In this study, we investigated therapeutic intervention for GIO. [Methods] We retrospectively investigated the intervention rate of osteoporosis treatment in patients aged 65 years or older (total 226 patients) who were prescribed prednisolone (PSL) for at least 3 months at our collagen disease and rheumatology department between September 2021 and August 2022. [Results] 179 patients were prescribed osteoporosis medications. The breakdown of treatment drugs (including duplicates) was as follows: BP: 110 patients, PTH: 9 patients, denosumab: 11 patients, Vit. D: 98 patients, and unknown details (due to prescriptions at other hospitals): 1 patient. There were 47 patients with no therapeutic intervention. [Conclusions] The compliance rate with guidelines is estimated to be 20-30%, but the rate was high at 79.2% at our hospital. However, there were some cases in which osteoporosis treatment, such as bone density measurement, was not evaluated. In the future, we would like to make efforts to manage GIO by measuring bone density and suggesting therapeutic agents.

P3-099

The calcium ingestion by the meal in the patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] Calcium is an important composition nutrient of a bony mineral ingredient, and is a nutrient indispensables to preventation and medical treatment of osteoporosis. The meal Ca content in the patients with RA was investigated using a Ca self-check table as a method of presuming the amount of calcium ingestion this time. [Methods] The 204 RA patients under going-to- hospital-regulrty treatment comprised 177 women and 27 men with a mean age of 69.2 years, a mean duration of 19.8 years. BMD, serum 25 (OH)vitamin D concentration, a bone metabolic marker, a renal function and Ca concentration were measured. [Results] There are quit few Ca intakes as an average of 507.2 mg. When mark were classified into 5 steps, A (20 < points) was 2 persons and B (16-19 points) was38 persons and C (11-15 points) became 110 persons, D (8-10 points) became 37 persons, E (0-7 points) became 17persons, and not more than Ca600 mg was 164persons (80.4%). 25 (OH)vit D concentration was 18.3 ng/ml and a deficiency state. [Conclusions] As for many of RA patients, Ca intake is liable to a scantiness. Moreover, vit D concentration is also in a scantiness state. Also in order to obtain the curative effect of osteoporosis, they are Ca intake and vit D by a meal. It is idea that it is important to raise concentration.

P3-100

A Study on the 2014 Glucocorticoid-Induced Osteoporosis (GIO) Guidelines

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Conflict of interest: None

[Objective] The accuracy of japan 2014 guidelines and physicians compliance were examined. [Methods] (1) Conducted an awareness questionnaire survey on gio treatment among 25 prescribing physicians in 9 departments of our hospital. (2) Survey of 526 patients who received steroid treatment from april to june 2020. [Results] (1) 60% of doctors do not refer to the guidelines. There was a tendency to prescribe bisphosphonate (bp) with steroid prescriptions. There is no tendency to ask for bone densitometry or history of fractures. (2) Four guideline items were reevaluated. In 3 or more points, 65% were treated for osteoporosis. (86% bp) and 35% had no treatment. Secondary fractures occurred in 11% of the bp treatment group and 19% of the no treatment group. Secondary fractures were correlated with the presence or absence of a history of fracture and age, but not with dose or lumbar bone density. In addition, there was a strong correlation between secondary fractures and the total score of the four guideline items. [Conclusions] Few doctors were aware of the guidelines and treated them, and many thought that bp should be prescribed by steroids. However, the accuracy of the guidelines is high, and we thought that evaluating all items would help prevent secondary fractures.

P3-101

Comparison of Efficacy for Bone Mineral Density Improvement between Teriparatide and Romosozumab in Female RA Patients

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Conflict of interest: None

[Objective] The aim of this study is to compare the efficacy for bone mineral density (BMD) improvement between teriparatide (TPTD) and romosozumab (ROMO) in female rheumatoid arthritis (RA) patients. [Methods] This retrospective case-controlled study comprised 77 patients with female RA patients treated with TPTD for 2 years or ROMO for a year. BMD of the proximal femur (F) and lumbar spine (LS) were evaluated by the DXA method. We compared BMD changes in each drug after initiation and changes in BMD among drugs at each time. To control for baseline patient characteristics associated with 2 drugs, propensity score matching was performed. [Results] The rate of BMD improvement in TPTD [LS, F] was [1.081, 1.005] at 1 year ($p<0.05$, $p=0.178$), and [1.091, 1.038] at 2 year ($p<0.05$, both), and in ROMO was [1.155, 1.020] at 1 year (both $p<0.05$). Among both drugs, the rate BMD-LS improvement was significantly higher in ROMO [1 year: 1.134] than in TPTD [1 year: 1.059, 2 years: 1.089] ($p<0.05$, both). There were no significant differences in the rates of BMD-F improvement between ROMO [1 year: 1.114] and TPTD [1 year: 1.025, 2 years: 1.042]. [Conclusion] ROMO was superior in BMD-LS improvement of female RA patients, but there was no difference in BMD-F among TPTD and ROMO.

P3-102

Association between bone metabolism markers and increases in bone mineral density in patients with postmenopausal osteoporosis treated with romosozumab

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Conflict of interest: None

[Objective] To evaluate association between effect of romosozumab (Rmab) on bone mineral density (BMD) and bone metabolic markers (BTM) in patients with postmenopausal osteoporosis (PMO). [Methods] Between March 2019 and August 2021, 34 patients with PMO and naïve to treatment were included. The correlation between changes (%-) in L-BMD and Th-BMD at 12 months (M) and baseline (BL) data and BTM was calculated. Multiple regression analysis was performed on the factors that showed significant correlations to BMD. [Results] The mean age was 72.5 years, BMI 20.6 kg/m^2, vertebral fractures 2.1, L-BMD 0.762 g/cm^2, TH-BMD 0.589 g/cm^2, P1NP 107.0 μg/L, and TRACP-5b 640.3 mU/dL. %L- and %TH-BMD at 12 M were 18.1% and 9.1%. %P1NP at 3 M was positively correlated with %L-BMD at 12 M, while %P1NP at 1 M and 6 M and TRACP-5b at each time point showed no significant correlation with %L-BMD at 12 M. Multiple regression analysis confirmed that an increase in P1NP at 3 M was associated with an increase in L-BMD at 12 M. No correlation between BTM and %TH-BMD at 12 M was observed. [Conclusion] We showed that an increase in P1NP at 3 M was a predictor of an increase in L-BMD at 12 M in patients with PMO treated with Rmab. On the other hand, there was no association between TH-BMD increase and BTM.

P3-103

Investigation of factors affecting the bone mineral density improvement effect of romosuzumab in female patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] Rheumatoid arthritis (RA) patients are frequently complicated with osteoporosis, but there are few reports on romosuzumab (ROMO). In this study, we investigated the efficacy of ROMO in female RA patients and factors affecting it. [Methods] From August 2019 to August 2021, 27 female RA patients who recerved ROMO at our hospital. Bone mineral density (BMD) (by DXA) of the lumbar vertebrae and proximal femur was evaluated 1 year later. In addition, we compared the clinical backgrounds of the effective group and the non-effective group divided by BMD, and searched for factors that affect the efficacy of ROMO. [Results] The background of all patients was age 74 years, duration of RA 13 years, DAS28-CRP 2.20, PSL use in 12 cases, BMD lumbar spine 0.665, proximal femur 0.644, prior treatment with bisphosphonate in 14 cases, 8 denosumab (DM), 1 teriparatide, 4 no treatment. One year later, the BMD in the lumbar spine was 0.782 (1.114 compared to the baseline), and the proximal femur was 0.649 (1.025) ($P<0.05$). As a result of comparing the both group, the change rate was low in cases using DM in the proximal femur ($P<0.05$). [Conclusion] ROMO improved BMD in RA patients. However, it was suggested that the BMD improvement rate of the proximal femur may decrease in patients who used DM.

P3-104

Analysis of Romosozumab Treatment for Osteoporosis in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To analyze the effect of one year of treatment with romosozumab on osteoporosis in patients with rheumatoid arthritis (RA). [Methods] In 23 patients treated with romosozumab, we analyzed age, gender, stage, class, disease duration, biologic agent, methotrexate, prednisolone and SDAI, CDAI, DAS28-ESR, rheumatoid factor, anticitrullinated protein antibodies, CRP, MMP-3, TNFα, IL-6, homocysteine and bone density before and after 1 year of osteoporosis treatment. [Results] There were no significant effects of osteoporosis treatment on disease activity, inflammatory response, serum factors, and cytokines throughout 1 year. The 1-year change from baseline in bone mineral density was +9.5% in the lumbar spine ($p < 0.05$) and +4.1% in the femoral neck ($p < 0.05$). The group with a higher rate of change than the median was divided into response group and the group with a lower rate of change was divided into non-response group, and analysis of patient background showed that only class was a predictor for response. [Conclusions] One year of treatment with romosozumab significantly improved bone mineral density at the lumbar spine and femoral neck in patients with RA, independent of disease activity, inflammatory response and cytokines, with class being the only predictor.

P3-105

Effects of initial treatment of osteoporosis by bisphosphonates or denosumab on bone mineral density with biological agent in rheumatoid arthritis

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Conflict of interest: None

[Objective] The aim of this 1-year retrospective study was to evaluate the differences in outcomes of bisphosphonate (BP) or denosumab (DMAB) with golimumab (GLM), abatacept (ABT), or tocilizumab (TCZ) in rheumatoid arthritis. Bisphosphonates and denosumab has long half-life in bone, and these can affect bone metabolism after we change to another drug in osteoporosis. Therefore, only patients who received initial treatment for osteoporosis were included. [Methods] We investigated patients treated with GLM, ABT, or TCZ which are relatively common among bDMARDs at our hospital. There was a total of 23 patients whose BMD were measured. Patients were divided into GLM and BP treated group (6 cases), ABT and BP treated group (4 cases), ABT-DMAB treated group (8 cases), TCZ and BP treated group (5 cases). We measured bone mineral density (BMD) of the lumbar 2-4 vertebrae (L-BMD) and total hip (H-BMD) at baseline and 1 year. [Results] There were no significant differences in the percent changes in 4 groups. The highest percent change was L-BMD in ABT-DMAB (median 108%), and the lowest percent change was H-BMD in ABT-DMAB (median 99%). [Conclusions] GLM and ABT, TCZ are said to have an effect on osteoclasts. BP and DMAB are thought to increase BMD similarly even under that influence.

P3-106

Re-recognition of pseudogout in daily rheumatology practice and analysis of efficacy of colchicine

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Conflict of interest: None

In recent years, with the aging of society, opportunities to treat polyarthritis in the elderly people are increasing. Typical rheumatoid arthritis (RA) with positive rheumatoid factor and anti-CCP antibody, seronegative RA, polymyalgia rheumatica (PMR), and RS3PE syndrome are well known diseases, however, crystal-induced polyarthritis such as pseudogout (acute or chronic CPPD arthritis), sometimes showing the status of pseudo-RA and pseudo-PMR, has been underestimated. The EULAR recommendations for CPPD (2011) recommends local treatment and NSAIDs as well as colchicine and corticosteroids for the treatment of pseudogout. In this study, we retrospectively examined 70 cases of pseudo-RA and pseudo-PMR, and analyzed the clinical course including the extent of affected joints and efficacy of colchicine. One-third of patients showed improvement of symptoms and CRP levels, which lead to a reduction of corticosteroids and DMARDs.

P3-107

Clinical Results of Kaarela's tendon interposition arthroplasty supplemented with Mini TightRope for carpometacarpal osteoarthritis of the thumb

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Conflict of interest: None

[Objective] Carpometacarpal osteoarthritis of the thumb is common among patients with hand arthritis. We report the clinical results of modified Kaarela's tendon interposition arthroplasty. [Methods] Five hands of 5 patients with carpometacarpal osteoarthritis of the thumb that was surgically treated in our hospital were included in this study. Besides the original Kaarela's procedure, Mini TightRope was supplemented to the intermetacarpal. Clinical results were evaluated by range of thumb abduction, grip strength, and Quick DASH score. Proximal migration of the first metacarpal was evaluated on radiographs. [Results] Range of the thumb palmar abduction was improved from 27.0 degree to 41.0, and grip strength from 17.0 kg to 19.3, on average. Quick DASH function/symptom score was significantly improved from 50.9 to 13.7. Proximal migration of the first metacarpal was minimum on radiograph. [Conclusion] Satisfactory clinical outcomes have been reported for many surgical treatments of this lesion, and likewise in our study. Our modification could minimize the proximal migration of the metacarpal without a need of postoperative external fixation, and may enhance patients' comfort.

P3-108

Different methods of arthroplasty for bilateral CM joint disorder associated with rheumatoid arthritis -a case report-

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Conflict of interest: None

Sixty years old female was diagnosed as having bilateral CM joint disorders associated with rheumatoid arthritis. We performed different ligamentoplasties after trapeziectomy. Left side was reconstructed using half slip of flexor carpi radialis tendon when she was 61 years old. Right side was reconstructed using a suture button after one year. QuickDASH score was 15.9 points and PRWE was 28 points in left side, both QuickDASH and PRWE were 0 point in right side at 6 months after surgery. Furthermore, both QuickDASH and PRWE were 0 point at the final follow-up (left side; 5.5 years, right side; 4.5 years). Patient was satisfied the surgical results, but ligamentoplasty using a suture button could recover faster than using half slip of flexor carpi radialis tendon.

P3-109

Characteristics of patients with rheumatoid arthritis for whom home visit-medical care were introduced and their risk of falling

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Conflict of interest: None

[Objective] In recent years, the number of elderly-onset rheumatoid arthritis (RA) and long-term RA patients has been increasing. Elderly patients have various physical functions, cognitive functions, social backgrounds, etc., and require different treatment than non-elderly patients. In this study, we evaluated and discussed the characteristics of RA patients for whom home-visit medical care was introduced, as well as their risk of falling. [Methods] We investigated the clinical characteristics, level of care, level of independence in daily living, and causes that led to the introduction of home-visit medical care for RA patients referred to our clinic between April 2021 and September 2022. We also assessed the risk of falls using the Fall Risk Index (FRI) 21. [Results] The number of patients who received home-visit care was 25, with a mean age of 83.8 ± 9.7 years and a mean duration of disease of 17.7 ± 12.5 years. Many of the patients had DAS28 (CRP) 2.7 ± 1.2, but had strong deformity. The most common reasons for the introduction of home-visit care were debility due to aging (52%), dementia (16%), and fracture (16%). [Conclusions] RA patients are at high risk for falls and require rehabilitation not only of the lower extremities but also of the upper extremities.

P3-110

Online music therapy for patients with rheumatoid arthritis by using body percussion under COVID-19 pandemic

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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 RA. Under COVID-19 pandemic, we switched the activity to online since 2020. In this study, we investigated the effects of online music therapy by using body percussion. [Methods] Zoom online meeting system was recruited. Eight songs were sung with a piano accompaniment and 2 were played with body percussion. GH condition was evaluated by 0-10 NRS, pain by face scale, positive and negative moods, and emotional relaxation were surveyed by self-rating questionnaire including NRS, face pain rating scale, PANAS, and ERS. [Results] Seven female patients were participat-

ed. The median of HAQ-DI was 0.125. Although the sound was delayed because of the predisposition of the online meeting system, the results of before/after the activity were; GH 2.0/1.8, pain 3.6/2.2, positive affect of PANAS 26.0/28.2, and negative affect of PANAS 22.2/18.6, and four subscales of ERS were 10.2,12.0,11.8,10.8 respectively, which showed possible improvement of physical and psychological condition. Neither arthralgia nor fatigue was not induced by body percussion. [Conclusions] On line active music therapy by using body percussion may improve the condition of patients with RA.

P3-111

Effectiveness of rehabilitation for Elderly Rheumatoid Arthritis (RA) Patients

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Conflict of interest: None

[Objective] As the population of ageing is increasing, elderly RA patients is also increasing. Advances in RA treatment have reduced disease activity and improved life expectancy, however there has been no improvement in ADL due to muscle weakness and fracture risk. Then, we examined whether rehabilitation can improve ADL for elderly RA patients. [Methods] Of 50 RA patients aged 65 years or older, 25 patients were classified into the rehabilitation group and 25 patients were into the non-rehabilitation group. Physical ability (5-meter walk), bone density (lumbar spine and femur), and muscle mass of both lower limbs were measured before and 6 months after rehabilitation, and the improvement rate of each measurement was compared. [Results] The rate of improvement in each measurement, bone density, lower limb muscle mass, and walking speed (average and fastest), after 6 months was not significantly different with or without rehabilitation. [Conclusions] Six months rehabilitation might be too short. More longer rehabilitation period would increase ADL. It might be difficult to continue self-rehabilitation for the elderly patients. Involvement of health care provider is required for efficient rehabilitation. Advances in RA treatment have also contributed to the maintenance of physical.

P3-112

Examining the effects of self-exercise using exercise assistance apps

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Conflict of interest: Yes

[Objective] When rheumatoid arthritis patients do self-exercise (self-EX) at home, they often forget how to do or do in the wrong way. Thereby pain aggravation and recurrence of inflammation occur. We compared the effects of Self-EX on physical function (FF) with or without smartphone (SP) app for exercise assistance when performing Self-EX at home instructed by a physical therapist. [Methods] 9 patients who were usable the SP app, DAS28-CRP < 2.7, and consented to this study were selected and randomly divided into an app user group of 5 and a non-app user group of 4. Using a Sony Group's EX assistance app that is adapted to our clinic Self-EX, the patients performed Self-EX at home for 4 weeks. Before and after Self-EX was performed, the 2 groups were compared by our clinic's original FF assessment. [Results] The FF of all 5 patients in the app group improved. The app group's average FF score before and after self-EX were 109.4 and 117.6, respectively, showing a significant improvement (p=0.01), while the control group's were 79.5 and 78.5, with no significant difference. [Conclusions] It is difficult to obtain good effects of Self-EX at home by providing guidance only at clinic, but self-EX using the app at home was effective in improving FF. The app is meaningful to check self-EX at home.

P3-113

Recovery ward patients with rheumatoid arthritis and non arthritis

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Conflict of interest: None

[Objective] The aim of study is to investigate the utilization ratio of recovery ward in RA patients. [Methods] Our recovery ward patients were 201 cases including RA 8 cases 2008 average age 72.5 yrs. 410 cases 2021 including RA 7 cases average 77.9 yrs. We investigated main disease, comorbidity, oral medicine, degree of care at discharge. FIM score. [Results] Comorbidity became increasing in 2021 comparing 2008, especialy, Diabetes and Parkinsonism. The number of oral medicine were increased to 7.2 drugs from 4 drugs. The prevalence of patients with RA at our recovery ward patient was 4‰. Vertebral fracture, femoral neck fracture were more common comparing RA originated arthroplasty. Biologics were used 0 cases at 2008,2 cases at 2021. FIM scores of rheumatoid arthritis patients and non arthritis patients were lower in patients with many comorbidity. [Conclusion] Aging and comorbidity, ex. dementia seriously illness were increased in patients with recovery ward., however, were not increased in patient with RA. Comprehensiveness of hospitalization fee restricted RA admission due to expensive RA drugs, Utilization ratio of recovery ward seems to be low in patients with RA.

P3-114

Development of an objective functional evaluation table for rheumatoid arthritis patients

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Azuma Rheumatology Clinic

Conflict of interest: None

[Introduction] The subjective evaluation batteries are used to evaluate Lifestyle/Activity in rehabilitation (Rehab) for rheumatoid arthritis (RA) patients. To improve physical function, objectively clarify where the declining physical function is required, no objective evaluation battery can be found in the literature so far. Therefore, in our clinic, we attempted to create a "RA function evaluation table (RAFET)" can objectively evaluate the physical functions of RA patients. [Method] Subjects were randomly selected from 14 RA patients who underwent Rehab at our clinic during October 1 to 25, 2022. Average age was 64.57 ± 11.87 years. Measured by a physical therapist based on the "RAFET". In addition, they were asked to answer a self-administered questionnaire that summarizes the evaluation of their existing life and activity functions. [Result] There was a slightly negative correlation (r=-0.35) between "RAFET" and the existing Assessments. When divided into upper and lower extremities, there was a negative correlation for the upper extremities (r=-0.61) and a slightly negative correlation for the lower extremities (r=-0.31). [Discussion] It was suggested that "RAFET" can objectively evaluate declining body function by region in RA patients.

P3-115

Clinical Outcomes of Surface Replacement Arthroplasty for Osteoarthritis of PIP Joint

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Conflict of interest: None

[Objective] Proximal interphalangeal (PIP) joint osteoarthritis (OA) causes significant disorder of activities of daily living (ADL). It is difficult to treat patients with severe PIP joint OA. We evaluated the clinical results of surface replacement (SR) arthroplasty for PIP joint. [Methods] Fifteen patients were studied (9 women, 6 men) with a mean age of 69 years at surgery and the mean follow-up period was 13 months. The operated digits were the index (3 digit), middle (6 digit), ring (4 digit), and little (2 digit) fingers. We underwent implant arthroplasty using a SR prosthesis (Nakashima medical) via volar approach. We evaluated functional and radiological outcome. The parameters evaluated included pain, range of motion, grip strength, Mayo wrist score. [Results] Treatment by SR arthroplaasty resulted in improvement of symptoms in all patients. Clinical results show a satisfactory functional outcome. ROM, and grip strength were improved. [Conclusions] SR arthroplasties are an efficacious treatment for in PIP joint OA and are thus a recommended surgical treatment.

P3-116

Arthrodesis of the distal interphalangeal joints of fingers in a patient with multicentric reticulohistiocytosis: A case report

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Conflict of interest: None

[Objective] We present a case of multicentric reticulohistiocytosis (MRH) in which a disabled distal interphalangeal joint (DIPJ) of a finger was functionally reconstructed via joint arthrodesis. [Case Report] A 41-year-old woman with MRH who had been medicated with disease-modifying antirheumatic drugs orally and bisphosphonate intravenously was referred to our hand surgery unit due to DIPJ instability. A simple X-ray revealed that DIPJs in both hands had been severely damaged, with bony absorption. We performed arthrodesis on all four fingers of her right hand, as well as cortico-cancellous bone graft interposition in two fingers. Two 1.2-mm-diameter Kirschner wires and one 24G intraosseous soft wire were used for internal fixation. At the latest follow-up 10 months postoperatively, complete bony union was observed in an X-ray photograph, and functional improvement in active daily life was achieved due to joint stability. There were no complications from the surgical procedure or the metallic implant. [Conclusions] Arthrodesis in MRH for DIPJ is a promising surgical procedure.

P3-117

A case of Juvenile Idiopathic Arthritis (JIA) who had reconstructive surgeries and rehabilitation for functional disturbances of the hands in a long period passed after the onset

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Conflict of interest: None

[Objectives & Clinical Significance] We aim to report on the importance of rehabilitation which contributed to continuing work and maintaining hand function for the JIA patient. [Case] A female in her thirties was diagnosed as having JIA at the age of 15. After having a diagnosis by pediatrics, she was transferred to rheumatology when she was 23. When a biopharmaceutical had been introduced at 24 the disease activity became stable. However, she interrupted her medication and continued her work which overloaded her joints. Because extensor tendon ruptures on both hands were found when she was around 30, functional reconstruction surgeries were conducted on her right hand at 35 and left hand at 36. She had a five-month-long inpatient rehabilitation after the surgery. Three months after her left-hand surgery her grip strength was increased in right hand (250/242 mmHg) and Disabilities of the Arm, Shoulder and Hand (DASH) score was 31.89. Even though the difficulty increased, the dexterity was improved. She returned to work at 4 months after her left-hand surgery. [Conclusion] It was suggested that the regular evaluations on grip strength and dexterity as well as rehabilitation were significantly useful for patients' maintaining their QOL and continuation of their work.

P3-118

Steroid pulse induces neutrophil extracellular traps in a mouse model of SLE

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Conflict of interest: None

[Objective] Steroid pulse is an essential treatment option for severe cases of SLE, but it affects the coagulation system. In this study, the effects of steroid pulse on neutrophil extracellular trap (NET) formation were determined using a mouse model of SLE. [Methods] Imiquimod (IMQ)-induced SLE model mice were employed. Six of them were given methylprednisolone (mPSL) intraperitoneally on Days 39, 40, and 41. Five were given PBS instead. Six normal mice were given mPSL and another six normal mice were given PBS similarly. NETs in the blood were detected by flow cytometry on Day 56. Proteome analysis was conducted to extract proteins specifically increased in the NETs-positive group. Their effects on NET formation were assessed in vitro. [Results] In the IMQ and steroid pulse-applied group, the leukocyte fraction was more distinct and NETs were significantly increased compared to the other groups. Proteome analysis identified Prenylcystein Oxidase 1 (PCYOX1) as a protein specifically increased in the NETs-positive group. In vitro, PCYOX1 induced NETs via H_2O_2 production. Furthermore, the addition of IMQ and mPSL enhanced the NET formation. [Conclusion] Steroid pulse increased NETs in the IMQ-induced SLE mice, and PCYOX1 could enhance NET formation via H_2O_2 production.

P3-119

Suppression of Toll-like receptor agonist imiquimod induced lupus phenotype by programmed cell death-1

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Conflict of interest: Yes

[Objective] To analyze the functional role of programmed cell death-1 (PD-1) in mouse model of systemic lupus erythematosus induced by Toll-like receptor 7 agonist imiquimod (IMQ). [Methods] After C57BL/6 (WT) mice and PD-1 knock out (KO) mice were treated with topical IMQ for 8 weeks, anti-double strand (ds) DNA IgG in sera were measured by ELISA. 2) Cytokines production from in vitro-stimulated splenic $CD4^+$ T cells isolated from IMQ-treated WT and KO mice was evaluated by flow cytometry (FCM). 3) PD-1 expression in B cell subpopulations was analyzed before and after the treatment of IMQ in WT mice by FCM. 4) IgG production from in vitro-stimulated B cells of WT mice and KO mice was examined by ELISA. [Results] 1) Anti-dsDNA IgG tended to be higher in KO mice compared with WT mice. 2) There was no significant difference in cytokines such as IFNγ, IL-10, IL-17, and IL-21 in CD4+ T cells between WT and KO mice. 3) Expression of PD-1 was up-regulated in germinal center B cells, plasmablasts, and plasma cells after IMQ treatment. 4) IgG production was significantly elevated in KO mice compared to WT mice. [Conclusions] PD-1 expression in B cells might play a role in regulation of lupus phenotype induced by IMQ via the inhibition of autoantibody production.

P3-120

SLE stratification based on BAFF and IFN-I bioactivity for biologics and implications of BAFF produced by glomeruli in lupus nephritis

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Conflict of interest: None

Objective: B-cell activating factor (BAFF) is implicated in systemic lupus erythematosus (SLE) pathogenesis. We identified patients with high BAFF-bioactivity to investigate their clinical characteristics and revealed the association of BAFF and lupus nephritis (LN). **Methods:** We established the reporter cell for BAFF and investigated the clinical characteristics of SLE patients with high BAFF-bioactivity. We identified BAFF-expressing kidney cells using publicly available scRNA-seq data and immunohistological analysis. SLE patients were stratified based on the bioactivity of BAFF and type-I interferon (IFN-I). **Results:** LN patients had significantly higher serum and urine BAFF-bioactivity than healthy controls and non-LN patients. Single-cell-RNA-seq data and immunohis-

tological analysis of kidney samples from LN patients revealed that BAFF is expressed in glomerular macrophages and mesangial cells. Stratification of SLE based on bioactivities of serum BAFF and IFN-I revealed clinical characteristics of BAFF or IFN-I high patients. **Conclusions:** Monitoring urinary BAFF-bioactivity may be valuable in diagnosing LN. Furthermore, stratification based on serum BAFF and IFN-I bioactivities may allow the identification of appropriate patients for two biologics for SLE.

P3-121

Analysis of spinal fluid exosomes in patients with NPSLE

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Conflict of interest: None

[Object] In this study, we analyzed exosomes and cytokines in cerebrospinal fluid in patients with NPSLE. [Method] Measurements of exosomes and IL-6 concentrations in the spinal fluid of patients with NPSLE and other diseases, and IRF activity and NFkB were measured by adding cerebrospinal fluid to THP1 cells. [Result] When the concentration of exosomes and IL-6 in the spinal fluid of NPSLE and other diseases was measured, the concentration of exosomes was significantly higher in NPSLE than in other diseases, but the concentration of IL-6 was not significantly different. In addition, when cerebrospinal fluid was added to THP1 cells and IRF activity was measured, no significant difference was observed, but NFkB activity was significantly reduced dominantly in the NPSLE group compared to other diseases. No significant difference was observed in exosomes, but IL-6 was found to be significantly higher in the focal group than diffuse group. [Conclusion] IL-6 in cerebrospinal fluid in the focal group was higher than in the diffuse group. The focal group has been shown to cause thrombotic angiopathy due to antiphospholipid antibodies and immune complexes, suggesting that elevated IL-6 in cerebrospinal fluid may be the result of thrombotic vascular disease.

P3-122

Investigation of genetic changes in T cells induced by hydroxychloroquine in systemic lupus erythematosus

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) is the anchor drug for systemic lupus erythematosus (SLE), and its mechanism of action has been reported to inhibit the activation of autoreactive T cells by increasing the pH of antigen-presenting cells, and to inhibit TLR function. However, there are few reports that examined it using comprehensive gene expression analysis. [Methods] The subjects were 3 newly diagnosed SLE patients who started treatment with HCQ alone and 3 SLE patients in the maintenance phase who received HCQ to reduce the steroid dose. CD4-positive T cells were isolated using microbeads, RNA-seq was performed, and gene expression before and after HCQ administration was compared. [Results] A total of 46,427 genes in 12 specimens from 6 patients were analyzed, and 40 genes that changed more than twice before and after HCQ administration ($p<0.05$) were extracted. It was suggested that the patterns of gene expression changes were different, and the number of genes that changed in the newly diagnosed group was greater than in the maintenance group. [Conclusions] It was suggested that there may be differences in the pattern of T cell gene expression changes due to HCQ administration between SLE at initial onset and in the maintenance phase of remission.

P3-123

Investigation into characteristics and pathological analysis of patients with RA and SLE who underwent cardiac surgery in our hospital

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Conflict of interest: None

[Objective] The purpose of this study was to know the pathological tissue and clinical features of heart disease associated with RA and SLE. [Methods] 33 of SLE patients, 47 of RA patients and a patient of both RA and SLE who underwent cardiac surgery among patients diagnosed from 2012 to 2021 at our hospital were included. Paraffin sections were prepared for patients who had undergone left atrial appendage resection during surgery, and immunohistochemical staining was performed using anti-human IgG antibodies, compared with histology of non-collagenous disease group investigated. [Results] Average age of RA (R) and SLE (S) were R/S: 70.4/58.4, average disease duration was 15.5/24.0. RF positivity rate was R/S: 85.2/16.7%, anti CCP antibodies rate was 73.3/0%, anti SS-A antibodies rate was 16.7/44.4%, anti RNP antibodies rate was 0/25.9%. IgG deposits were found in the myocardial fibers of 7 of the 8 patients in the SLE complication group, no deposits were found in any RA patients. IgG deposits were found in the myocardial fibers of a patient of both RA and SLE. [Conclusions] The possibility of the onset of immunological mechanism in muscle tissue of heart which were operated may be the cause of heart disease in SLE patients much more than in RA patients.

P3-124

A Case of 4 overlapping cancers during a 3-year course of TIF1 antibody-positive dermatomyositis

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Conflict of interest: None

[Case] A 71-year-old man. He was diagnosed with dermatomyositis based on Godron's sign, elevated CK and aldolase and CRP, and iliopsoas muscle weakness, and anti-TIF1γ antibody was positive. He was a past smokier In September X, PSL 50 mg was started, combined with IVIG, then symptoms and laboratory findings improved. In February X+1, he complained of dysphagia, and was diagnosed as squamous cell carcinoma of the nasopharynx and was treated with radiotherapy. In August X+1, endoscopic submucosal dissection for early-stage esophageal cancer was performed. In October X+1, he was diagnosed with recurrent hypopharyngeal cancer and underwent pharyngolaryngo-esophagectomy. In June X+2, he was diagnosed as a medium-differentiated tubular adenocarcinoma, and a laparoscopic gastrectomy was performed. In June X+3, he had right cervical pain, and was diagnosed with mesopharyngeal carcinoma of the root of the tongue, and cetuximab was administered. During the course, TIF1γ antibody titer wasn't increased. [Clinical Significance] Patients with anti-TIF1 antibody-positive dermatomyositis may develop multiple cancers, even in the absence of cancer at the time of diagnosis, or elevated antibody titers during the clinical course, and should be followed carefully with attention to clinical symptoms.

P3-125

A case of anti-TIF1-gamma antibody-positive dermatomyositis with repeated relapses leading to the diagnosis of right pericoronary B-cell lymphoma by PET-CT

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Conflict of interest: None

A female in her 70s was referred to our hospital for dyspnea on exertion, myalgia and weakness. She was diagnosed with dermatomyositis (DM) with positive anti-ARS and anti-TIF1-γ antibodies. Gastrointestinal endoscopy and enhanced computer tomography (CT) could not detect any malignant tumors. Prednisolone 50 mg and intravenous cyclophosphamide resolved her symptoms. However, intravenous immunoglobulin therapy was added due to dysphagia, interstitial pneumonia, and myositis one month after the diagnosis. Four months after the diagnosis, dysphagia and weakness of the upper arm were observed again, and MRI detected myositis in both the neck and upper arm. PET-CT imaging showed abnormal accumulation around the right coronary artery, multiple lymph nodes and bone regions. Bone marrow examination led the diagnosis of B-cell lymphoma. She was treated with chemotherapy but died due to respiratory failure. Discussion: Because malignant tumors are associated with the disease in 18-80% of patients with anti-TIF1-γ-positive DM, making the search for tumor is important. Non-Hodgkin's lymphoma and pericoronary lymphoma are also very rare. Even when malignancy cannot be identified by the general search, repeated tumor search is necessary in relapsed or refractory cases of DM.

P3-126

A case of anti-TIF1-gamma antibody-positive dermatomyositis following SARS-CoV-2 vaccination

Yuki Desaki[1], Kayoko Tabata[2], Misaki Yasutake[2], Ryo Matsumiya[2], Katsunori Tanaka[2], Nobuo Kuramoto[2], Shigeru Iwata[2], Takao Fujii[2]
[1]Postgraduate Clinical Training Center, Wakayama Medical University, [2]Rheumatology and Clinical Immunology, Wakayama Medical University

Conflict of interest: None

[Case] A 82-year-old man had an itchy skin rash and muscle weakness after the third vaccination of SARS-CoV-2 (BNT162b2). The patient had Heliotrope rash, Gottron's sign, proximal muscle weakness, elevated myogenic enzymes, inflammatory response, myogenic changes on needle electromyogram and positive anti-TIF1-γ antibody, meeting ACR/EULAR2017 classification criteria and MHLW PM/DM diagnostic criteria 2015. The skin tissue showed perivascular lymphocytic infiltrate consistent with dermatomyositis (DM). Comprehensively, we diagnosed anti-TIF1-γ antibody-positive DM. We started treatment with daily prednisolone of 60 mg, and the skin rash and laboratory data were improved. Since muscle weakness remained, we added high-dose immunoglobulin therapy. Until now, he showed no evidence of malignancy. [Discussion] Although new-onset DM including anti-MDA5 antibody-positive cases after SARS-CoV-2 vaccination has been reported, the number of cases is still small. Here, we report a rare case of anti-TIF1-γ antibody-positive DM after the third vaccination of SARS-CoV-2 with no complication of malignancy and discuss with the related literature.

P3-127

A case of paraneoplastic anti-TIF-1gamma antibody-positive dermatomyositis (DM) as immune-related adverse events (irAEs) following administration of pembrolizumab, an immune checkpoint inhibitor (ICI)

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Conflict of interest: None

[Case] A 70-year old man had been diagnosed with prostate cancer and had underwent partial prostatectomy. Gemcitabine/Cisplatin was given for the multiple metastases, which was discontinued due to thrombocytopenia. After the second administration of Pembro 1 months before hospitalization, he experienced pain in both thighs and shoulders and skin rashes on the extensor surface of the fingers, and then he was referred to our department. He was suspected of having DM based on his symptoms, laboratory findings (elevated CK, aldolase, and CRP levels), and myositis of the both thighs on MRI. He was positive for anti-TIF-1γ antibody and the diagnosis was histologically confirmed by the muscle biopsy in which perifascicular necrosis was evident. Prednisolone was started. [Clinical Significance] Anti-TIF-1γ antibody-positive DM is strongly associated with malignancies, but, in the current case, the possibility that his DM was induced by ICI should be considered to decide whether to stop ICI in cases of DM developing after the initiation of ICI, clinician should distinguish two conditions: a new onset disease induced by ICI and a worsening of pre-existing disease. When ICI-induced DM cannot be ruled out, clinicians should discontinue ICI and start the treatment with corticosteroids.

P3-128

A case of anti-TIF1-gamma antibody-positive dermatomyositis associated with renal pelvis and ureter cancer successfully treated with intravenous immunoglobulin

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Conflict of interest: None

A 82-year-old Japanese woman underwent nephroureterctomy for the right renal pelvis and ureter cancer at January X-1. Lung metastasis was detected March X-1, and received chemothrapy. A skin rash appeared in August X-1 and diagnosed with Steven-Johnson syndrome. Methylprednisolone pulse therapy was initiated, followed by administration of prednisolone (PSL) 20 mg/day. However, the patient in October X-1, recurrence of skin rash, facial swelling, myalgia of shoulder girdle muscles and arthralgia gradually appeared, positive for anti-TIF1-γ antibody, and referred to our department. Diagnosis of anti-TIF1-γ antibody-positive dermatomyositis (DM) was made and the recurrence of cancer was highly suspected due to macrohematuria. PSL was administered at 30 mg/day, however, dose escalation to 40 mg/day was required because of inadequate response. Intravenous immunoglobulin (IVIg) was added. Her symptoms were improved, and she was able to reduce PSL. She has had an uneventful course after discharge without recurrence. IVIg seems to be an effective therapy for cancer associated anti-TIF1-γ antibody-positive DM.

P3-129

Evaluation of liver dysfunction during the course of treatment in patients with polymyositis and dermatomyositis

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Conflict of interest: None

[Objective] In patients with polymyositis/dermatomyositis (PM/DM), we experience cases of suspected exacerbation of liver dysfunction despite improvement in CK and aldolase levels. In this study, we retrospectively investigated the presence and severity of liver dysfunction occurring during the course of treatment in PM/DM patients. [Methods] Between December 2017 and October 2021, 28 PM/DM patients (myositis group) and 20 patients with other collagen vascular diseases (control group) who were treated with high-dose steroid therapy were examined for changes in CK and transaminase levels after the initial treatment by comparing ALT/AST and ALT/CK ratios before and after treatment. [Results] Although there was no significant difference in the ALT/AST ratio between the two groups, the ALT/CK ratio was significantly higher in the myositis group than in the control group at 4-8 weeks (P=0.018-0.05) when the rate of increase in the ALT/CK ratio after treatment in both groups was calculated based on the pre-treatment value. [Conclusions] In comparison with other collagen vascular diseases, it was suggested that liver dysfunction due to some unknown mechanism is more often observed transiently in inflammatory myopathies during the course of treatment including high-dose steroids.

P3-130

Clinical study of 16 cases of dermatomyositis/polymyositis complicated with macro-creatine kinase in our hospital

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Conflict of interest: None

[Objective] PM/DM has elevated levels of serum CK due to myositis. But PM/DM often complicates macro-CK, then myositis can be difficult to assess. We studied the clinical features of PM/DM with macro-CK. [Methods] Out of 55 consecutive cases of PM/DM treated in our hospital from Apr. 2017 to Sep. 2022, 20 cases were examined with CK isozymes. Then we retrospectively studied 16 cases complicated with macro-CK. [Results] Of the 16 cases (DM 11, PM 5), mean age was 65 (21-85) years, 12 cases were female. 10 cases had interstitial pneumonitis, 3 cases had dysphagia, and 3 cases had malignant tumors. Other connective tissue diseases were complicated in 3 cases. Hypergammaglobulinemia and hypocomplementemia were complicated in 4 and 3 cases, respectively. Myositis-specific autoantibodies were positive in 8 cases. All cases were treated with prednisolone, and 5 cases received steroid pulse therapy. Immunosuppressive drugs were used in 14 cases. 9 cases were received IVCY, and 2 cases were received IVIG. 1 case died. [Conclusions] Out of 20 PM/DM patients in which CK isozymes were measured, 16 (80%) cases had macro-CK. We should use the combination of blood tests and imaging tests for general evaluation of PM/DM with macro-CK. We also have to perform the test of swallowing and check for cancer.

P3-131

Three cases of adult-onset anti-NXP-2 antibody-positive dermatomyositis

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Conflict of interest: None

We experienced three adult cases of anti-NXP-2 antibody-positive dermatomyositis and report clinical features. [Case 1] 85-year-old woman had muscle weakness in proximal muscles of dysphagia and bilateral PIP, MCP, hand and shoulder joints, edema of hands and feet, and Gottron's sign. CK 728 U/mL, anti-NXP-2 antibody, CD4/CD8 positive. Prednisolone (PSL) 40 mg and methotrexate (MTX) 6 mg/week were started and remitted. [Case 2] 50-year-old male, bilateral PIP, MCP and shoulder joints, myalgia and weakness, CK 623 U/mL, rheumatoid factor, anti-CCP antibody, anti-NXP-2 antibody, muscle biopsy showed positive. PSL 60 mg and MTX PSL 60 mg and MTX 6 mg/week were started and remitted. [Case 3] A 67-year-old woman, who developed muscle pain and weakness in bilateral upper arms and thighs, V-neck sign, and Gottron's sign. CK 1833 U/mL, anti-NXP-2 antibody, muscle biopsy showed positive. PSL 65 mg and MTX 6 mg/week were started, but refractory to treatment and immunoglobulin therapy was started Anti-NXP-2 antibody-positive myositis is associated with distal muscle weakness, interstitial pneumonia, Gottron's sign and heliotrope rash, malignant complication, and response to steroid therapy is good. The PSL response to treatment was good in two patients and refractory in one patient.

P3-132

Clinical features of anti-Mi-2 antibody positive dermatomyositis

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Conflict of interest: None

[Objective] To examine the clinical features of anti-Mi-2 antibody positive patients. [Methods] Newly diagnosed Polymyositis/dermatomyositis (PM/DM) patients who visited Tokai University Hospital and Tokai Hachioji hospital between 2012 and 2022 were screened. Autoantibodies were identified by immunoprecipitation assays and all clinical and immunological data were collected retrospectively. [Results] Of 218 patients with PM/DM, 4 (1.8%) anti-Mi-2 antibody positive patients were identified. All 4 patients were diagnosed as DM and serum creatinine kinase (CK) level of 4 patients were high. No interstitial lung disease or malignancy were detected in all patients. Although the effect of initial treatment with prednisolone (PSL) was good, one patient showed persistent high CK level with a gradual reduction of PSL. [Conclusions] Although the clinical characteristics of anti-Mi-2 antibody positive DM at our hospital were almost the same, the frequency of anti-Mi-2 antibody in DM was lower compared with previous reports.

P3-133

A case of anti-HMGCR antibody-positive immune-mediated necrotizing myopathy successfully treated with intravenous immunoglobulin therapy

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Conflict of interest: None

(Case) A 58-year-old woman who was healthy until one month earlier, when she developed neck and shoulder pain, muscle weakness, and difficulty swallowing. She was referred to our hospital because her CK level was extremely high (9290 u/L). Manual muscle test revealed 2 to 3 in the neck and proximal lim muscles. MRI showed STIR high in the arm. Both anti-ARS and dermatomyositis-specific antibodies were negative. Since needle electromyogram suggested the presence of myositis, muscle biopsy from the left biceps was performed. Steroid pulse therapy was administered, followed by 40 mg of PSL with tacrolimus. Despite the therapy, muscle weakness and dysphagia worsened. Intravenous immunoglobulin (IVIg) was also ineffective. Muscle pathology showed mild inflammatory cell infiltration, whereas severe muscle atrophy and positive anti-HMGCR antibody, leading to the diagnosis of immune-mediated necrotizing myopathy. Despite six weeks of treatment, her condition worsened and developed difficulty walking and eating. Elevation of PSL and addition of methotrexate stopped worsening, although did not improve her condition. We decided to administer second IVIg, which was dramatically effective. After that, she was able to walk again and eat meals without troubles.

P3-134

A case of interstitial pneumonia in a patient with anti-PM-SCl75 antibody-positive dermatomyositis

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Conflict of interest: None

[Introduction] Due to the low prevalence of the related HLA in Japanese, reports of Anti-PM-Scl antibodies positive cases in Japanese are rare. [Case] 57 years old, woman. [History of present illness] Ten months before coming to our hospital, she was found frosted shadows. She was referred to our hospital because of anti-ARS antibodies and mechanic's hands. Diagnosis of anti-ARS antibody-positive dermatomyositis was made. She was negative for anti-Jo1 antibody, and additional test revealed positive for anti-PM-Scl antibody. Treatment was started with prednisolone (PSL) 50 mg/day. After the start of treatment, interstitial pneumonia (IP) markers showed a decreasing trend, and Skin symptoms showed improvement, and the PSL dose was reduced. When PSL was reduced to 20 mg/day, interstitial pneumonia markers worsened, so tacrolimus was added. [Clinical Implications] Although PM-Scl antibody-positive dermatomyositis (DM) is known as a marker of DM with good prognosis with good response to treatment, this case differed from previous reports in that not responsive to treatment after PSL administration and not complicated by scleroderma features. There are a few case reports of anti-PM-Scl antibody-positive DM and IP in Japan. We report this case with some discussion of the literature.

P3-135

2 cases of focal myositis (FM)

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Conflict of interest: None

[Case 1] A 32-year-old female developed self-limiting myalgia and

mass on left lateral thigh. T2 weighted image (T2WI) of MRI showed high signal intensity on left middle gluteus and left lateral great muscle. 3 years later, the same self-limiting symptoms recurred. Inflammatory infiltrates were observed in biopsy specimen of left lateral great muscle. 3 years later, the similar symptoms recurred on right brachioradialis muscle with elevated CK and CRP, high intensity signal on T2WI. The symptoms were persistent, but improved by administration of prednisolone 20 mg/day for 2 weeks. [Case 2] A 78-year-old male developed fever, myalgia and mass on left lateral lower limb with elevated CK and CRP, and T2WI of MRI showed high intensity signal in left peroneus longus muscle. We planned to perform electromyogram and biopsy, but his symptoms were self-limiting. [Discussion] FM is a rare acute localized inflammatory myopathy and often recognized as inflammatory pseudotumor with unknown etiology. Generally, CK and CRP do not elevate in FM, but in some case reports, elevated CK and CRP were observed. Usually, symptoms regress spontaneously, but persistent cases need to be treated. Continuous observation seems to be important in FM because some cases have relapse and progression to polymyositis.

P3-136

Inflammatory myopathy involving the masseter muscle following COVID-19 mRNA vaccination

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Conflict of interest: None

[Case Presentation] An 80-year-old woman presented with a history of fever and fatigue for 3 months soon after receiving the third COVID-19 mRNA vaccination. Her symptoms progressed to jaw pain and inability to open the mouth. She also experienced mild proximal muscle weakness in the lower limbs. CK level was normal. Fat-saturated T2-weighted magnetic resonance imaging (T2-weighted MRI) showed bilateral high-intensity signals for the masseter and quadriceps muscles. A muscle biopsy was planned, but the patient experienced spontaneous resolution of fever and improvement of symptoms 5 months after onset. Since then, the patient has been followed up for 4 months without any recurrence of symptoms or any additional treatment. [Conclusion] According to previous reports, most cases of inflammatory myopathy following mRNA vaccination are similar to cases of idiopathic inflammatory myopathy (IIM) in their clinical features and courses. We report a rare case of transient inflammatory myopathy involving the masseter muscle following the third dose of COVID-19 mRNA vaccination, without creatine kinase (CK) level elevation and skin lesion, which resolved spontaneously 5 months after onset.

P3-137

Human Immunodeficiency Virus (HIV) associated myopathy, A mimicker of idiopathic inflammatory myositis

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Conflict of interest: None

A 58-year-old man presented to our hospital because of myalgia and creatinine kinase (CK) elevation. A year prior to admission (PTA), he had had myalgia on bilateral shoulders and thighs. Six-month PTA, antiretroviral therapy had been initiated after a diagnosis of Human Immunodeficiency Virus (HIV) infection. Three-month PTA, he had had persistent myalgia and CK elevation of 1,000 U/L without muscle weakness. Myositis-specific antibodies had been negative. Antiretroviral therapy had been stopped because of suspected drug-induced myopathy. However, his symptoms had not been abated. He was admitted to our hospital with a-month history of dyspnea and left-hand weakness. A physical examination revealed poor muscle strength in left-hand lumbrical and interosseous muscles. Chest-X ray showed pulmonary congestion. A transthoracic echocardiography revealed ejection fraction of 11%. A endomyocardial biopsy demonstrated severe lymphatic inflammation with myocardial necrosis. We diagnosed the patient with HIV-associated myopathy, followed by acute myocarditis with severe heart failure. HIV-associated myopathy is rare although myalgia is frequently observed during HIV infection. Patients with HIV also exhibit various symptoms like polymyositis and sporadic inclusion body myositis.

P3-138

A case of Aortitis syndrome after SARS-CoV-2 vaccination

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Conflict of interest: None

A 80-year-old women presented with general malaise and back pain in July X. After the second SARS-CoV-2 vaccination in June X-1, erythema with tenderness on her bilateral lower legs appeared one month later, and the same erythema also appeared after the third vaccination. A contrast-enhanced thoracic CT revealed wall thickness with contrast effect (double ring enhancement sign) in the aortic arch, and FDG-PET/CT scan showed FDG accumulation. We diagnosed her with aortitis syndrome and prednisone treatment (30 mg/day) was initiated. But her back pain and elevated C-reactive protein (CRP) levels were not improved. Therefore, we added subcutaneous injections of tocilizumab. Her back pain was disappeared and CRP levels became negative. Wall thickness on aortic arch was also improved and normalized in contrast-enhanced thoracic CT. Discussion: Previous reports have suggested that SARS-CoV-2 vaccination may be involved in the development of various types of vasculitis, including aortitis syndrome. The present case supports these reports, and aortitis syndrome is an important differential diagnosis between unknown fever and inflammation after SARS-CoV2 vaccination.

P3-139

A case of Pegylated G-CSF associated aortitis

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Conflict of interest: None

[Patient] A 71-year-old woman started to receive postoperative chemotherapy for breast cancer from January. In June, she was given pegfilgrastim because of neutropenia due to chemotherapy. A few days after receiving pegfilgrastim, she developed general body pain and fever, and serum C-reactive protein level was elevated. Contrast-enhanced CT revealed wall thickness of the right subclavian artery and descending aorta. She was diagnosed as Granulocyte Colony Stimulating Factor (G-CSF) associated aortitis and was treated with 40 mg/day of oral prednisolone, which improved her symptoms, laboratory findings and wall thickness of the arteries and aorta. Prednisolone was tapered and discontinued without relapsing the aortitis. [Discussion] Aortitis is known to be a rare adverse event associated with G-CSF, but little is known about the pathogenesis, the morbidity and the treatment. Some cases need glucocorticoids while other cases improve without treatment. In our case, glucocorticoid was quickly tapered and discontinued without relapse, which suggested that it may be possible to discontinue glucocorticoids early in G-CSF associated aortitis.

P3-140

Myelodysplastic syndrome complicated with Behçet's disease-like symptoms and Takayasu's arteritis

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Conflict of interest: None

A 73-year-old woman with fever appeared to our hospital in X. A blood test showed granulocytic dysplasia, anemia, and increased platelet count. A bone marrow examination revealed megakaryocytic dysplasia and increased blasts (9%), leading to the diagnosis of myelodysplastic syndrome (MDS). G-band staining method showed no genetic abnormalities including trisomy 8. A few days after starting azacitidine and prednisolone (PSL) 10 mg for MDS, polyarthralgia, erythema nodosum-like rash and uveitis appeared. A CT scan revealed wall thickening of the thoracic aorta and HLA-B52 antigen was positive. She was diagnosed with Behçet's disease-like symptoms and Takayasu's arteritis associated with MDS and treated with colchicine 1 mg and PSL 40 mg (1 mg/kg). After the initiation of treatment, the clinical manifestations were ameliorated. Thus, PSL was tapered, however, the inflammatory response recurred in X+2. Tocilizumab (TCZ) was added to intensify treatment, and remission of symptoms was achieved. MDS is known to be associated with a variety of autoimmune diseases, whereas its complication with Behçet's disease-like symptoms and Takayasu's arteritis is rare. Here, we report the case, in which PSL, colchicine and TCZ successfully led to remission, with some literature review.

P3-141

Large-vessel giant cell arteritis in a patient undergoing treatment for renal abscess

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Conflict of interest: None

A 71-year-old woman was admitted to our hospital because of lumbago and fever. On admission, her laboratory examination showed moderate leukocytosis and elevation of her serum C-reactive protein (CRP) levels. Contrast-enhanced CT showed a right cystic renal mass which had heterogeneously low attenuation. We treated for her a renal abscess with antibiotics for two weeks. However, her fever persisted and serum CRP was not improved. Contrast-enhanced MRI revealed a remission of right renal abscess and hyperintense lesions on Fat-Saturation T1 weighted image and diffusion weighted image in the aortic wall. Temporal artery ultrasonography showed no abnormality. We diagnosed her as large-vessel giant cell arthritis (LV-GCA) and initiated with oral prednisolone (40 mg/day). Her fever subsided and serum CRP values became negative. At our outpatient clinic, she was treated with addition of tocilizumab and tapering off prednisolone without relapse. GCA is a systemic vasculitis of large and medium-sized arteries. Two main phenotypes of GCA (cranial GCA and/or large-vessel GCA) are distinguished. Patients with solitary LV-GCA often present with non-specific signs and symptoms. We herein report a case of solitary LV-GCA in a patient undergoing treatment for renal abscess.

P3-142

A case of giant cell arteritis with lack of characteristic subjective symptoms

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Conflict of interest: None

The patient was an 83-year-old man. Due to diabetic nephropathy, dialysis was introduced in year X-5. A blood test in April of year X showed an elevated CRP of 18.34 mg/dL, and he was referred to our hospital. He was suspected of having a bacterial infection, and treated with antibiotics. Body temperature is 36.4 degrees. He had a mild occipital-forehead headache, and his temporal artery was palpable, but no temporal artery tenderness was noted. He had no jaw claudication nor extremity arthritic symptoms and stiffness. He had few symptoms of vasculitis, but PET-CT examination showed hyperuptake along temporal arteries and hyperuptake along bilateral vertebral arteries. He underwent a right temporal artery biopsy, which showed luminal stenosis due to thickening of the temporal artery wall and inflammatory cell infiltration in the media of the artery wall. The internal elastic lamina was torn, confirming the presence of multinucleated giant cells, and he was diagnosed with giant cell arteritis (GCA). He started oral prednisolone 30 mg. After starting prednisolone, CRP decreased and prednisolone was tapered. In this case, mild occipital and forehead pain were noted, but there were no characteristic findings of GCA, such as jaw claudication, joint pain or stiffness in the extremities.

P3-143

A case of Crohn's disease with prolonged inflammation and acutely complicated aortic regurgitation

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Conflict of interest: None

Case: A 47-year-old woman was diagnosed with Crohn's disease and was treated with 5-ASA. Blood tests showed fluctuations in CRP values, however the cause was unknown. In January 202X, she was hospitalized with acute epiglottitis and treated with antimicrobial agents and glucocorticoids. After tapering off glucocorticoids, the epiglottitis did not flare up again. However, in June 202X, she complained of shortness of breath and weight gain, and a new diastolic murmur was detected. Transthoracic echocardiography revealed severe aortic regurgitation (AR), then she was admitted. Gastrointestinal endoscopy revealed no active Crohn's disease. Contrast-enhanced CT showed wall thickening of the aorta with contrast effect, and HLA-B52 and HLA-B67 were detected. She was diagnosed as Takayasu arteritis, and prednisolone (PSL) 0.8 mg/kg/day was started in combination with methotrexate and TNF inhibitor. Discussion: Patients with Takayasu arteritis with HLA-B52 have been reported to have severe AR, and AR is also known to be an extraintestinal manifestation of Crohn's disease. We considered acute AR to be caused by Takayasu arteritis or Crohn's disease. In patients with IBD with a prolonged inflammation, the complications of aortitis and the occurrence of acute AR would be carefully monitored.

P3-144

Ultrasonography in the early diagnosis of giant cell arteritis

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Conflict of interest: None

A previously healthy 65-year-old woman presented with one month history of polyarthralgia and subtle temporal/occipital headache without visual symptoms or jaw claudication. Physical examination revealed no temporal tenderness. Blood tests revealed elevated inflammatory markers, and negative rheumatoid factor, anti-CCP antibody, and ANCA. Ultrasonography of temporal artery was unremarkable, and the patient was diagnosed with polymyalgia rheumatica (PMR). Prednisolone 15 mg daily ameliorated her symptom. Seven weeks later, jaw claudication developed, and repeat ultrasonography revealed halo and compression signs. Temporal artery biopsy confirmed giant cell arteritis (GCA). Prednisolone was increased, and tocilizumab was added. GCA complicates 5-30% of patients with PMR. Early diagnosis of GCA is essential to prevent serious complications. Ultrasonography is simple and reliable for the screening of GCA. Reevaluation of GCA is vital in cases of poor response to steroids.

P3-145

A case of Takayasu arteritis localized to the pulmonary artery

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Conflict of interest: None

[Case] A 74-year-old female presented to our hospital with weight loss and persistently elevated CRP levels. No fever, skin rash, or other symptoms except mild palpitations on exertion. No specific findings on physical examination. Blood tests showed elevated inflammatory reaction. Positive

for ANA, negative for anti-ds-DNA antibodies, and negative for ANCA. Plain CT showed no findings, and PET-CT revealed inflammatory findings in the arterial wall of the aortic arch and pulmonary arteries. Vascular ultrasound showed no wall thickening in the same area, and contrast-enhanced CT showed mild wall thickening in the pulmonary arteries. We diagnosed Takayasu arteritis and started treatment with PSL 30 mg/day. Palpitations on exertion resolved quickly, and CRP became negative. [Clinical Significance] Takayasu arteritis causes inflammatory wall thickening of the aorta and its primary branches, but rarely does it cause wall thickening of the pulmonary arteries only. The case presented with nonspecific symptoms, which were difficult to detect by conventional examinations such as plain CT, vascular ultrasound, and echocardiography. PET-CT was useful for diagnosis.

P3-146

A case of scurvy: one of vasculitis mimickers even today

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Conflict of interest: None

[Case] The patient is 28-year-old man. One month before the visit, he noticed increasing petechial purpura on his lower leg. Two weeks before, he developed lower leg pain. He was suspected to have vasculitis because of the rash and was referred to our department. On physical examination, purpura was limited to around hair follicles. There were corkscrew hairs on lower legs. MRI showed a hematoma in the left gastrocnemius fascia. Based on physical examination, scurvy was suspected. Detailed medical interview clarified that he had been eating only white rice, natto, and eggs for a long time, and had not eaten raw vegetables or fruits for more than six months. His serum ascorbic acid concentration was less than 0.2 mcg/ml, and a definite diagnosis of scurvy was made. In addition, he had carnitine, vitamin B12 and zinc deficiency. Oral supplementation of these nutrients and nutritional guidance successfully treated his symptoms. [Discussion] Various symptoms including fatigue, anemia, myalgia, bleeding tendency and purpura make scurvy a mimicker of vasculitis. It has been pointed out that not a few people today may be potentially vitamin C deficient. It can be diagnosed with a detailed interview and physical examination and should be considered as a differential disease of vasculitis.

P3-147

Immunopathological feature of vasculitic myopathy

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Conflict of interest: None

[Objectives] We investigated the immunopathological features of musculoskeletal tissues in patients with myopathy related to small- or medium-sized vasculitis (VM). [Methods] Biopsied specimens of musculoskeletal tissues from 15 patients with VM and 14 patients with immune-mediated inflammatory myositis (IIM) were stained with anti-CD56, anti-C5b-9, and anti-MHC-Class I antibodies. Frequencies of their expressing muscle fibers were compared between patients with VM and IIM. [Results] Frequencies of CD56 and MHC-Class I expressing muscle fibers were significantly lower in patients with VM than in those with IIM. C5b-9 expressing muscle fibers was hardly displayed in patients with VM despite not being significantly different from those with IIM. [Conclusions] VM can be characterized as having less irreversible damage to muscle fibers than IIM. Neither MHC-Class I interaction nor membrane attack complex may be implicated in the development of VM.

P3-148

Four cases of suspected vasculitis following SARS-CoV2 vaccination

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Conflict of interest: None

[Objective] This study aimed to identify characteristics of the clinical manifestations and MRI findings in four cases of suspected vasculitis following SARS-CoV2 vaccination. [Methods] We investigated retrospectively the clinical manifestations and MRI findings in four patients with suspected vasculitis following SARS-CoV2 vaccination. [Results] The patients were 3 females and 1 male, the average age being 75.3 years. Two patients had a medical history of autoimmune disease, one had Sjögren's syndrome and the other had palmoplantar pustulosis. The average number of SARS-CoV2 vaccinations was 3.25. The period from the last SARS-CoV2 vaccination to the onset of clinical symptoms was approximately 10 days in two cases and 6 months in two cases. Patients had arthralgia and either lower leg pain or reticulocytosis. A laboratory examination showed elevated serum levels of MPO-ANCA in three of four patients. PR3-ANCA was negative in all cases. Short inversion-time recovery image of lower legs showed dot-like high signal intensity in the muscles, suggesting vasculitis. Three patients were self-limiting, and one patient was treated with prednisolone. [Conclusions] We experienced four cases of suspected vasculitis of lower legs following SARS-CoV2 vaccination.

P3-149

The clinical features and long-term prognosis of vasculitis confined to muscle: a retrospective observational study

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Conflict of interest: None

[Objective] To clarify clinical features and long-term prognosis in vasculitis confined to muscle. [Methods] We retrospectively reviewed hospitalized patients with vasculitis confined to muscle between January 2004 and September 2022. [Results] We included 36 patients with no organ involvement of vasculitis other than skeletal muscle. The mean age was 70.9±17.0 years. Thirty-three patients (91.7%) had fever, 32 (88.9%) had myalgia, 23 (63.9%) had arthralgia, and 22 (61.1%) had weight loss. Twenty-one patients (28.3%) were ANCA-positive (ANCA+), all with MPO-ANCA. ANCA+ patients were significantly underweighting (49.9±8.65 kg vs. 57.6±12.3 kg, p=0.035) and had significantly more weight loss and respiratory underlying conditions (16/21 vs. 6/15, p=0.041; 16/21 vs. 3/15, p=0.002). The mean initial dose of prednisolone at induction therapy was 34.6±11.1 mg. Thirteen patients relapsed during the observation period. The Cox proportional hazards model showed that ANCA+ was a possible risk factor for relapse (HR 3.778 [1.032-13.82], p=0.045), and the 5-year cumulative relapse rate was significantly higher in the ANCA+ group (log-rank test, p=0.031). [Conclusions] ANCA may be a risk factor for relapse in patients with vasculitis confined to muscle.

P3-150

A case of fever and multiple ruptured aneurysms after COVID19 infection, which was suspected to be vasculitis but turned out to be Ehlers-Danlos syndrome

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Conflict of interest: None

33-year-old male. He was admitted to the hospital with fever and left-sided abdominal pain. He was turned out to be COVID19 positive, and splenic artery dissection was confirmed by CT and underwent IVR coiling. And 12 days after A8 pseudoaneurysm of the liver ruptured and coiling

was performed by IVR. And on CT abnormal vessels were found in the right internal carotid artery, right vertebral artery, gastroduodenal artery aneurysm, left lingual artery pseudoaneurysm, left rectus abdominis intramuscular hematoma, right shallow artery, and lumbar artery. On suspicion of vasculitis, he was started on betamethasone 20 mg/day, and was transferred to our hospital. When he admitted to our hospital, he had no fever and no subjective symptoms. Pathological examination of the right shallow temporal artery revealed no inflammatory cell infiltration, no loss of elastic fibers, and no tears. With the patient's consent, we performed a genetic search and confirmed the COL3A1 gene mutation. Steroids were discontinued at an accelerated pace, but the patient did not show any increase in inflammatory response or subjective symptoms, and was discharged from the hospital without any worsening of the vascular lesions.

P3-151

A case of hypocomplementemic urticarial vasculitis (HUV) with purpura which appeared after various symptoms disappeared

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Conflict of interest: None

[Case] A 75-year-old woman noticed difficulty opening bottles in the spring of the year, lower leg edema, and shoulder pain on both sides in September. She was referred to our hospital because of fatigue and fever. Anti-nuclear antibody, anti-double-stranded DNA antibody, and rheumatoid factor were positive. C4 level was slightly low. CRP was 3.27 mg/dL. She was admitted to our hospital. Musculoskeletal ultrasonography did not reveal tenosynovitis, and articular pain resolved itself. CT scan detected pleural effusion on the left lung, but it vanished five days later. During hospitalization, she had no fever, and her leg edema was reduced. One week after hospitalization, she recognized purpura with pruritus on both lower legs. A skin biopsy was performed the next day, and the purpura disappeared within two days. Pathological findings were as follows; Perivascular infiltration of neutrophils, eosinophils, and lymphocytes at the subpapillary layer and upper reticular dermis. Nuclear dust and erythrocyte leakage were consistent with leukocytoclastic vasculitis. She was diagnosed with HUV. [Clinical Implications] In spite of almost normal complement levels, the patient had systemic manifestations. A skin biopsy was essential to make a diagnosis. We discuss the pathophysiology of HUV.

P3-152

A case of eosinophilia in a maintenance hemodialysis patient required differentiation of eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

The patient was diagnosed with minimal change nephrotic syndrome in childhood and has been treated with PSL since then. Maintenance hemodialysis was introduced in February X. He was diagnosed as bronchial asthma by pulmonologist due to cough and result of respiratory functional test and treatment was started. After that, the increase in eosinophils did not improve, and fever was also observed, so he was referred to our department. The possibility of EGPA was suspected, but there were no other significant symptoms, and an increase in eosinophils associated with hemodialysis was suspected. So we changed nafamostatmesilate to heparin. After that, a decrease in eosinophils was observed, and we diagnosed eosinophilia due to allergy to nafamostatmesilate. This is a case in which a significant increase in eosinophils was observed, and it was a rare case, so we report it.

P3-153

A case of T-cell lymphoma during treatment of cutaneous polymyalgia nodosa with a history of erythema nodosa and polymyalgia rheumatica

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Conflict of interest: None

We report an 80-year-old woman who has a history of erythema nodosum and polymyalgia rheumatica (PMR) 4 years ago. She was in remission with having been taken oral steroids for about 1 year. She was developed arthritis of wrists, swelling of fingers, and edema of lower legs. Skin biopsy showed vasculitis with infiltration of eosinophils. We suspected eosinophilic granulomatosis with polyangiitis. Steroid made improved the skin lesions, but steroid reduction worsened them. Angiography of the forearm revealed multiple small aneurysms. Although there is no pathological findings, we diagnosed cutaneous polyarteritis nodosa (PAN). The lesion of her fingers improved with intravenous cyclophosphamide. On the other hand, she had intermittent fever and persistent positive CRP. Antibiotic therapy was ineffective. After that, her cervical lymph nodes became enlarged. CT imaging revealed enlarged lymph nodes all over the body. Lymph node biopsy revealed T-cell lymphoma. We experienced a case of T-cell lymphoma that developed during treatment of erythema nodosum, PMR, and PAN. Malignant lymphomas can present with a spectrum of immune abnormalities. Sometimes immunosuppressive therapy can mask the development of lymphoma. We report the pathogenesis of this case with a review of the literature.

P3-154

A Case of Sjögren's Syndrome with NMOSD Triggered by Pneumonia

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Conflict of interest: None

A 63-year-old woman with Sjogren's syndrome and rheumatoid arthritis received regular treatment at this hospital. She had a fever in the low 37's since December 6, X. On December 8, she visited her local doctor's office. He was prescribed an antipyretic (Kalonal), but there was no improvement. On December 9, he had numbness and malaise in both hands and fingers, so he visited his doctor on December 10. There were no significant neurological findings, but a CT scan showed pneumonia in the right lower lung, so the patient was hospitalized and started antibiotic therapy (CTRX) for pneumonia. The next day, dysuria appeared, followed by worsening numbness in the groin and lower limbs. MRI showed T2 high signal area over Th4-L1, and the patient was referred to the Department of Neurology with suspicion of transverse spondylitis. The patient was diagnosed as having neuromyelitis optica syndrome (NMOSD), since no optic neuritis was found and blood tests were positive for anti-aquaporin 4 antibodies. The neuropathy improved with high-dose steroid therapy and endoxan infusion. There is little evidence that endoxan is effective for NMOSD, and anti-aquaporin 4 antibodies may be useful in differentiating NMOSD from NPSLE.

P3-155

Primary Sjögren's syndrome. Types and frequency of osteoarticular symptoms Part 2

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Conflict of interest: None

[Introduction] Sjögren's syndrome is an autoimmune disease that can cause lesions that span multiple organs. In ESSDAI, there are activities measurement items distributed in at least 10 organs. Joint symptoms are one of them. However, we believe that the survey report on the frequency and content of joint symptoms focused on primary Sjögren's syndrome (pSS) is still insufficient. [Purpose] We aimed to dig deeper into these cases and analyze them. [Methods] Patients with pSS visiting our hospital were included. Osteoarticular symptoms, specifically synovitis and ten-

donitis that can be confirmed by ultrasonography of the joint, were extracted from the medical record. [Results] Of the 60 patients with pSS, 24 had positive ultrasonography examination, of which 12 had persistent arthritis. Three of these cases were thought to have transitioned to RA, but unlike normal RA, treatment was not progressive and treatment could be discontinued in the middle. Nine other patiens did not overlap RA. Many indicated tendonitis. [Conclusion] The transition from pSS to RA was rare. Furthermore, we concluded that both arthritis and tendonitis persisted for a long time but were transient in the end, and that these points were characteristic of arthritis and tendonitis associated with pSS.

P3-156

A 90-year-old woman with Sjögren's syndrome with complex neuropathy

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Conflict of interest: None

[Case] A 90-year-old woman. She was able to do housework and care for her husband by herself. Four months before her first visit, she felt discomfort in her toes. She consulted an orthopedist and a dermatologist without pointing out abnormality. Two months before her first visit, she began feeling unsteady and gradually developed weakness and difficulty walking. She had Raynaud's phenomenon and electric shock pain in the lower extremities. On her first presentation, she was positive for an anti-SS-A antibody, Schirmer's test, and lip biopsy, and we diagnosed her with SS. We consulted a neurologist regarding neurological disorders. Lumbar spine MRI revealed nerve root symptoms associated with lumbar spondylosis. A nerve conduction velocity test and somatosensory evoked potential test showed complex neuropathy, including peripheral nerves of the right lower extremity, lumbar plexus, and central disorder. We diagnosed her with neuropathy associated with lumbar spinal canal stenosis and restless leg syndrome in addition to SS neuropathy. Pregabalin and pramipexole made her symptoms improve. [Clinical Interpretation] SS neuropathy treatment depends on the disorder's mechanism, so it is crucial to make an accurate diagnosis.

P3-157

Effectiveness of dual B-cell targeting therapy for TAFRO-like Sjogren syndrome

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Conflict of interest: None

[Introduction] TAFRO syndrome is a subtype of multicentric Castleman's disease, and is characterized by thrombocytopenia, cavernous fluid, myelofibrosis, hepatosplenomegaly, and enlarged lymph nodes. [Case] 65-year-old male [Disease course] He had progressive hearing loss since X-1 year prior to admission. X-1 month, he had fever, lower leg edema, and abdominal fullness, and he visited his previous general hospital. CT scan showed lymphadenopathy, massive pleural effusion, and ascites, and left adrenal infarction. Blood test revealed inflammatory response, severe thrombocytopenia, high antinuclear antibody (x1280 Ho/Sp), anti-DNA, and anti-SS-A/SS-B antibody. Despite high-dose steroids and intermittent platelet infusion, his anasarca and thrombocytopenia did not improve. Bone marrow biopsy revealed fibrosis and megakaryocytes. Considering TAFRO syndrome, we initiated steroid pulse therapy and rituximab. He still had refractory thrombocytopenia, so we added subcutaneous belimumab. He showed gradual improvement in consciousness and hearing loss. [Conclusion] In this case, an autoimmune mechanism was assumed. There is less consensus about treatment protocol for TAFRO syndrome, but dual B-cell targeting therapy could be a successful option for steroid-resistant patients.

P3-158

Characteristics of IgG4-Related Disease with Hypocomplementemia

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Conflict of interest: None

[Object] Hypocomplementemia frequently occurs in IgG4-related disease (IgG4-RD). We examined the characteristics of IgG4-RD with hypocomplementemia. [Method] We analyzed 82 patients diagnosed IgG4-RD in our facility. We compared patients who decreased either C3 or C4 (HC group) with the others (non-HC group). Laboratory data and clinical course were analyzed from their medical records retrospectively. [Results] Thirty one patients in the HC group, 30 patients in the non-HC group. Compared to the non-HC group, the HC group had lower hemoglobin level and platelet count. The HC group also had higher serum IgG4, IgG and sIL-2R. In cases followed for more than 1 year, 18/22 patients in the HC group required treatment, while 14/21 in the non-HC group. Recurrence rates were 7/18 in the HC group and 8/14 in the non-HC group. Three patients of the HC group and 1 patient of the non-HC group died during the course. [Conclusion] Compared to the non-HC group, the HC group tended to have lower blood cell counts and higher levels of IgG4. Because the HC group had more cases requiring treatment and more deaths than the non-HC group, this study suggested the HC group may have poor prognosis.

P3-159

Onset of IgG4-related retroperitoneal fibrosis under administration of TNF inhibitor in a rheumatoid arthritis patient

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Conflict of interest: None

[Case Report] Retroperitoneal fibrosis (RPF) is a disease in which idiopathic inflammation spreads around the abdominal aorta, iliac arteries and ureter, and sometimes cause hydronephrosis and postrenal renal failure. IgG4-related disease may show the appearance of systemic inflammatory disease with various organ damage such as thyroid gland, salivary gland, and kidney. The etiology isn't yet elucidated, but glucocorticoid is the standard treatment for RPF. Recently, successful treatment with TNF inhibitors have been reported. However, it remains uncertain whether TNF inhibitor is effective to RPF. We experienced a case of IgG4-related RPF with periaortic inflammation, hydronephrosis, and postrenal renal failure in a patient with rheumatoid arthritis while using a TNF inhibitor. [Clinical Significance] This report is a rare case in which inhibition of TNF may have pathogenic roles in IgG4-related RPF as a paradoxical reaction, providing important suggestions for considering the etiology, pathophysiology, and treatment of IgG4-related RPF.

P3-160

A case of retroperitoneal fibrosis requiring differentiation from IgG4-related disease during administration of a tyrosine kinase inhibitor

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Conflict of interest: None

[Case Presentation] A 63-year-old male was diagnosed as having chronic myelogenous leukemia (CML) in X-3 year. He was treated with nilotinib, a tyrosine kinase inhibitor (TKI), and CML was well controlled. In May X year, his back pain occurred and CT showed mass around the left common iliac artery. IgG4 and sIL-2 receptor were within normal range and anti-nuclear antibody, MPO-ANCA and PR3-ANCA were negative. Fibrous tissue was predominant with little inflammatory cells. IgG4/IgG

positive cells ratio was less than 40%. Nilotinib related retroperitoneal fibrosis (RPF) was suspected and prednisolone (PSL) was started. His back pain improved. PSL was gradually tapered to 1 mg/day in two years. [Discussion] Three cases of TKI related RPF have been reported. We summarized 3 cases and ours. The patients were all male, aged 11-63 years, and the duration from start of TKI to detection of RPF was 12-41 months. In one patient who stopped TKI, RPF was reduced in size. In two patients who continued TKI and PSL, one improved, and one remained unchanged. The course of the other patient was unknown. TKI related RPF can be improved by discontinuation or PSL. [Clinical Significance] It is important to know TKI related RPF can occur, which should be differentiated from IgG4-related diseases.

P3-161

A case of IgG4-related disease with a dissecting aneurysm of the intracranial vertebral artery

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Conflict of interest: None

[Case] 3 years ago, a 62-year-old man had a plain brain MRI that incidentally revealed a dissecting aneurysm of the intracranial vertebral artery (VA) and enlarged lacrimal glands, and was followed up at the neurology center. This time, a contrast-enhanced CT scan for a gastric tumor revealed aortitis/periaortitis in the abdominal aorta and multiple poor contrast areas in the kidneys, and he was referred to our department. Since we observed submandibular gland enlarged, hyper IgG4emia and marked IgG4-positive plasma cell infiltration in salivary gland tissues, we diagnosed IgG4-related disease (IgG4-RD). Also, contrast-enhanced head MRI and CT showed aortitis/periaortitis and worsening of aneurysm diameter in the VA. Prednisolone 40 mg was started, resulting in rapid improvement of their aortitis/periaortitis and renal lesions. [Discussion] Aortitis/periaortitis in IgG4-RD occurs in large vessels of the thorax and abdomen, but has not been reported in the VA. Because asymptomatic dissection or aneurysm resulting in stroke can occur, it is suggested to include not only the trunk but also the head in the evaluation of IgG4-RD. In addition, when lacrimal gland enlargement is seen along with vascular lesions on head MRI, vascular lesions due to IgG4-RD should be considered.

P3-162

A case of laryngeal polyp with suspected relation to IgG4-positive cells

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Conflict of interest: Yes

21-year-old female was referred to the otorhinolaryngology department with a chief complaint of hoarseness. Bilateral raised lesions were observed in arytenoids, and laryngeal polypectomy was performed. Granulation tissue with aggregation of plasma cells including IgG4-positive cells was observed histologically. Serum IgG4 level was only mildly elevated, and no other lesion suspected of IgG4-related disease was present. One month after, raised lesions reappeared and increased, and oral administration of glucocorticoid was started to avoid reoperation. Although one lesion disappeared, the other was slightly reduced of size and was re-excised 15 months after the first operation. [Clinical Significance] It was very rare course that laryngeal polyps reappeared and increased in short period of time. And the relation to IgG4-positive cells could not be denied histologically. Since there are few reports of laryngeal lesions associated with IgG4-related diseases, we report this case with a review of the literature.

P3-163

A case of the serum IgG4 negative IgG4-related disease with a cardiac mass

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Conflict of interest: None

[Case] A 65-year-old woman with chest discomfort, back pain and complete atrioventricular block was referred to our hospital. Chest auscultation detected systolic and diastolic murmurs in the aortic valve region. Echocardiography showed a mass measuring 38 mm×24 mm in the aortic valve to left atrium. 18F-FDG-PET/CT showed a high accumulation in the cardiac mass and anterior mass of 12th thoracic vertebra and both side on the lung apices. A biopsy of the anterior mass of 12th thoracic vertebra showed lymphoplasmacytic infiltration and fibrosis. IgG4-related disease (IgG4-RD) was suspected, and immunostaining was performed. Although the IgG4/IgG ratio was less than 40%, IgG4-positive cells were more than 10 per field of view at high magnification. Serum IgG4 was 61.8 mg/dL, within normal range. Based on the 2019 ACR/EULAR IgG4-RD classification criteria, she was diagnosed with IgG4-RD. She was treated with prednisolone and rituximab, and then the mass shrank. [Discussion] IgG4-RD rarely presents with a cardiac mass. As far as we searched, there were 14 cases. Among them, there was only one case of serum IgG4-negative, and this case was an extremely rare. [Conclusion] Combination glucocorticoid and rituximab therapy may be effective for IgG4-RD with a cardiac mass.

P3-164

A case of IgG4-related disease (IgG4-RD) diagnosed 8 years after resection of a pancreatic tail mass with pericoronary arteritis and pericardial effusion

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Conflict of interest: None

Case: A 77-year-old man with a pancreatic tail mass and mild pericardial effusion was found on computed tomography (CT) in (X-8) year, and he was performed resection of the pancreatic tail. In June of X year, a follow-up CT incidentally showed thickness of pericoronary artery tissue and increased pericardial effusion. He had no symptoms and serum CRP was 0.30 mg/dL, but serum IgG4 was high as 934 mg/dL. Additional immunostaining of pancreatic tissue at X-8 years showed 160 IgG4 positive cells/HPF and IgG4/IgG positive cell ratio of 73%, compatible for IgG4-related disease. Coronary angiography showed significant stenosis, but antiplatelet agents was chosen instead of stenting considering the risk. Initiation of treatment with PSL 20 mg and azathioprine 50 mg gradually improved both pericoronary arteritis and pericardial fluid. Discussion: Although pericoronary arteritis is a potentially fatal complication of IgG4-RD, they often lack chest pain, heart failure symptoms, or elevated CRP. This case with IgG4-related pericoronary arteritis was incidentally diagnosed as IgG4-RD by CT 8 years after the onset of his undiagnosed pancreatic mass. We consider it worth to report in the point that they show a natural course of untreated IgG4-RD where pericoronary arteritis silently progressed.

P3-165

A Case of abdominal aortic aneurysm associated with IgG4 related disease

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Conflict of interest: None

[Case] A 70-year-old man was referred to our department for increasing total protein, albumin/globulin ratio, serum IgG4 level, and abdominal aortic aneurysm (AAA) on computed tomography (CT). He had a history of tabacco abuse, hypertension, hyperlipidemia and borderline diabetes. The patient denied any active symptoms. Physical examinations revealed no abnormal findings. The serum level of IgG and IgG4 concentration were increased to 2521 mg/dL and 308 mg/dL, respectively. Enhanced contrast CT revealed a 57 mm dilatation of the abdominal aorta, but there were no sign of peri-aortitis or retroperitoneal fibrosis. He underwent a surgery for an AAA. An aorta pathology demonstrated plasma cells and lymphocytes infiltrate involving the adventitia, fibrosis and increased number of IgG4/IgG ratio (79.5%). Based on these findings, he was diagnosed with IgG4 related AAA. Postoperative positron emission tomography-CT scan demonstrated intense FDG avidity of abdominal aortic wall. Therefore, treatment with low-dose prednisolone was initiated. A 6-months follow up, repeat CT revealed reduction of the aortic wall thickening. [Clinical Significance] We reported a case of IgG4-related AAA that was difficult to distinguish from an atherosclerotic AAA.

P3-166

A case in which CT-guided biopsy led to the diagnosis of non-Hodgkin's lymphoma, although IgG4-related disease was suspected from the imaging findings

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Conflict of interest: None

[Case] A 70-year-old man [CC] back pain [Present illness] He became aware of back pain and visited local physician, but symptoms didn't improve. He was referred to our hospital for close examination of periaortitis and retroperitoneal fibrosis (RF), including IgG4-related diseases (IgG4RD) after CT scan. Blood tests showed no hyper IgG4emia. A contrast-enhanced CT scan showed soft-tissue shadows around the aorta, pancreas, and paravertebral body, and FDG-PET scan showed abnormal FDG accumulation in the same areas and in the bones. A CT-guided biopsy of the periaortic soft tissue showed no IgG4-positive cells, storiform fibrosis, or phlebitis obliterans, leading to the diagnosis of malignant lymphoma. [Consideration] Although there was no hyper IgG4emia or swelling of the lacrimal or salivary glands, we suspected IgG4RD because of periaortitis, RF, and a capsule-like lim enhancement of pancreas. However, there were several findings suggestive of lymphoma in the retrospective view, including abnormal accumulation of FDG in bone, and M-proteinemia, which could not be explained by IgG4RD. There are reports of lymphoma presenting with periaortitis and RF, which is an important differential disease for IgG4RD, we report with a literature review.

P3-167

A case of IgG4-related lymphadenopathy localized in lymph nodes and literature review

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Conflict of interest: None

Case: A 65-year-old male underwent surgery and postoperative chemoradiotherapy for mid-pharyngeal cancer twelve years ago, resulting in no recurrence or metastasis. Six years later, CT scan revealed 1 cm of a left axillary lymph node. Seven months before consulting us, it had grown to 4 cm in diameter, and subsequent FDG-PET/CT showed delayed phase accumulation suggestive of malignancy, prompting a biopsy. No malignant findings were found, but a CD138-positive plasma cell infiltrate was noted (IgG4-positive >10 cells/HPF, IgG4/IgG ratio about 40%). Serum IgG4 was elevated (376 mg/dL), but there were no masses or thickened lesions other than the lymph nodes. He started to have oral prednisolone 40 mg/day with a tentative diagnosis of IgG4-related lymphadenopathy. The left axillary lymph node quickly diminished and the serum IgG4 levels normalized. Six months after treatment, it was tapered to 10 mg/day, but no recurrence was observed. Clinical Significance: We report a rare case of IgG4-related lymphadenopathy restricted to lymph nodes, which developed during long-term follow-up after treatment of a patient with mid-pharyngeal cancer. IgG4-related disease is frequently associated with lymphadenopathy, but lymph node involvement alone is considered extremely rare.

P3-168

Spontaneous Benign Pneumoperitoneum in a Patient with IgG4RD

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Conflict of interest: None

We report a case of spontaneous benign pneumoperitoneum in a patient with IgG4RD in whom there was no evidence of either visceral perforation nor of pneumatosis cystoides intestinalis. A 50-year-old woman with 7-years history of Mikulicz's disease / IgG4RD was admitted to our hospital to study an incidental subphrenic free gas on a chest X-ray during a routine follow-up examination in the outpatient clinic. The patient was asymptomatic and had no relevant gastro-intestinal surgical history. Her physical examination and laboratory workup were normal. CT revealed significant free intra-abdominal gas without fluid collection. The findings suggested spontaneous pneumoperitoneum. After one week of observation the radiographic manifestation of free gas was disappeared. Spontaneous pneumoperitoneum is a rare complication in patients with intestinal scleroderma. The aetiology of these circumstances is obscure; it has been suggested that recurrent microperforations along the gastrointestinal tract allow air to leak into the peritoneal cavity. It may well be important that physicians should be aware of spontaneous pneumoperitoneum in patients with IgG4RD in which heterogenous immune-mediated fibro-inflammatory conditions can affect multiple organs including the gastrointestinal tract.

P3-169

A case of mixed connective tissue disease with difficulty in differentiating renal dysfunction

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Conflict of interest: None

[Case] A 57-year-old woman. She's diagnosed with MCTD, which was associated with Raynaud's symptoms, puffy finger, polyarthritis, dermatosclerosis and positive anti-U1-RNP antibody in X-4 years. Proteinuria was observed at the time of diagnosis, and later resolved spontaneously. He was admitted to the hospital for close examination and treatment because of headche, hypertension, thrombocytopenia, renal dysfunction and retinitis. After admission, a thorough examination revealed no specific antibodies for SLE or SSc. Cerebrospinal MRI revealed high-signal areas in the basal ganglia and cervical to thoracic medulla on T2-weighted images. Based on these findings, she was suspected to have SLE, and high-dose steroid therapy was started on the 1st day. Otherwise, we suspected TMA from hypertension, hemolytic anemia with fractured RBCs, thrombocytopenia, and renal dysfunction. A renal biopsy was performed on the 9th day, which revealed thrombotic occlusion and thickened vascular endothelium at the transition zone. ACEi and plasma exchange were started on the 17th day. After these treatmet, she was weaned off from plasama exchange. [Clinical Significance] MCTD has a variety of clinical manifestations, and this is a difficult case to distinguish SLE from SSc in terms of renal dysfunction.

P3-170

A case of panniculitis presenting with periodic fever and diagnosed as Weber-Christian disease

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Conflict of interest: None

[Case] A 68-year-old woman with a history of fever, painful swelling of dorsum of the foot, livedo reticularis on both lower legs, and a tender subcutaneous nodule on the left temporal area, which spontaneously disappeared 8 days later. This time, she was hospitalized because she presented with a periodic fever that lasted for about 4 days at 2-week intervals for the past 6 months. On Day 7, she developed a fever of 38°C that lasted for 4 days accompanied by left neck pain, which was visualized as subcutaneous high intensity nodule on contrast-enhanced CT scan. Subsequently she still had recurrent fever with left neck pain that persisted for several days at approximately 2-week intervals. When she developed fever accompanied by a painful erythema on her left lower extremity, we performed a skin biopsy, which revealed the presence of lobular panniculitis, as evidenced by infiltration mainly consisting of T-lymphocytes and histiocytes. Considering pathological and radiographic findings, she was diagnosed with Weber-Christian (WC) disease, and oral prednisolone 20 mg was started. Her periodic fever did not recur after 8-month follow-up, when the dose of prednisolone gradually tapered to 8 mg. [Conclusion] WC disease should be considered as a differential diagnosis of periodic fever.

P3-171

Nodular-type muscular sarcoidosis: two cases

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Conflict of interest: None

We report two cases of nodular-type muscular sarcoidosis. [Case 1] A 73-year-old man developed multiple nodules subcutaneously in his buttock and extremities, and subsequently weakness of the lower limbs. The histology of the nodules, which were surgically resected, confirmed non-caseating epithelioid cell granuloma, resulting in the diagnosis of sarcoidosis. Musculoskeletal MRI T2-weighted images (Mus-MRI) indicated increased signal intensity in the affected lesions including muscle. Prednisolone at 30 mg daily was administered, achieving remission. [Case 2] A 71-year-old woman, having a history of uveitis, developed mass lesions proximal in the legs. Increased signal intensity by Mus-MRI and Ga scintigraphy accumulation were focally demonstrated in the nodular lesions, which were located in the quadriceps muscle. An increase in serum levels of ACE was also revealed. Histology of the biopsied nodular lesion indicated non-caseating epithelioid cell granuloma, confirming the diagnosis of sarcoidosis. An immunosuppressant (IS) was not ultimately required because of being asymptomatic. [Discussion] Nodular-type muscular sarcoidosis is often asymptomatic, while IS can lead to remission in patients showing muscular symptoms.

P3-172

A case of bilateral leg myositis induced by minocycline

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Conflict of interest: None

A 30-year-old woman had been taking minocycline for palmoplantar pustulosis for six months. She was referred to our department two months ago due to persistent swelling and pain in both legs, which increased at night. Physical examination revealed diffuse swelling and tenderness from half of the lower leg to the dorsum of the foot and flexion and extension problems in both ankles; however, neither arthritis nor neuropathy was observed. She had an inflammatory response, such as a CRP level of 4.66 mg/dl, but her CPK level was not elevated. Immunological tests, such as RF, anti-CCP antibody, ANA, and autoantibodies associated with myositis, showed no abnormalities. The nerve conduction studies were normal. Contrast-enhanced MRI of both lower legs showed diffuse high signal intensity on STIR, and that of both lower leg muscle bundles showed pale staining at T2 high, indicating myositis. The patient stopped minocycline intake, and the swelling improved dramatically within a week. Three months later, contrast-enhanced MRI showed no STIR hyperintense signals or contrast enhancement. [Clinical Significance] There are few reports of minocycline-induced myositis. However, drug-induced myositis should be suspected, and the drug should be discontinued when the cause of myositis is unknown.

P3-173

A case of TMA during anti-GBM antibody-positive RPGN treatment, diagnosed as cobalamin metabolism disorder

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Conflict of interest: None

Case A 31-year-old woman was admitted to the medical intensive care unit due to acute renal failure. RPGN was diagnosed and emergency dialysis was started. On the 6th day, laboratory test showed anti-GBM antibody was positive, she was diagnosed with Goodpasture syndrome, and received methylprednisolone (mPSL) 1 g for 3 days followed by PSL 1 mg/kg and plasma exchange (PE). On the 19th day, These treatment archived anti-GBM antibody and CRP were negative, and withdrew PE but not dialysis. Thrombocytopenia progressed from the 21st day, and thrombotic microangiopathy (TMA) was diagnosed based on thrombocytopenia (10,000/μL), hemolytic anemia with schistocytes. She received mPSL 1 g for 3 days followed by PSL 1 mg/kg and PE, but platelet count showed no improvement. On the 41st day, a hyperhomocysteinemia of 130 nmol/L was observed, and abnormal cobalamin metabolism was diagnosed, hydroxocobalamin and betaine were started. Theses treatment improved platelet count (50,000/μL). Clinical Significance TMA is a rare complication of Goodpasture syndrome and immunosuppressive therapy was ineffective for TMA. Although there are many causes of TMA that are difficult to identify, cobalamin metabolism disorders have been reported in a number of cases, even in adults, and should be kept in mind.

P3-174

Calcaneus osteomyelitis and pyogenic ankle arthritis induced by a cutaneous ulcer with eosinophilic fasciitis. A case report

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Conflict of interest: None

[Case] 47-year-old male. He was introduced to our hospital because of a callus on his left heel had been ruptured and infected. The skin of his foot was hard, and both ankle joints were stiff. An ulcer was shown on his left heel, and MRI showed Gd-enhancement on his left calcaneus, leading to a diagnosis of left calcaneal osteomyelitis. Otherwise, one year after his first visit, an ulcer on the right medial malleolus appeared and the purulent discharge was drained. MRI showed Gd-enhancement on his ankle joint, leading to a diagnosis of pyogenic arthritis. After the curettage and antibiotic treatment, a free flap followed by the necrosis of pedicle flap was performed with calcaneal osteomyelitis, and arthrodesis and free flap were performed with pyogenic arthritis, respectively. One year after the surgery, he has never achieved wound healing. During this course, a skin biopsy performed by the dermatologist suspected eosinophilic fasciitis, and the patient was proposed for taking prednisolone, but he refused. Eosinophilic fasciitis is a very rare disease characterized by plate-like skin stiffness of the extremities and joint stiffness. In this case, a cutaneous ulcer caused by the eosinophilic fasciitis, and wound healing was considered to be difficult.

P3-175

A case requiring differentiation between autoinflammatory syndrome and peritoneal cancer

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Conflict of interest: None

A 59-year-old woman was referred to our hospital with arthralgia, swelling of joints in both hands, and fever. She was admitted to our hospital in August X for close examination and treatment. The physical and imaging findings revealed polyarthritis, pleurisy, and pericarditis. The fever, arthralgia, and serositis suggested the diagnosis of autoinflammatory syndrome, and colchicine was started. CA125 was elevated and an abdominal MRI revealed peritoneal nodules. Her general condition improved with continued administration of colchicine, and she underwent a PET-CT scan. FDG accumulation in the para-aortic lymph nodes suggested peritoneal carcinoma and pericardial and pleural metastasis. However, since colchicine alone improved the serositis, an autoinflammatory syndrome is strongly suspected in this case, and we are planning to conduct genetic testing for autoinflammatory diseases. We have experienced a case that required differentiation between an autoimmune syndrome and peritoneal cancer. The patient had fever, arthralgia, pleural effusion, and pericardial effusion as symptoms associated with malignant tumor, suggesting the importance of clinical course, imaging tests, and genetic tests in differentiating autoimmune syndrome from autoinflammatory disease.

P3-176

Two cases of polymyalgia rheumatica during use of immune checkpoint inhibitors for advanced hepatocellular carcinoma

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Conflict of interest: None

[Background] The combination therapy of the immune checkpoint inhibitor (ICI), atezolizumab and bevacizumab (Atz/Bev), was indicated for the treatment of unresectable hepatocellular carcinoma (HCC). We report two cases of polymyalgia rheumatica (PMR), a possible immune-related adverse event caused by ICI. [Case 1] An 84-year-old man noticed myalgia with proximal muscles, fever, weight loss, and morning stiffness after 4 months of Atz/Bev for HCC. Though blood tests showed elevated CRP (13.86 mg/dl), both antinuclear antibodies and autoantibodies were negative. PMR was diagnosed and prednisolone (PSL) 20 mg/day was started. The next day his symptoms of myalgia improved. [Case 2] A 77-year-old man complained of bilateral shoulder pain, morning stiffness, and fever 5 months after Atz/Bev. CRP and CK were elevated, but CK decreased spontaneously. Rheumatoid factor and anti-CCP antibodies were negative. MRI and electromyography showed no myogenic changes and the revised diagnostic criteria of for polymyositis were not met. After PSL 15 mg/day was started, CRP became negative and symptoms did not recur after PSL tapering. [discussion] In addition to PMR, other rheumatic diseases caused by ICI include rheumatoid arthritis and myositis; these are the first two cases of PMR reported by Atz/Bev.

P3-177

A case of rheumatic irAE with early tendinopathy and bone erosion occurred lately during ICI treatment, leading to early diagnosis and therapeutic intervention by musculoskeletal ultrasound

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Conflict of interest: None

A 71-year-old man had received chemotherapy including pembrolizumab, an immune checkpoint inhibitor (ICI), for primary lung adenocarcinoma since November 2020. After four courses, the patient had achieved partial response and switched maintenance therapy including pembrolizumab. In late September 2022, he showed fever and malaise, and polyarthralgia. Although rheumatoid factor and anti-CCP antibody were both negative, multiple swollen joints, elevated serum CRP levels, bone erosions on wrist x-ray, and moderate to severe synovitis, peritendinitis, and tenosynovitis mainly in swollen joints on musculoskeletal ultrasound (MSUS) were observed. We diagnosed inflammatory arthritis, major rheumatic irAE, and discontinued the ICI and started 20 mg of PSL, his joint symptoms and inflammatory response improved. Rheumatic irAE often occurs lately after ICI administration, and its diverse clinical manifestations require differentiation from other diseases. Especially in inflammatory arthritis, tendon involvement and bone erosion may occur early in the course, and also affect the decline in performance status. This case suggests the need for early diagnosis and therapeutic intervention using MSUS and other techniques from the perspective of resuming treatment for the tumor.

P3-178

Nine Cases of New-onset Rheumatic Diseases Following COVID-19 Vaccination

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Conflict of interest: None

We have experienced 9 cases of new-onset rheumatic diseases following COVID-19 vaccination. Among those, 5 cases of adult-onset Still's disease (AOSD), one case each of rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), microscopic polyangiitis (MPA), immune-mediated necrotizing myopathy (IMNM) were noted. Eight of the 9 cases were female. The age ranged from 32 to 79 years. The symptom onset ranged from 1 day to 10 weeks following vaccination. Three of AOSD improved with high-dose glucocorticoid (GC). Other two of AOSD were complicated with hemophagocytic syndrome, both of which were treated with intravenous methylprednisolone pulse therapy, tocilizumab, and cyclosporin. The case of RA improved with low-dose GC and abatacept. The case of SLE improved with high-dose GC and hydroxychloroquine. The case of MPA improved with high-dose GC. The case of IMNM, who had received methotrexate and adalimumab for her underlying RA, discontinued them and responded to high-dose GC. [Clinical Significance] Since over 80% of the Japanese population has received at least second dose of COVID-19 vaccination, the onset and relapse of rheumatic diseases following this vaccination may be very rare. Further accumulation and examination of cases are necessary to understand this phenomenon.

P3-179

A case of polymyalgia rheumatica (PMR) after vaccination with COVID-19 mRNA vaccine (BNT162b2)

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Conflict of interest: None

An 80-year-old woman received the fourth dose of COVID-19 vaccine 4 weeks earlier and developed generalized myalgia and stiffness in her shoulders on the night of the same day. Although she was followed up as a transient adverse reaction to the vaccine, she did not get better. A blood test performed 19 days after vaccination revealed a CRP of 9.9 mg/dL and an ESR of 121 mm/h. She was referred to our hospital because her symptoms did not improve after administration of antimicrobial agents and NSAIDs. Contrast-enhanced CT showed no obvious abnormalities in major organs or large blood vessels, and bursitis was observed around the right humeral head and left femoral condyle. Since RF and anti-CCP antibodies were also negative, she was diagnosed as PMR. After starting treatment with 15 mg/day of prednisolone, her symptoms rapidly improved

and her CRP and ESR decreased. PMR has been reported to occur after viral infection, and since the 1990s, it has also been reported as an adverse event after immunization. However, even according to WHO guidelines, the incidence of PMR after immunization is less than 0.01%. Although there are only a few reports of cases of PMR after COVID-19 vaccination, PMR should be included in the differential diagnosis of post-vaccination myalgia.

P3-180

A case of TAFRO syndrome-like condition after COVID-19 infection

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Conflict of interest: None

[Case] In May 2021, she developed fever and was diagnosed with COVID-19 by RT-PCR. Chest CT showed no evidence of pneumonia, and she was admitted to a nearby hospital as a mild case and was treated with favipiravir. High CRP levels did not improve and remdesivir and steroid pulse therapy were used on day 6 of onset, but she developed pleural effusion, ascites, thrombocytopenia, and multiple lymphadenopathies, which resulted in transfer to a general hospital. Due to persistent fever and thrombocytopenia with systematic rash after RT-PCR of SARS-Cov-2 turned negative, a multisystem inflammatory syndrome was suspected, and prednisolone 80 mg/day was administered on day 17. Symptoms improved after 2 weeks of initial treatment, but during the process of reducing the dose of prednisolone, ascites, thrombocytopenia and lymphadenopathies flared up, accompanied by acute renal failure. Bone marrow biopsy revealed megakaryocytosis, renal biopsy showed interstitial nephritis, and we diagnosed her with TAFRO syndrome-like condition and treated her with an increased dose of prednisolone and tocilizumab 640 mg/body, which resulted in improvement. [Discussion] It is known that COVID-19 can cause cytokine storms, however a case of TAFRO syndrome-like disease after COVID-19 has not been reported.

P3-181

Pneumocystis pneumonia after rituximab treatment in a patient with microscopic polyangitis

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Conflict of interest: None

[Background] Rituximab (RTX) has been used for induction treatment of microscopic polyangitis (MPA) because of less severe infection than cyclophosphamide. Recent reports showed RTX had a risk of infection for patients with older age or renal dysfunction. I report a case of pneumocystis pneumonia (PCP) after administration of RTX for MPA. [Case] An 82-year-old woman had a history of PMR. She was suspected of a relapse due to appetite loss and the elevation of CRP. When she admitted to our hospital, laboratory examinations showed proteinuria, hematuria, elevation of serum creatinine and MPO-ANCA, and interstitial pneumonia. She had transferred to another hospital and a diagnosis of MPA was made clinically. Weekly dose of 480 mg of RTX was administered for four weeks with 30 mg daily of PSL. Sulfamethoxazole/trimethoprim (ST) was started on the next day of 4th RTX. Three days later, she was febrile when she has returned to our hospital. She was diagnosed as PCP in combination with the elevation of beta-D-glucan and bilateral multiple reticular shadows. Half dose of steroid pulse treatment and ST was not effective and she died three weeks later. [Clinical Significance] RTX has a risk of severe infection in patients with MPA, especially older age or renal dysfunction.

P3-182

A case of concurrent enteritis and secondary hemophagocytic lymphohistiocytosis caused by cytomegalovirus during treatment of systemic lupus erythematosus

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Conflict of interest: None

A 34-year-old woman suspected of systemic lupus erythematosus (SLE) as she had polyarthralgia and positive anti-DNA antibodies was admitted to our hospital. A renal biopsy was performed because proteinuria was observed, and the biopsy findings showed diffuse proliferative glomerulonephritis (type IV-G (A)). Treatment with prednisolone (PSL) and mycophenolate mofetil resulted in rapid improvement of SLE activity, following which she was discharged from our hospital. After one month, she was admitted again to our hospital for fever and diarrhea due to cytomegalovirus (CMV) colitis. Six days after hospitalization, a substantial small intestinal bleeding was observed, and she went into hemorrhagic shock. Although the patient received embolotherapy and recovered from the hemorrhagic almost immediately, high fever and thrombocytopenia continued. Subsequently, hepatic dysfunction and ferritin increase were also observed, leading us to suspect CMV-induced hemophagocytic lymphohistiocytosis (HLH). Although mPSL pulse therapy was performed promptly, hepatic dysfunction worsened. Accordingly, we applied both plasma exchange and administered cyclosporin, resulting in HLH recovery. Severe CMV infections can occur in compromised hosts, necessitating attentive and careful treatment.

P3-183

A case of elderly-onset rheumatoid arthritis who developed pneumocystis pneumonia during treatment with steroid and immunomodulator

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Conflict of interest: None

96-year-old female visited our department with chief complaints of low-grade fever and polyarthralgia. A blood test showed leukocytosis and high CRP level. RF and ACPA were negative, but MMP-3 levels were high, and synovitis was confirmed by joint echocardiography. She was diagnosed with rheumatoid arthritis and was started on SASP and PSL 20 mg. SASP was changed to IGU after 2 weeks due to skin itching. The dose of PSL was reduced from 20 to 10 mg every 2 weeks. About 10 days later, she presented to the emergency department with cough and dyspnea. Her chest CT scan revealed diffuse GGO, and she was rushed to the hospital. She stopped taking IGU and started steroid pulse therapy. Pentamidine was also used in combination. On the 3rd day, a high βD-glucan level was found, suggesting Pneumocystis pneumonia. On the fifth day, she passed away due to respiratory failure. Very elderly patient with rheumatoid arthritis was treated with steroid and immunomodulator. Despite the fact that she did not take immunosuppressants and the steroid dose was tapered relatively quickly, she developed pneumocystis pneumonia 2 months after starting treatment. In the very elderly, it was suggested that even relatively low doses of steroid may be at risk of pneumocystis pneumonia.

P3-184

A case of rheumatoid arthritis-associated interstitial lung disease (RA-ILD) with Diffuse Alveolar Hemorrhage (DAH) after SARS CoV-2 infection (COVID-19)

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Conflict of interest: None

A 72-year-old man who diagnosed with RA and RA-ILD had been followed in our hospital and had been treated with csDMARDs. The patient was infected with SARS CoV-2 and was diagnosed with viral pneumonia. He recovered from COVID-19 but subsequently developed more

severe respiratory failure, which was considered to be a COVID-19 triggered acute exacerbation of RA-ILD. Chest CT showed diffuse ground glass opacities in both lungs. Bronchoalveolar lavage showed hemorrhagic fluid, macrophages with hemosiderin in cytology. Based on these findings, we made a diagnosis of DAH. Furthermore, He suffered from numbness in the feet that was suspected peripheral neuropathy simultaneously. Immunoserology revealed positive immune complexes and elevated anti-CCP antibody and RF titer. These blood investigations results and his symptoms suggest that DAH was associated with rheumatoid vasculitis. He was successfully treated with pulse dose mPSL and CY. This patient is the rare case of RA-ILD developing DAH and probably it occurred with rheumatoid vasculitis after SARS CoV-2 infection. There is growing evidence that COVID-19 can lead to the development of rheumatic autoimmune diseases. The main diseases reported were vasculitis. COVID-19 pandemic is still ongoing, and our case is a suggestive example.

P3-185

A case of Cytomegalovirus retinitis during treatment of Anti-MDA5 antibody-positive dermatomyositis

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Conflict of interest: None

A 60-year-old woman was aware of dyspnea and skin rash in August X-1 and was diagnosed with Anti-MDA5 antibody-positive dermatomyositis (DM) and interstitial pneumonia in September. She was treated with prednisolone, tacrolimus and intravenous cyclophosphamide. She was transferred for rehabilitation because of muscle weakness caused by steroids in March X. A CT scan at the new hospital revealed new nodules of the lung and liver, and she was transferred to our hospital on April X for examination. A detailed interview revealed she had been aware of blurred vision since February X. After an ophthalmologic examination, she was diagnosed with cytomegalovirus (CMV) retinitis and started valganciclovir. The location of lung nodules was difficult for bronchoscopy and the biopsy of liver nodules showed no specific findings. No abnormal findings were observed on upper and lower endoscopies. Although all bacteriological tests including CMV pp65 antigen were negative, there remained the possibility that these nodules were caused by CMV. As the ocular findings had improved, she was discharged in May X and we follow her if these nodules would be smaller. CMV retinitis associated with DM is rare, so we report this case with some literature review.

P3-186

A case report of severe Pneumocystis jirovecii pneumonia successfully rescued with a combination of strong immunosuppressive therapy and veno-venous extracorporeal membrane oxygenation

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Conflict of interest: None

The case is a 48-year-old male who was recently treated for immune-mediated necrotizing myopathy with high-dose prednisolone (PSL), IVIG, rituximab at another facility, and was taking PSL20 mg, tacrolimus 6 mg, and methotrexate 24 mg. After developing fever and dyspnea, the patient was transferred to our hospital for evaluation of hypoxemia and bilateral ground-glass opacities on chest CT. Upon admission, broad-spectrum antibiotics, sulfamethoxazole-trimethoprim, and methylprednisolone (mPSL) pulse therapy (1 g/day for 3 days) were started. Tacrolimus and methotrexate were discontinued. On day 2, deterioration of oxygenation required intubation and mechanical ventilation (MV). With elevated serum β-D glucan and PCR analysis of bronchoalveolar lavage fluid, *Pneumocystis jirovecii* pneumonia (PCP) was diagnosed. Despite treatment, respiratory failure progressed, necessitating a second steroid pulse and placement of veno-venous extracorporeal membrane oxygenation (V-V ECMO). After the steroid pulse, high-dose steroid was continued, and a dose of intravenous cyclophosphamide was administered. Subsequently, respiratory function and chest radiograph improved, and both ECMO and MV were discontinued. ECMO may be a beneficial treatment option in the progressive phase of severe PCP.

P3-187

A case of miliary tuberculosis with tuberculous arthritis treated as seronegative rheumatoid arthritis

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Conflict of interest: None

A 71-year-old woman was diagnosed with seronegative rheumatoid arthritis with polyarthritis involving right ankle joint at an orthopedic clinic5 months ago. She was treated with several DMARDs, but her symptoms were worsened. A week ago, MRI scan revealed right talus fracture. After a few days, she developed fatigue, shortness of breath, and respiratory failure, so she was transferred to our hospital. Chest CT showed ground-glass opacities and slight granular opacities in both lungs. We suspected interstitial lung disease and started steroids. After that fever and arthralgia in the left knee developed. A bone marrow biopsy revealed caseating granuloma, and mycobacterium tuberculosis was detected in the synovial fluid of left knee and even right ankle joint. We diagnosed miliary tuberculosis with tuberculous arthritis and started antitubercular medication and she was transferred to a hospital with a tuberculosis ward. She had no history of tuberculosis and no family history. The mycobacterium tuberculosis-specific interferon-gamma release assay test (IGRA) was negative and the chest radiograph showed no abnormalities before the start of therapy. We should be aware that IGRA may be negative in elderly tuberculosis and that miliary tuberculosis may not visible on chest radiograph.

P3-188

Clinical features of connective tissue diseases in patients with cytomegalovirus infection in our department: A retrospective observational study

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Conflict of interest: None

This retrospective observational study aimed to investigate the clinical features of patients with CTDs who developed cytomegalovirus (CMV) infection. This study included patients with CTDs who were admitted to our department from August 2008 to September 2022. According to histopathological examinations or positive for CMV antigenemia test by CMV pp65 antigen (C7-HRP), 27 patients were diagnosed with CMV infection. Clinical data were collected from medical records. Of the 27 patients, 6 were males, with an average age of 59 years. CTDs included 7 cases of SLE, 6 cases of vasculitis, 4 cases of Still's disease, 3 cases each of RA, dermatomyositis, and Sjögren's syndrome, and 1 case of MCTD. Corticosteroids were administered in all patients. At the CMV infection diagnosis, 18 cases were asymptomatic. Cytopenia was most commonly reported in 13 cases, enteritis in 6 cases, and pneumonia in 2 cases. The laboratory data before the CMV infection diagnosis revealed a median lymphocyte count of 628/μl and an albumin level of 2.59 mg/dl. Ganciclovir and valganciclovir were administered in 23 patients. Cytopenia may be the most commonly reported abnormal laboratory findings associated with CMV infection, and distinguishing it from autoimmune disease exacerbation may be necessary.

P3-189

Delayed wound healing after surgical resection of gouty tophus of the foot

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Conflict of interest: None

[Background] The management of gouty tophi has generally shifted from surgical excision to conservative therapy due to surgery's traditional association with high wound complication rate. Nevertheless, there are still patients who are indicated for surgical excision of gouty tophi. [Case Presentation] A 37-year-old obese man (BMI, 32.0) had multiple gouty tophi with bone erosion. He had a history of gout since he was 18-year-old. Hyperuricemia was well-controlled by medication. However, footwear use was limited by the presence of tophus of the right foot. He underwent surgical resection of gouty tophus of the right foot. We permitted early weight bearing after surgery. However, increasing exudate was seen and small white particles were found in the exudate. Then, surgical debridement was performed. During the surgery, we irrigated the area with a continuous flow of water. This was because urate crystals are slightly soluble in water, making the removal of the remaining material easier. His foot was fixed with bandage and restricted from weight bearing until healing of the wound. Three weeks later, wound healing was completed. [Clinical Significance] We recommend the continuous irrigation during the excision of tophi and long period of immobilization of the surgical sites.

P3-190

A case of gouty tophus formed on the extensor hallucis tendon enthesis

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Conflict of interest: None

[Introduction] Gout is thought to be caused by phagocytosis of sodium urate crystals in joints by leukocytes. We report a case of gouty tophus in the distal phalanx of the 1st toe. [Case] A man in his 20s had pain in his left 1st toe for 10 years, and noticed a nodule on the distal phalanx of the 1st toe one year ago. Serum uric acid level was 9.2 mg/dl. There was no family history of gout. An X-ray showed bone erosion at the left 1st MTP joint and a 7 mm-sized circular translucent image in the center of the left 1st distal phalanx. Ultrasonography revealed a subcutaneous nodule with a power Doppler signal was observed adjacent to the extensor tendon attached to the 1st distal phalanx. In addition, a part of the nodule was seen to enter the bone from the bone erosion, suggesting continuity with the nodule on the plantar side. HR-pQCT images of the left 1st distal phalanx showed the bone erosion had penetrated from the dorsal side to the plantar side, and the trabecular bone had almost disappeared. [Conclusions] Gouty tophus were observed at the tendon enthesis of the 1st toe, similar to those observed at the tendon enthesis of elbows and knees.

P3-191

A case of gout thought to be associated with enthesitis in deposition of monosodium urate crystals and formation of tophi

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Conflict of interest: None

[Introduction] The tophus of the 1 MTP joint is continuous with the intra-articular joint. We experienced tophi that were not connected to the joints of fingers and elbows. [Case] The case is a 50-year-old male who has had recurrent gout attacks for the past 15 years. He had tophi in the 2 MCP and 2 PIP joints of the right hand, the 2 MCP and 3 PIP joints of the left hand, the left olecranon, and the left 1 MTP joint. Plain X-P showed bone formation in the left olecranon, patella, tibia, calcaneus, and tarsal bone, but bone erosion was observed only in the left 1 MTP joint. Joint ultrasonography showed that the tophi were in contact with the finger extensor tendon and triceps brachii tendon enthesis, and most of the tophi did not connect to the inside of the joint. In addition, hyperechoic spots and inflammation were observed at the quadriceps tendon enthesis, patellar ligament enthesis, and Achilles tendon enthesis. [Conclusions] In this case, The tophi were observed around the tendon and at the enthesis. Monosodium urate crystal deposition was accompanied by exudation of plasma due to enthesitis. It was thought that the tophi were formed by recurrent enthesitis and gout attack.

P3-192

Gouty flexor tenosynovitis of the hand -a case report

Masashi Morishige
Ube Kohsan Central Hospital

Conflict of interest: None

[Case] A 50-year-old man diagnosed with gout attack in left foot with high uric acid (UA) level of 13.8 mg/dl 9 days earlier visited a nearby orthopedist for swelling and pain of the left middle finger 3 days ago. Pyogenic tenosynovitis was feared and antibiotic therapy was started, but not effective. He was referred to our hospital. On initial examination, there was swelling, redness and pain in the left middle finger with all Kanavel's 4 cardinal sign. Laboratory date showed elevated WBC 15320/μl, Neutro 86.8%, CRP 0.79 mg, and UA was 8.7 mg/dl. T2-weighted MRI showed hyperintense changes along the flexor tendon sheath of the middle finger. Admitted on the same day and surgery performed the next day. White powdery deposits were observed between and in tendon sheaths and that had infiltrated both flexor tendons. The white deposits and pathological synovial membrane were removed as much as possible. Antibiotic administration was completed the day after surgery. He was no recrruence at 2 monthes later. Pathological examination showed no crystal deposits, but intraoperative findings and postoperative course led to a diagnosis of gouty tenosynovitis. [Clinical Signification] Gouty flexor tenosynovitis is uncommon and difficult to differentiate from pyogenic tenosynovitis in acute onset.

P3-193

Crystals can be identified even in long-term cryopreserved joint fluid

Takayasu Kise[1,2], Naoto Yokogawa[2], Yuji Miyoshi[2], Masako Utsunomiya[2], Yoshiki Nagai[2], Yuichiro Imamura[3], Toshinori Morito[4], Ikuko Masuda[5], Kota Shimada[2]

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Conflict of interest: Yes

[Objective] There is no report comparing whether crystals can be identified in long-term cryopreserved joint fluid. [Methods] Identification of calcium pyrophosphate crystals (CPP) and monosodium urate (MSU) before and after cryopreservation (CRYO) of joint fluid from knee suspected with crystal induced arthritis from April 2019 to March 2021 at three rheumatology institutions. Specimens (SP) before CRYO were evaluated by outsourcing (centrifuged sediments were examined using U-GAN®). In March 2022, all CRYO SP were defrosted, centrifuged at 3000 rpm for 5 min and examined by two skilled rheumatologists using polarizing microscope (MT9300) as consensus reading. [Results] 68 SP were evaluated. 30 (44.1%) were crystal-positive before CRYO (CPP was 83.3% (25/30) and MSU was 16.7% (5/30)), and 38 (55.9%) were crystal-negative. In the sediment of defrosted SP, 31 (45.6%) were crystal-positive (CPP was 80.6% (25/31), MSU was 19.4% (6/31)), and 37 (54.4%) were crystal-negative. If the results before CRYO was the reference, crystals could be identified in defrosted SP with the sensitivity of 80.0% (24/30; CPP was 76.0% (19/25) and MSU was 100% (5/5)) and the specificity of 81.6% (31/38). [Conclusions] Identification of CPP and MSU was possible even in long-term CRYO joint fluids.

Morning Seminar

MS1

Usefulness and points to consider of methotrexate subcutaneous formulation

Hideto Kameda
Division of Rheumatology, Department of Internal Medicine, Toho University

Conflict of interest: Yes

In 2022, methotrexate (MTX) subcutaneous injection formulations became available in Japan. The formulations are 7.5 mg, 10 mg, 12.5 mg, and 15 mg, and the injection volume for each is 0.15 mL, 0.2 mL, 0.25 mL, and 0.3 mL, respectively. Because of the higher bioavailability, especially at higher doses compared to the oral formulation, the subcutaneous injection would effectively be a higher dose than the oral one at the same dose. Therefore, the recommended dose for a *de novo* MTX start is 7.5 mg once a week, but for a switch from the oral formulation, the recommended dose is 7.5 mg for 6 mg, 7.5-10 mg for 8-10 mg, and 10-12.5 mg for 12-16 mg, which should be determined including whether there is any intention to increase the dose. Starting with a 15 mg injectable formulation is not permitted, as this would be equivalent to 20 mg or more of the oral dose, based on the area under the blood concentration curve. It has been suggested that some adverse events may be reduced, but this will be clarified in post-marketing surveillance. In this seminar, I would like to discuss the proper use of MTX and its possibilities and challenges, focusing on the results of domestic Phase III clinical trials and referring to overseas trials and the revised MTX use and practice.

MS2

Reactivation of Hepatitis B Virus Caused by Immunosuppressive Therapy and Chemotherapy - Current Status and Future Perspectives -

Naoto Kawabe
Department of Gastroenterology and Hepatology, Fujita Health University School of Medicine

Conflict of interest: None

Hepatitis B virus reactivation (HBVr) has been reported as a complication of immunosuppressive therapy and chemotherapy, leading to fulminant hepatitis in some patients and resulting in fatal outcome. Although many cases of HBVr had been reported in HBsAg-positive patients, hepatitis due to HBVr in HBsAg-negative patients with past HBV infection has been reported since the introduction of molecular-targeted therapies such as anti-CD20 and anti-TNF antibody. A multicenter, prospective observational study in patients with past HBV infection showed that the risk of HBVr (defined as HBVDNA elevation) was 10% and 5% following anti-CD 20 and anti-TNF treatment, respectively. In accordance with the "Guidelines for prevention of HBV reactivation in patients receiving immunosuppressive therapy or chemotherapy" in the "Guidelines for the Management of HBV Infection (4th edition)" revised by the Japan Society of Hepatology in 2022, the risk of HBVr should be evaluated in advance by quantitative tests for HBc antibody, HBs antibody, and HBVDNA in addition to HBs antigen at screening. In addition, preventive administration of antiviral drugs in HBs antigen-positive patients and HBVDNA monitoring in patients with past HBV infection should be taken for the prevention of HBV related hepatitis and for the safe continuation of immunosuppressive therapy and chemotherapy. However, according to a nationwide survey, even recently fatal cases of acute liver failure due to HBVr have not been eradicated, and educational activities are needed to prevent severe hepatitis due to HBVr in all disease areas. In this session, the latest evidence on the risk of HBVr is reviewed, and our approaches and future prospects are introduced.

MS3

Positioning of TNF inhibitors in the treatment of rheumatoid arthritis and significance of dosage adjustment

Shintaro Hirata
Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital

Conflict of interest: Yes

The 20th anniversary of the launch of infliximab, a chimeric anti-TNF-α monoclonal antibody, as the first full-fledged molecular targeted therapy for rheumatoid arthritis in Japan is now being celebrated. Rheumatoid arthritis is a systemic autoimmune disease characterized by polyarthritis and joint destruction, and its pathogenesis is known to involve a variety of inflammatory cells such as neutrophils, lymphocytes, monocytes and macrophages, as well as osteoclasts, osteoblasts and synovial fibroblasts. At the time, the world was suprised by the therapeutic effect, described as a "paradigm shift", achieved by inhibiting a single cytokine in such a complex disease state. Since then, not only TNF inhibitors but also various other molecular targeted drugs have been approved for the treatment of rheumatoid arthritis and other rheumatic diseases, with success. There are now six originator TNF inhibitors listed for rheumatoid arthritis (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol, and ozoralizumab), plus biosimilar options. Most are administered subcutaneously via a pre-filled syringe or pen device, with only infliximab available via intravenous (IV) administration. Although the intravenous formulation is less convenient than the subcutaneous formulation because of the need for venipuncture and longer administration time, it has the advantage of allowing fine-tuned dosing according to body size and clinical condition. Several clinical studies conducted in Japan with infliximab, such as the RISING and RRRR studies, have contributed greatly to our understanding of the relationship between dosing and clinical outcomes in antibody therapy. In this seminar, I will discuss the position of TNF inhibitors in current rheumatoid arthritis therapy and the significance of dosage adjustment.

MS4

Shared decision in PsA

Masato Okada
Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: Yes

Treatment of Psoriati arthritis is based on involved domains of each patient, and non-steroidalanti-inflammatory drugs, conventional synthetic disease modifying anri-rheumatic medications, biologics disease modifying anri-rheumatic medications, targeted synthetic disease modifying anri-rheumatic medications are selected as individual medicine. Major cytokines including IL-23, IL-17, TNF etc., and we have biologics which target the cytokines and a JAK inhibitor covers multiple cytokines directly and indirectly.

MS5-1

Concept of difficult-to-treat (D2T) RA and issues to be resolved

Eiichi Tanaka
Division of Rheumatology, Department of Internal Medicine, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

The sufficient use of methotrexate and the introduction of biological DMARDs (bDMARDs) and/or tsDMARDs (JAK inhibitors) have resulted in significant advances in treatment strategies for rheumatoid arthritis (RA). In the IORRA cohort, the proportion of the patients who achieved DAS28 remission increased from 8.4% in 2000 to 63.1% in 2021, and approximately 80% of the patients with RA were well-controlled. However, despite these advances in RA treatment, some patients still experience moderate or high disease activity. Therefore, appropriate treatment should be considered an unmet need of these patients. Since uniform terminology and a clear definition for such patients are lacking, a EULAR Task Force was established to derive comprehensive recommendations addressing unmet needs in the management of difficult-to-treat (D2T) RA. The EULAR definition of D2T RA was proposed in 2020. At this seminar, we will first discuss the process of making the EULAR definition of D2T RA and the content of this definition. In addition, I would like to explain various issues that may contribute to D2T RA, including (1) treatment for RA when methotrexate cannot be prescribed, (2) treatment for multidrug-resistant RA, especially for inadequate response to bDMARDs, and (3) treatment for RA with various types of complications and elderly patients with RA,

using data from clinical trials and registries, such as the IORRA cohort.

MS5-2

Unmet needs in management of rheumatoid arthritis

Masataka Kuwana
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Conflict of interest: Yes

Management of rheumatoid arthritis (RA) has made great strides in the last 20 years. A therapeutic strategy to prevent the progression of joint destruction and to maintain functional ability has been established by aiming for remission by early diagnosis and intervention. On the other hand, a term "difficult-to-treat RA" has been proposed to describe patients who remain symptomatic despite treatment according to the current management recommendations. One of the factors linked to this condition is age-related comorbidities that prevent treatment intensification. The age of RA onset has been getting older, and its speed is prominent in Japan. RA patients who developed the disease over the age of 60 are regarded as elderly-onset RA (EORA), which occurs in the acute to subacute course with involvement of large joints and impaired activity of daily living. The current treatment strategy of RA is to intervene promptly before joint destruction occurs and to adjust the treatment frequently. However, in the elderly, it is often difficult to pursue treat-to-target treatment algorithms due to impaired physiological functions, aging of immunity, and multiple complications. Sustained disease activity further promotes the frailty cycle, resulting in irreversible exercise incapacity, cognitive decline, and susceptibility to infection. Therefore, management of EORA is an extremely difficult mission to complete. Challenges to treat EORA include which DMARDs to be selected as an initial treatment, whether corticosteroids should or should not be used, how to maintain drug adherence, and how to manage risks for major cardiovascular events and malignancy that are common in the elderly.

MS6-1

Discuss the safety of JAK inhibitors in the treatment of rheumatoid arthritis

Naoki Ishiguro
Aichi Developmental Disability Center

Conflict of interest: Yes

These agents have changed the course of rheumatoid arthritis (RA) treatment through the use of biologics with defined therapeutic targets. On the other hand, pain at the time of injection since it is an injectable drug and the problem of drug management remain. Therefore, JAK inhibitors have been developed as a new oral RA drug class. At present, five types of JAK inhibitors can be prescribed in Japan as therapeutic agents for RA, making Japan a country with many options worldwide. The newest of these is Filgotinib (FIL). Currently, it is approved as a therapeutic agent for RA in Europe and Japan, and can be prescribed. JAK inhibitors are often classified according to the kinase that the drug exhibits inhibitory activity on, but pharmacokinetics (PK) is also important as a factor related to actions and side effects when considering drug properties. In addition to inhibitory activity, PK analysis can capture other aspects of drug-to-drug differences. Consideration of pharmacokinetic characteristics may be helpful in considering differences in efficacy and safety of individual drugs. We believe it is important to understand the differences between the various JAK inhibitors, as this will greatly assist in prescribing them. In addition, the existence of Japanese data on safety is a valuable source of information for drug evaluation. We were fortunate to have enough Japanese data to analyze the safety of FIL. All RA patients (Japanese (including RA patients), and explain the analysis results regarding safety. In addition, the results for Japanese data only are also detailed. Currently, overseas regulatory authorities have expressed concerns about the safety of some JAK inhibitors, but considering differences in drugs and racial differences in side effects, it is necessary to build data in Japan. Regarding this drug, we expect that with your cooperation in all-case surveillance (PMS), the tabulation will be carried out promptly and sufficient information will be disclosed.

MS6-2

The era of JAK inhibitors has come in the treatment of rheumatoid arthritis

Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center

Conflict of interest: Yes

Now 5 JAK inhibitors (JAKinibs) are available for RA in Japan. JAKinibs are highly effective both clinically and radiographically in RA patients who had inadequate response to MTX (MTX-IR). The FINCH1 study has shown non-inferiority of Filgotinib (FIL) compared to adalimumab in the treatment of MTX-IR RA. FIL has more selective for JAK1 than other JAKinibs. Traves PG, et al. (Ann Rheum Dis 2021) demonstrated that the inhibitory effects of FIL on phosphorylation of both STAT5 in NK cells by IL-15 and STAT1 in monocytes by IFNg were less than that of other JAKinibs. This might be associated with no significant increase of malignancies, and lower incidence rate of herpes zoster. However, selectivity of JAK1 may not guarantee safety in the real world clinical practice. FIL should be carefully used in RA patients with impaired renal function such as the elderly because 87% of the active metabolites are excreted in the urine. As several studies like FINCH3 have demonstrated the superiority of JAKinibs than MTX in DMARD-naïve early RA, the era of JAKinibs as the mainstay in the treatment of RA might be coming in the future.

MS7

Overview on interstitial lung disease associated with connective tissue disease

Vincent Cottin
University of Lyon, France

Conflict of interest: Yes

Interstitial lung disease (ILD) occurs in 25% to 50% of patients with systemic sclerosis and is characterized by a NSIP pattern, and an overall mortality of 30% at 5 years. Systematic screening for ILD using chest CT is recommended. The antifibrotic agent nintedanib reduces forced vital capacity (FVC) decline in patients with systemic sclerosis and ILD. An expert consensus states that patients in whom pharmacological therapy is required may receive first-line treatment with mycophenolate mofetil, cyclophosphamide, or nintedanib. Tocilizumab and rituximab are alternative treatments in selected patients. ILD occurs in 5-10% of patients with rheumatoid arthritis and is mostly characterized by a UIP pattern, and an overall mortality of 60% at 5 years. No systematic screening is recommended, however patients older than 58 years, male, with a smoking history, have active rheumatoid arthritis, and carrying the MUC5B rs35706950 allele, have an increased risk of ILD. In the absence of guidelines, patients with severe ILD often receive immunosuppressive therapy using rituximab, abatacept, or glucocorticoids. ILD is frequent and symptomatic in patients with autoimmune inflammatory myositis, and requires corticosteroid and immunosuppressive treatment. ILD may also be present in patients with Sjögren syndrome or systemic erythematosus lupus, and may benefit from immunosuppressive therapy. In all connective tissue diseases-associated ILD, monitoring of ILD is key to identify early disease progression, and is based on the combined longitudinal assessment of clinical evaluation and pulmonary function especially FVC and DLCO. Worsening of fibrosis extent on chest CT also contributes to the assessment of disease progression. Patients with progressive pulmonary fibrosis despite first-line management are eligible for antifibrotic therapy using nintedanib, which reduces disease progression assessed by FVC decline, and reduces the risk of acute exacerbation of fibrosis.

MS8

The Role of IL-6 Receptor Inhibitors in Rheumatoid Arthritis

Allan Gibofsky
Weill Cornell Medical College and Hospital for Special Surgery

Conflict of interest: Yes

Interleukin 6 (IL-6) is a cytokine that has been implicated in the pathogenesis of several inflammatory diseases, including rheumatoid arthritis,

vasculitis and inflammatory bowel disease. IL-6 has been shown to be significant in numerous mechanisms of host defense, including cell trafficking, T-cell differentiation, inducing acute-phase proteins as well as mechanisms of homeostatic regulation. IL-6 biology has been extensively studied over that past two decades, resulting in significant clinical implications for therapy in inflammatory diseases and certain malignancies. The relationship of IL-6 receptor inhibition to reducing inflammation has been a major focus of clinical investigation. This presentation will review advances in IL-6 research, the differential effects of IL-6 activation and how IL-6 receptor inhibition targeted therapies have resulted in significant clinical advances and improvement in the quality of life of patients with rheumatoid arthritis.

MS9-1

Shared decision making in rheumatoid arthritis care

Masato Okada
Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: Yes

Personalized medicine is imperative to accomplish satisfactory disease control and quality of life without substantial risk of adverse event in rheumatoid arthritis. Initial treatment plan is made based on duration of the synovitis before treatment, prognostic factors of joints such as pre-existing bone erosion and anti-CCP antibody positivity, disease activity, comorbid condition such as interstitial lung disease, patient age and social situation which affect urgency of establishing remission, etc. Disease modifying anti-rheumatic drugs (DMARD) are sorted into conventional oral DMARD and biologic DMARD. Oral DMARD monotherapy, combination of oral DMARDs, and biological DMARD with or without oral DMARD can be options. Abatacept has repeatedly been shown to be effective to patients with positive anti-CCP antibody, and that is consistent with the mode of action. Patients' understanding of the balance of effectiveness and safety of each choice of treatment regimens are imperative to shared decision making. The relatively good safety profile of abatacept in conjunction with appropriate patient selection, such as anti-CCP antibody status, facilitates satisfactory decisions. After remission of rheumatoid arthritis is achieved, de-escalation of DMARD can be an issue to discuss with patients. Careful de-escalation and prepared plan of re-escalation in case of flare are recommended.

MS9-2

Pathophysiology and treatment strategies for rheumatoid arthritis patients with interstitial lung disease

Shigeru Iwata
Department of Rheumatology and Clinical Immunology, Wakayama Medical University

Conflict of interest: None

Interstitial lung disease (ILD) associated with rheumatoid arthritis (RA) is an important prognostic organ disorder. The risk factors for the development of ILD are male, age, smoking history, as well as rheumatoid factor and anti-citrullinated peptide antibody (ACPA). It is often difficult to treat for such RA patients with ILD. Antigen-nonspecific ACPA has been produced in RA patients several years before the onset of the disease. Subsequent exposure to citrullinated proteins derived from joints and airway mucosa leads to the following steps: (1) presentation of citrullinated proteins to T cells via HLA-DRB1 (shared epitope) on antigen-presenting cells, (2) interaction of the T cells with B cells that recognize citrullinated protein antigens, (3) B cells differentiate and produce antigen-specific ACPA. ACPA-IgG produced by antigen-specific B cells is characterized by highly glycosylated variable regions and low affinity. Glycosylation of the variable region potentially modulates the signaling threshold of the B cell receptor (BCR), promoting B cell activation and differentiation and facilitating positive selection, while reducing affinity for non-self antigens and escaping negative selection. We focused on the tyrosine kinase Syk, which is downstream of the BCR, to investigate the abnormality of BCR signaling in RA patients and its involvement in the pathogenesis of RA. Syk phosphorylation in B cells was decreased after 6 months of treatment with abatacept (ABT). In a subanalysis of the AMPLE study, the highest DAS28 improvement with ABT was seen in RA patients with higher ACPA levels. In a small number of patients, the efficacy of ABT in RA-ILD was confirmed. These results suggest that ABT may have an effect on disease activity and ILD via regulation of B cell and ACPA production in RA. In this session, we would like to discuss the role of B cells including ACPA production, the mechanism of ILD in the pathogenesis of RA, and therapeutic strategies.

MS10-1

Current status of disease activity of Behçet's disease as determined from the Yokohama City University Behçet's Disease Registry

Yohei Kirino
Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine

Conflict of interest: Yes

Behçet's disease (BD) is a recurrent inflammatory disease with oral aphthous ulcers, genital ulcers, and skin and eye lesions as the major symptoms. Starting in 2019, we are promoting the YCU-BD registry, which consists of four institutions: Yokohama City University (YCU), Hokkaido University and Kitasato University, and Niigata University. The study will include a BD general disease activity index Behçet disease current activity form (BDCAF: how many of the 12 BD-related symptoms were present in the past month; a score of 0 on the BDCAF indicates no BD symptoms in the past month), a disease activity face scale (1-7) that patients themselves will judge, and a disease activity The YCU-BD registry analysis revealed a median BDCAF of 2 points for enrolled patients. Despite the fact that these patients were receiving adequate currently available medications, 53.2% of the patients had oral ulcers and 40.3% had residual arthralgia. The median BDCAF was 2 points, not only at Yokohama City University but also at other universities. Furthermore, the median score of the Face scale was 4 [IQR2-5], and the patient assessment also showed residual disease activity, which was also 4 at both Yokohama City University and the other universities. This indicates that many BD patients in Japan have residual disease activity even after currently available treatments. The clinical significance of this residual BD disease activity is unknown, but treatment strategies to reduce disease activity may improve patient prognosis, and a registry study is underway. With the use of apremilast, a treatment strategy aiming for a BDCAF score of 0 has become feasible. In this talk, I would like to discuss the current status of disease activity indices for BD and future T2T development.

MS10-2

Pathophysiology of articular symptoms in Behcet's disease

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Conflict of interest: Yes

Behcet's disease is a systemic inflammatory disease characterised by oral ulcers and a broad range of clinical manifestations. Vasculitis has been widely implicated in the pathophysiology of Behcet's disease, and activated neutrophils have been reported to be increased. On the other hand, Behcet's disease has both autoimmune and autoinflammatory features and is heterogenous as a disease, suggesting the involvement of multiple processes in its pathogenesis. Arthropathy is a common symptom of Behcet disease, which was reported the most prevalent in the knee, the ankle, and the wrist in a recently published Japanese study. However, only a small number of studies have reported whether the arthritic symptoms actually accompanied objective signs of inflammation such as swelling, and few studies have assessed the extra-articular inflammation. We and a group from Yokohama City University are now conducting a study together to localize the inflammation in Behcet's disease patients with arthritic symptoms using ultrasound. In this session, the preliminary results of this study in our hospital and representative cases will be presented and the pathophysiology of articular symptoms in Behcet's disease will be discussed.

MS11

SARS-CoV-2 infection and COVID-19 vaccination in people with rheumatic diseases

Takahiko Horiuchi
FCHO Fukuoka City Hospital, Fukuoka, Japan

Conflict of interest: Yes

A novel coronavirus known as SARS-CoV-2, which unexpectedly arose in end of 2019, is still troubling the entire human population and has affected healthcare system and the global socioeconomic balance. COVID-19 was quickly designated as a global pandemic by WHO and to date, has resulted in more than 30 million of infection and over 70 thousand fatal deaths in Japan. Since then, numerous new strains of SARS-CoV-2 have emerged, showing increased transmissibility and resistance to therapies. While new treatment drugs and vaccines have been developed, there are still many issues to explore, especially to understand the consequence of the infection on individuals for short term and long COVID. This pandemic has also led to more concern about people with an immune or inflammatory rheumatic disease. These patients, especially for those who have been treated with immunomodulatory drugs, are more prone to the development of severe COVID-19 than the general population. For these patients, it's important to continue their own treatment and reduce the risk of SARS-CoV-2 infection and severe COVID-19 with vaccination. Here we provide the updated information of COVID-19 in immune or inflammatory rheumatic disease patients in this seminar.

Luncheon Seminar

LS1

The Impact of Filgotinib for Achieving Clinical and Structural Remission

Daniel Aletaha
Division of Rheumatology Department of Internal Medicine 3, Medical University Vienna

Conflict of interest: Yes

On behalf of Gilead Sciences K.K. and Eisai Co., Ltd, please join us for a dynamic, live presentation by Prof Daniel Aletaha. This presentation will focus on the importance of early intervention for rheumatoid arthritis (RA) to prevent joint damage, as well as how a treat-to-target strategy and shared decision-making can help achieve optimal patient outcomes. It will also cover the latest clinical data for filgotinib, a once-daily oral Janus kinase inhibitor approved for the treatment of RA, in patients who have had an inadequate response to conventional therapies. Prof Aletaha will review recent EULAR recommendations that emphasize patient education and active patient involvement in the selection of treatment options, as well as the importance of early intervention in mitigating consequences of difficult-to-treat RA. Along with highlighting the role of early treatment with effective therapies to prevent structural damage, he will also discuss the importance of specific, stringent clinical trial remission endpoints, particularly Boolean remission, for evaluating RA disease activity. Prof Aletaha will summarize recent clinical evidence for the efficacy of 200 mg of filgotinib in combination with methotrexate (MTX) in reducing radiographic progression of joint damage and achieving clinical remission in the presence of poor prognostic factors. Data will also be presented regarding the safety of filgotinib from the clinical trials and ongoing long-term safety studies. The presentation will also provide an understanding of patient groups who may be good candidates for receiving filgotinib therapy, particularly patients who have experienced an inadequate response to MTX.

LS2

Beyond the glucocorticoid-dependent treatment in EGPA

Takahiko Kurasawa
Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan

Conflict of interest: Yes

Eosinophilic granulomatosis with polyangiitis (EGPA) is classified as anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis in CHCC 2012. However, the prevalence of ANCA in EGPA is only about 40%. EGPA patients have asthma, systemic symptoms (fever, body weight loss, and so on), and multiple organ lesions, such as paranasal sinuses, skin, heart, and nerves due to small to medium-sized vascular inflammation. A genome-wide association study revealed HLA-DQ was a risk allele in MPO-ANCA positive EGPA. On the other hand, GPA33 gene, which encodes a cell surface glycoprotein that maintains intestinal epithelial barrier function, and IL5 gene have a role in eosinophil inflammation[1]. Glucocorticoid (GC) and immunosuppressive agents such as cyclophosphamide for remission induction treatment and azathioprine for remission maintenance improve prognosis[2]. To improve the long-term prognosis, it is important not only to make an early diagnosis but also to control disease activity by induction therapy and remission maintenance therapy without flare. But GC-related adverse events are also a problem. Mepolizumab, anti -interleukin-5 monoclonal antibody has been approved for EGPA patients with refractory to GC therapy in Japan. In this seminar, I would like to discuss the role of mepolizumab to overcome conventional GC-dependent treatment. 1) Furuta S. et al. *Allergology International.* 2019; 68 (4), 430-436 2) Jpe White, S Dubey. *Autoimmun Rev.* 2022. Oct 22; 103219. Online ahead of print.

LS3-1

Treatment Strategies for Rheumatoid Arthritis by Nephro-rheumatologist

Naoki Sawa
Nephrology Center and Department of Rheumatology, Toranomon Hospital, Tokyo, Japan

Conflict of interest: Yes

In recent years, the prevalence of chronic kidney disease (CKD) in patients with rheumatoid arthritis (RA) has been reported to be approximately twice that in the general population, and disease activity of RA has been reported to be an independent factor in the progression of CKD in addition to general CKD risk such as hypertension and smoking. The ANSWER study reported that the lower RA disease activity, the slower rate of decline in eGFR. Therefore, the management of RA disease activity is important for suppressing the progression of CKD. However, RA patients with CKD are limited in the use of the key drug methotrexate (MTX). This is a dilemma for many rheumatologists, and biologics and JAK inhibitors are often required for RA patients with CKD. The characteristics of drugs that are desirable in RA patients with CKD include: 1. Maintenance of efficacy with monotherapy, and 2. Low urinary excretion of unchanged drug. In this lecture, I will discuss treatment strategies for RA in consideration of changes in physiological functions associated with decreased renal function.

LS3-2

Treatment strategies to avoid D2T RA and expectations for JAK inhibitors

Shingo Nakayamada
The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), clinical, structural and functional remission has become a realistic goal with appropriate early therapeutic intervention with conventional synthetic anti-rheumatic drugs (csDMARDs) such as methotrexate (MTX), and biological anti-rheumatic drugs (bDMARDs). However, only about 60% of patients achieve these goals, and the existence of difficult-to-treat RA (D2TRA), a group of patients who do not achieve remission with current pharmacological therapies, is becoming increasingly clear. D2TRA is an important unmet need in the treatment of RA and treatment for D2TRA is an urgent priority, but it is also important to establish treatment strategies to avoid D2TRA. Because of their multi-target effect on innate and acquired immune systems, Janus kinase (JAK) inhibitors have the potential to meet unmet needs of conventional therapies. The efficacy and safety of upadacitinib has been shown in multiple phase III trials (SELECT clinical trial program) and this drug was approved for insurance coverage for RA in 2020. Upadacitinib has been shown to be effective in patients with inadequate response to bDMARDs, thus is expected to be effective in D2T RA. Recently, long-term extension study of the SELECT-COMPARE phase III trial in patients with inadequate MTX response has been reported, in which upadacitinib maintained a significantly higher rate of remission achievement compared to adalimumab over a three-year period. Our FIRST registry suggested that upadacitinib may be more effective in the pre-D2T phase and may be more likely to achieve CDAI remission at earlier stages when fewer molecularly targeted drugs are used. In this seminar, we would like to discuss the remaining challenges in the treatment of RA, such as D2T RA, and discuss the expectations of JAK inhibitors in the strategy of avoiding D2TRA by inducing early remission.

LS4

Recent drug treatment strategies for osteoporosis

Satoshi Soen
Soen Orthopaedics, Osteoporosis and Rheumatology Clinic

Conflict of interest: Yes

The goal of osteoporosis treatment is to prevent fragility fractures. Alendronate, risedronate, zoledronate, denosumab, and romosozumab are the only drugs that have been confirmed to be effective in preventing all kinds of fractures including vertebral, non-vertebral, hip fractures in postmenopausal osteoporosis. Regarding the effect of preventing non-vertebral fractures, the type of non-vertebral fractures evaluated in each clinical trial is different. So, the preventing effect on non-vertebral fractures may be not useful for the drug selection. Nitrogen-containing bisphosphonates, SERMs, eldecalcitol, denosumab, teriparatide, abaloparatide, and romosozumab can reliably prevent vertebral fractures. Basically, the type of fracture to be prevented in each patient should be considered, and drugs should be selected based on the evidence of fracture preventing effects. On the other hand, when treatment is started because bone mineral density is in the osteoporosis range, the treatment goal is to get the bone mineral density out of the osteoporosis range. In addition, it is recommended to select drugs that have at least a 50% chance of achieving treatment goals within 3 to 5 years. It is also necessary to select drugs by taking into account the speed of bone mineral density increasing effect. For patients with recent fractures, it is desirable to select drugs that can rapidly reduce fracture risk. The clinical effects of zoledronate, risedronate, recombinant teriparatide, and romosozumab on patients with so-called imminent fracture risk have been confirmed in clinical trials. Since April of 2022, it has become possible to calculate secondary fracture prevention and maintenance fees after hip fractures, and the efficacy of zoledronate in such cases has been demonstrated in clinical trials. Various clinical trials have shown that sequential therapy from an anabolic agent to an antiresorptive agent produces a sustained effect of increasing bone mineral density. This sequential therapy is recommended for patients with a very high fracture risk according to overseas guidelines. Although the specific criteria for patients with a very high fracture risk differ according to each guideline, they are almost identical to the specific criteria for osteoporosis with a high fracture risk in Japan.

LS5

What about Hot Topics in PsA - focus on Guseikumab -

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Conflict of interest: Yes

Abstract. This presentation will focus on a number of important elements in the management of psoriatic disease. It will highlight the importance of a multi-domain approach so that any novel therapy must have efficacy across these domains. The transition from psoriasis to psoriatic arthritis will be explored and attempts with biologic disease modifying drugs (bDMARDs) to prevent progression will be shown. Further the importance of the IL23 pathway in the pathogenesis of the disease will be discussed leading to a presentation of guselkumab's efficacy and safety profile across domains in both bDMARD naïve and bDMARD inadequate responder PsA populations. Efficacy on patient reported outcomes such as work productivity will be demonstrated as well as considerations of efficacy compared with other IL23 inhibitors and place in the treatment algorithm.

LS6

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.

LS7-1

Management of elderly rheumatoid arthritis patients in a rural area: a case in Soso District, Fukushima, Japan

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Conflict of interest: None

The recent development of anti-rheumatic drugs has dramatically improved life and functional prognosis of rheumatoid arthritis (RA) patients. This improvement, in parallel with the increase in the number of elderly-onset RA (EORA), has raised the average age of RA patients. Management of elderly RA patients is different from that of younger patients in the following points: · Prolonged arthritis may increase the risks for fall and for becoming bedridden; · Asymptomatic pleural/ascites fluid due to decline in heart and renal function are often observed, which may increase risks of adverse effect of drugs; · Infection can easily lead to death or bedridden life; · Osteoporosis and fracture caused by corticosteroid usage may even aggravate life prognosis; · Visit adherence may decrease with age due to decline in physical functions; · Risk of medication error may increase with decline in cognitive functions; · Patients may at risk of polypharmacy before the development of RA; and · Coexistence of malignancy may cause aggravation of the symptoms. Especially, EORA patients are sometimes at higher risk of poor prognosis, because: · EORA patients often exhibit acute inflammation affecting large joints, and treatment delay may easily cause physical and cognitive dysfunction; and · Patients who are new to treatment are at higher risk of non-adherence and drug misuse. Given these conditions, management of elderly RA patients need to take account of all physical, mental, and social backgrounds and design hospital visit intervals, route of drug administration, social and familial support to fit the needs of each patient. In addition to this, streamlining human and medical resources by multidisciplinary approach is important at local healthcare facilities with few resources. In this seminar, the speaker will present tips of how to provide safe, effective, and patient-friendly care in a rural area, based on the speaker's own experience in Soso district, Fukushima.

LS7-2

JAK inhibitor therapy for aging population

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Conflict of interest: Yes

In recent years, Japan has the problem of aging. The proportion of elderly (population aged 65 and over) was 4.9% in 1950, has risen to 28.4% in 2019, and is expected to continue rising in the future (Cabinet Office data). It is natural that the average age of rheumatoid arthritis (RA) patients has been increasing, but interestingly, the age at onset of RA is also increasing (Kato E, et al. Int J Rheum Dis. 2017). In general, diseases in elderly need to be treated considering renal dysfunction, polypharmacy, cognitive dysfunction, and medication adherence. RA itself is an important risk factor for chronic kidney disease. Further consideration is necessary for elderly RA, as it affects the large/proximal joints and is accompanied by high blood IL-6 levels. In addition, advanced age as well as methotrexate were recently revealed to be risk factors for RA-associated lymphoproliferative disease (Honda S, et al. Mod Rheumatol. 2022). Taken together, the treatment of RA in elderly should mind renal dysfunction and the dependence on methotrexate. In this seminar, we will introduce the problems of RA treatment in an aging society, the characteristics of elderly RA, and the position of peficitinib, a JAK inhibitor whose metabolism does not depend on cytochrome P450 and the kidney.

LS8-1

Better practices in molecular targeted-therapy in rheumatoid arthritis: from a safety perspective

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Conflict of interest: Yes

Biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) are positioned as the standard treatment option of rheumatoid arthritis (RA). The market of b/tsDMARDs has expanded, thus seventeen b/tsDMARDs and biosimilars are available in Japan as of November 2022. It seems that those agents provide sufficient number of treatment option: on the other hand, rheumatologist should deeply understand the characteristics of those agents and suggest the appropriate agent to each patient considering their background characteristics including comorbidities. Japan has been a super-aged society since 2007, and its aging rate is still rising. Indeed, RA population has also aged, and approximately half of the patients are with age of over 65. Rheumatologist also need to understand the characteristics of elderly RA and suggest appropriate agent: however, insufficient evidence in this area has impeded domestic and foreign guidelines/recommendations to describe a specific flow in product selection in such. There is a global consensus that DMARDs are similarly effective in elderly as well as young. On the other hand, elderly RA comprise the issues: comorbidities such as chronic kidney diseases, lung diseases and malignancies; adverse reactions to DMARDs at a frequent rate; impaired treatment adherence due to polypharmacy, depression, or cognitive disorder. Elderlies are at high risks frailty and subsequent dependent or bedridden, therefore rapid RA disease control is important. Paradoxically, there is the trend that rheumatologist refrain from aggressive treatment in elderly RA and it may cause the delay of treatment. Given those backgrounds, this session will discuss better practices in RA treatment form the safety perspective, addressing findings from a cohort study: FIRST registry.

LS8-2

Therapeutic strategy for preventing chronic kidney disease progression in elderly patients with rheumatoid arthritis

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Conflict of interest: Yes

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. Caution should be exercised when increasing 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. Here, we discuss therapeutic strategy for elderly RA patients to prevent CKD progression.

LS9

Antiphospholipid antibody syndrome: An up-to-date overview

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Conflict of interest: None

Antiphospholipid antibody syndrome (APS) is an autoimmune disease characterized by arterial thrombosis, venous thrombosis and obstetric complications mediated by antiphospholipid antibodies (aPL), including

anticardiolipin antibodies (aCL), anti-β2 glycoprotein I antibodies (ab2GPI), and lupus anticoagulant (LA). LA can be detected by their anticoagulant properties in coagulation tests such aPTT (with low concentration of PL, aPTTL) and DRVVT (dilute Russell's viper venom time). aCL is the most employed aPL antibody assay, performed by coating an ELISA plate with CL. The aCL ELISA detects both direct aCL and aβ2GPI. aβ2GPI assay involves coating purified human β2GPI on the surface of an irradiated plate. aβ2GPI assay should detect a greater number of pathogenic samples than the aCL assay. However, there exists nonpathogenic antibodies. Persistent positivity for aPL in conjunction with clinical events forms the cornerstone for the diagnosis of APS. APS patients can be stratified in terms of the risk of future thrombotic events, according to the aPL profile and the individual risks of thrombosis. Triple positivity, including LA, aCL, and aβ2GPI was a strong independent risk factor for arterial or venous thrombotic events. The antiphospholipid score (aPL-S) and the Global APS score (GAPSS) were developed for an individual thrombotic risk assessment. There is no specific treatment for APS. Since antithrombotic medications are still the only established therapy, clinicians prevent thrombosis according to the risk stratification. Further studies, particularly prospective randomized controlled trials, are highly warranted to establish an effective and tolerable treatment regimen for high risk aPL carriers. We aim to generate evidence in Japan by establishing a large Japanese cohort of patients with APS (J-RAPS).

LS10

Optimal management for patients with rheumatoid arthritis to improve patient satisfaction

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Conflict of interest: Yes

In recent years, pharmacological treatment of rheumatoid arthritis (RA) has rapidly progressed, and it has become possible to achieve comprehensive remission, but it is necessary to implement optimal management in order to increase patient satisfaction. Early pharmacological intervention and strict treatment are the main principles of RA management. Diagnosis should be performed as early as possible and then treatment should be initiated in accordance with the algorithm for pharmacological treatment of the RA Clinical Practice Guideline 2020. Cost-effectiveness is important for increasing patient satisfaction. By practicing treat-to-target using a composite measure that includes joint findings, it is possible to control disease activity with a lower level and to increase cost-effectiveness. In order to increase cost-effectiveness, the use of biosimilars is important. Comparable efficacy has been confirmed in trials comparing the original and biosimilar TNF inhibitors. In the RA Clinical Practice Guideline 2020, biosimilar DMRDSs are recommended as same as bio-original DMARDs. Some RA patients whose functional disability progresses despite strict treatment are observed. According to the algorithm for non-pharmacological and surgical treatment in the RA Clinical Practice Guidelines 2020, conservative treatment such as rehabilitation therapies and joint injections are recommended in phase I when joint dysfunction is confirmed. There is a lot of evidence that exercise therapies improve HAQ and muscle strength as well as RA patient satisfaction. Occupational therapies have also been shown to improve HAQ, AIMS-II, and grip strength. In the RA Clinical Practice Guidelines 2020, both therapies are strongly recommended. Surgical treatment is recommended in cases that are refractory to pharmacological treatment and rehabilitation therapies. When functional impairment and deformity are severe, evidence-based surgery should be selected for each joint and performed at the appropriate timing. It is thought that the surgical treatment for refractory cases can improve patient satisfaction. In this lecture, I would like to discuss the optimal management of RA to improve patient satisfaction, presenting recommendations and evidence.

LS11

Which Way to Go at the Junction of Pulmonary Arterial Hypertension Treatment Flow - Comorbidities, Initial Treatment, and Treatment Intensification-

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Conflict of interest: Yes

Pulmonary arterial hypertension (PAH) is one of the most serious organ involvements in connective tissue disease (CTD). Selective vasodilators have provided a significant impact on clinical practice. In this context, CTD-PAH, along with other forms of PAH including idiopathic PAH, has been included in clinical trials and registry studies to accumulate evidence and has shared updates in diagnostic criteria, risk assessment, and treatment algorithms. Recently, a European registry identified a subgroup of idiopathic PAH with cardiopulmonary comorbidities that are older and present with left ventricular diastolic dysfunction and decreased respiratory function. These populations are considered at risk and have worse outcomes compared to younger patients without comorbidities. Therefore, it is recommended to start with monotherapy, followed by sequential combination therapy depending on the pathophysiology of each patient. The European guidelines for pulmonary hypertension, revised in 2022, distinguish between combination therapy for patients without comorbidities and monotherapy for those with comorbidities. A recently reported post-hoc analysis of the GRIPHON trial of selexipag showed efficacy regardless of comorbidities. Initial treatment is divided into oral and intravenous, depending on the grade of risk. The post-hoc analysis of the GRIPHON trial showed efficacy of adding selexipag in patients with inadequate response to treatment with PDE-5 inhibitors and endothelin receptor antagonists, and this was incorporated into the new treatment algorithm. Thus, the treatment of PAH patients now requires individualization of vasodilator based on each condition and disease state. Furthermore, CTD-PAH is more complex and specific than other forms of PAH, and requires detailed evaluation and management. In this talk, I will discuss how to evaluate the pathophysiology, determine which way to proceed at a critical junction at the flow of PAH treatment algorithms.

LS12-1

Optimal molecular-targeted drug selection for D2TRA derived from clinical data

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Conflict of interest: Yes

The advent of biologics has brought about a paradigm shift in the treatment of rheumatoid arthritis. However, there are still some patients with rheumatoid arthritis who are refractory to treatment, such as patients with difficult-to-treat rheumatoid arthritis (D2TRA), a group of RA patients who are refractory to molecularly targeted drugs with different mechanisms of action, but who have residual disease activity and are unable to reduce glucocorticoids. The treatment of choice for this D2TRA patient is one of the major clinical questions. In the FIRST registry, a cohort of RA patients in our department, we focused on patients with D2TRA who were refractory to multiple molecularly targeted drugs and analyzed which molecularly targeted drugs were appropriate for these patients. Among 2128 RA patients, there were 353 RA patients were ineffective with two or more molecularly-targeted agents. After adjusting for PS-IPTW, the JAK inhibitor group significantly improved CDAI compared to the other biologic groups. This suggests that JAK inhibitors may be suitable for RA patients who have failed multiple molecularly targeted agents. Although in vitro analyses of JAK inhibitors have revealed differential effects on cytokine signaling, differences in efficacy and safety in real-world clinical practice are unclear. We compared the efficacy and safety of 156 RA patients treated with tofacitinib and 138 RA patients treated with baricitinib from the FIRST registry, adjusted for selection bias using PS-IPTW. The results of the study then revealed a patient population for whom baricitinib may be suitable. These results suggest that JAK inhibitors may be suitable for treating D2TRA, in which baricitinib may play an important role.

LS12-2

The role of JAK2 inhibition in the treatment of RA ~Therapeutic strategies to prevent patients from developing difficult-to-treat RA~

Ryu Watanabe

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Conflict of interest: Yes

Difficult-to-treat rheumatoid arthritis (D2T RA) refers to patients with RA whose disease activity is uncontrolled despite the use of two or more biologics or JAK inhibitors with different mechanisms of action. D2T RA not only reduces patients' QOL but also confers a socioeconomic burden. Therefore, it is extremely important to develop treatment strategies to prevent D2T RA, rather than to treat D2T RA. We have previously reported the following predictive factors for D2T RA: (1) seropositivity (especially RF), (2) high disease activity at initial diagnosis, and (3) the presence of pulmonary lesions. For patients with multiple predictive factors, earlier therapeutic intervention with b/tsDMARDs is mandatory. But how should we treat such patients? Baricitinib primarily inhibits JAK1 and JAK2, and the RA-BEAM study, which included a large number of seropositive, MTX-IR patients with high disease activity, demonstrated superiority over adalimumab in ACR20 response rates after 12 weeks of treatment as a secondary endpoint. In addition, evidence has accumulated not only for rapid improvement in patient-reported outcomes and long-term inhibition of joint destruction, but also for safety in Japan and overseas. Furthermore, recent studies have revealed that JAK2 is highly expressed in RA-associated interstitial lung disease (ILD). In animal models, the efficacy of selective JAK2 inhibitors has been reported in bleomycin-induced ILD. There are also some emerging reports in humans regarding the use of JAK inhibitors in RA-ILD patients. This suggests that among many JAK inhibitors, baricitinib may be effective for patients who have multiple predictive factors for D2T RA. In this seminar, in addition to recent topics of RA, the latest findings on D2T RA will be presented, and we would like to discuss the significance of JAK2 inhibition using baricitinib to prevent patients from developing D2T RA.

LS13-1

Considering pathogenesis-based treatment of elderly rheumatoid arthritis

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Conflict of interest: Yes

The number of elderly patients with rheumatoid arthritis (RA) and elderly-onset RA is rapidly increasing due to the aging of the population. It is well known that the acute onset, large joint-dominant lesion distribution, male patients, and autoantibody-negative cases are relatively higher in elderly-onset RA than in nonelderly-onset RA, making it difficult to differentiate polymyalgia rheumatica from other types of RA in many cases. Because of the difference in genetic background between non-age-onset and age-onset RA patients, changes in gene expression of immune cells are expected to occur. In addition, age-associated B cells (ABCs) and cytotoxic CD4+ T cells increase with age, and these immune cells are thought to contribute to the pathogenesis of RA. In elderly RA patients, clinical reserve is limited due to physiological decline in liver, kidney, and other functions, and immune aging. Delays in appropriate treatment are quickly linked to a decline in activities of daily living. Therefore, it is desirable to select a treatment with an excellent balance of efficacy and side effects according to the pathophysiology of each individual case, such as the presence or absence of autoantibodies, at an early stage of RA onset. In this lecture, I would like to outline the pathophysiology of elderly RA and discuss the treatment strategy.

LS13-2

Treatment strategies for elderly rheumatoid arthritis using b/tsDMARDs derived from the FIRST registry

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Conflict of interest: None

The population aging rate is increasing all over the world. As of October 1, 2021, Japan's total population is 125.5 million, the population aged 65 and over is 36.21 million, and the aging rate is 28.9%, the highest in the world since 2005. The aging rate of the world population has risen to 9.3% in 2020 and is anticipated to grow to 17.8% in 2060. Furthermore, it is anticipated that the aging of the population will progress in an unprecedentedly shorter period in the developing regions. Various kinds of bDMARDs and tsDMARDs that are highly effective have become available, and remission is an achievable and realistic goal. In Japan, a super-aging society, establishing a treatment strategy for elderly patients with rheumatoid arthritis is an urgent issue. Establishing this treatment strategy could be a model case for other countries. Methotrexate and bDMARDs, tsDMARDs are essential treatment options for achieving treatment targets in elderly RA. On the other hand, in elderly RA, the risk of adverse events may inevitably increase due to lower ADL, comorbidities, and organ dysfunction. Inadequate control or relapse of RA disease activity may also exacerbate comorbidities. Therefore, it is essential to use drugs appropriately and continuously in elder RA patients. By June 2022, 1147 RA patients had been treated with b/tsDMARDs in our department for more than five years (FIRST registry). Five hundred sixty-eight cases (49.5%) were less than sixty-five years old, 361 patients (31.5%) were semi-elderly, aged between 65 and 75 years old, and 218 cases (19.0%) were aged 75 years or older. There was no difference in treatment retention rates among age groups. On the other hand, COX proportional model in each age group revealed that; the decrease in non-responder by IL-6 receptor antibody contributed to increasing the retention rate in semi-elderly people; the use of TNF inhibitors was associated with drug-free remission. In the elderly population, the decrease in discontinuation due to adverse events with the use of CTLA4-Ig contributed to the increase in the treatment retention rate. In treating elderly RA patients, since the characteristics of each drug vary among the age groups, it is crucial to establish a treatment strategy according to the features of the drugs.

LS14

SLE/LN Treatment UPDATE - Overview of the latest treatment targets -

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) exhibits a diverse clinical course and organ damage due to its complex pathogenesis. The goals of treatment for SLE include ensuring long-term survival, achieving the lowest possible disease activity, preventing organ damage, minimizing drug toxicity, improving quality of life, and educating patients about their role in disease management. In the treatment of SLE, the EULAR treatment recommendations and Japanese guidelines for SLE treatment should be consulted. Once treatment is initiated, medications should be adjusted periodically based on the Treat-to-Target (T2T) algorithm, targeting the disease activity index. Recent advances in omics research have led to a better understanding of the etiology and pathogenesis of SLE, as well as the development of cell- and molecular-targeted agents, and newly approved therapies provide more treatment options. Lupus nephritis (LN) is occurring in approximately 40% of patients with SLE, with LN (+) having twice the mortality rate as LN (-), making LN the only prognostic SLE organ disorder. In LN, it is important to achieve a rapid decrease in urinary protein and to maintain renal function. Glucocorticoids (GCs), hydroxychloroquine, mycophenolate mofetil, and intravenous cyclophosphamide are used to achieve remission, and if not achieved, third-line therapy is added. In recent years, a variety of drugs are being developed for LN as SLE, including biologics, but only a limited number are currently in the clinical. The optimal use of both SLE and LN therapies, including those in developing will be necessary to maintain low disease activity while minimizing the use of GCs. In this seminar, I will review the key points to be considered in the daily treatment of SLE/LN, and present an overview of the latest therapeutic targets, as well as the future prospects for research required for further personalized medicine, referring to examples of other diseases.

LS15

The Evolution of RA Therapy From Biologics to the JAK Inhibitor Filgotinib: Aiming for Clinical and Structural Remission

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Conflict of interest: Yes

On behalf of Gilead Sciences K.K. and Eisai Co., Ltd, please join us for an interactive, discussion-based session chaired by Prof Yoshiya Tanaka. This session will include a short presentation from Prof Daniel Aletaha followed by a panel discussion with Japanese experts Prof Funakubo and Drs Ikeda, Kirino, and Kubo. Key topics in the session will include the evolution of rheumatoid arthritis (RA) therapy over time, the importance of early intervention for RA to prevent structural damage, and how a treat-to-target strategy and shared decision-making can help achieve optimal patient outcomes. He will also discuss the importance of specific, stringent clinical trial remission endpoints, particularly Boolean remission, for evaluating RA disease activity. The session will highlight the utility of filgotinib, a once-daily oral Janus kinase inhibitor approved for the treatment of RA, and will include a review of the latest clinical data for filgotinib in patients who have had an inadequate response to conventional therapies. The program will begin with a short presentation by Prof Aletaha that will summarize recent clinical evidence for the efficacy of 200 mg of filgotinib in combination with methotrexate (MTX) in reducing radiographic progression of joint damage and achieving clinical remission in the presence of poor prognostic factors. Data will also be presented regarding the safety of filgotinib from the clinical trials and ongoing long-term safety studies. The presentation will also provide an understanding of patient groups who may be good candidates for receiving filgotinib therapy, particularly patients who have experienced an inadequate response to MTX. Following the presentation there will be an interactive panel discussion featuring Japanese experts discussing the key topics identified above and sharing their clinical perspectives on the use, efficacy, and safety of filgotinib, as well as its position in the RA treatment landscape.

LS16-1

The novel perception and choice of therapy in peripheral psoriatic arthritis (PsA) ~The most useful procedure no need to get lost about early diagnosis and treatment of PsA by using the musculoskeletal ultrasound (MSKUS)~

Kenta Misaki
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Conflict of interest: Yes

The underlying pathogenesis and disease concept of PsA make a great change during the one decade. Specifically, it is already reported the PsA prevalence from psoriasis: PsO achieved up to around 30% also in Japan, also revealed PsA is one of the severe bone destructive diseases as in the case with rheumatoid arthritis: RA. It is easily suggested PsA should be required both early diagnosis and early treatment-strategy under the consideration of the available treatment agents such as MTX, biologics and JAKi as well as RA. Moreover, the PsA risk factors about the onset or subclinical course of PsA were newly defined recently, we Rheumatologist should approach to PsA with the same intensity as RA. The Imaging procedures make it possible to lead to early diagnosis of PsA. Especially, MSKUS can depict the real-time pathological findings of PsA with no harm, it has been reported the precious evidence concerned with MSKUS these days. MSKUS focused on peripheral region make a huge contribution to both the early diagnosis and early treatment in terms of detecting subtle pathological findings of PsA and enable to stratify the each component of PsA, administrate Bio appropriately based on the PsA treatment recommendations: EULAR2019, GRAPPA2021. I'll introduce the strategy of early peripheral PsA diagnosis focused on MSKUS pathological findings and differential diagnosis including the utility and novel evidence of Secukinumab to the peripheral PsA.

LS16-2

Advances in the Treatment of Axial Spondyloarthritis

Hiroaki Dobashi
Kagawa University

Conflict of interest: Yes

Spondyloarthritis (SpA) is often discussed separately into diseases that are predominantly axial lesions or predominantly peripheral lesions. Psoriatic arthritis (PsA) is a well-known representative of spondyloarthritis that mainly consists of peripheral joint lesions. On the other hand, ankylosing spondylitis (AS) is considered to be the representative disease with axial lesions predominate. However, even in PsA, in which peripheral joint lesions are considered to be the predominant form of spondyloarthritis, there are a small number of axial lesions. Moreover, axial lesions are clearly a major burden in PsA and are considered a target for treatment. In addition, non-radiographic axial spondyloarthritis (non-radiographic axial SpA) is now recognized as a new disease category of axial spondyloarthritis. The concept of non-radiographic axial spondyloarthritis (non-radiographic axial SpA) was conceived for early diagnosis before progression to AS, but not all cases of non-radiographic axial SpA will progress to AS. Therefore, the diagnosis of non-radiographic axial SpA and therapeutic intervention should be carefully considered. In other words, enough attention should be paid to over diagnosis and over treatment, including differential diagnosis. On the other hand, advances in clinical immunology and the results of clinical trials of new therapeutic agents have established treatment strategies based on cytokine taxonomy, and various options exist for therapeutic intervention for these SpA. Among them, TNF-α inhibitors were approved for AS and PsA ahead of other biologics. Subsequently, as basic and clinical research related to the pathogenesis of SpA progressed, medicine that inhibit IL23-IL-17axis and JAK inhibitors were developed one after another in addition to the aforementioned TNF-α inhibitors. Among them, IL-17 inhibition has demonstrated short- and long-term efficacy and safety in the treatment of peripheral joint lesions and axial spondyloarthritis. However, the optimal use of these numerous biologics remains inconclusive. Especially in non-radiographic axial SpA, there are many problems such as criteria for therapeutic intervention and evaluation of efficacy. In this seminar, I will discuss the importance of diagnosis and the necessity of therapeutic intervention for axial spondyloarthritis, including non-radiographic axial SpA with case presentations at our own hospital.

LS17

Tofacitinib, a clinically effective JAK inhibitor in the treatment of Rheumatoid Arthritis and safety lessons learned from Oral Surveillance

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Conflict of interest: Yes

RA therapy has changed dramatically since the introduction of aspirin (1897), gold salts (1930s), GCs (1950's), MTX (1980's), bDMARDs (1998) and earlier treat to target this century. However, we still see patients not effectively treated and have concerns with toxicity. Tofacitinib, introduced in 2013 in Japan, was the first oral advanced therapy for RA. The phase 3 ORAL trials demonstrated clinical and radiographic effectiveness in patients who failed csDMARDs as monotherapy (ORAL-SOLO), in combination with csDMARDs (ORAL-SCAN), and in patients who failed TNF inhibitors (ORAL-STEP). ORAL-STRATEGY demonstrated tofacitinib and adalimumab are equally effective in an incomplete responder to MTX. The trials also showed that the effects of tofacitinib in combination with MTX is non-inferior to TNFi but also demonstrated instances of lipid, creatinine, CPK, and hepatic enzyme elevations, hematopoietic effects, and a higher risk of HZ. ORAL-SURVEILLANCE demonstrated the relative safety of tofacitinib to TNFα in older patients at high risk for CV events. The results showed that the incidence of MACE and malignancies were higher with the combined tofacitinib 5 and 10 mg BID doses vs TNFi and did not meet non-inferiority criteria; these risks were predominantly seen in a subset of patients with age ≥65, smokers, a preceding or high degree of risk of CV events, a past VTE and in patients with persistent disease activity. Because of the clinical trial results, tofacitinib has become an important therapeutic in the treatment of RA because of its efficacy in those who respond, its potential as monotherapy and its convenience as an oral therapy. In a patient with an incomplete response to MTX, there are

patients who prefer tofacitinib over a bDMARD for these reasons. In a situation where a TNF is required to be prescribed first, such as the US, tofacitinib may be the option of choice for the above reasons with its demonstrated efficacy in TNF failures.

LS18

TNF Inhibitors -Thinking about the Present of this Old and New Drug

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Conflict of interest: None

More than 20 years have passed since the introduction of biologics for RA treatment. In Japan, it started with TNF inhibitors, and as of December 2022, 6 TNFis are available, excluding Bio Similar. Recently, completely new antibody biologic adopting nanobody for RA has been also a TNFi, which shows that TNFis still an attractive target in RA treatment. Whereas, although they target the same TNF, they have a wide variety of characteristics and are used based on theirs in actual clinical practice, which is in contrast to IL6 inhibitors. In this presentation, I will discuss the common characteristics of TNFis and the characteristics of individual of them, which have not lost their value even after more than 20 years and continue to be developed anew. Generally, TNFis have rapid onset of efficacy and solid prevention of joint destruction. Whereas it's necessary to pay attention of tuberculosis, therefore it made physicians assess risk of infection while biologics introduction, and ensure the procedure of prophylactic administration. Later of this presentation, I'll recent consider notable characteristics of Golimumab (GLM). GLM is a drug for which post-marketing surveillance has shown that age is not a risk factor for severe infections. It's interesting to note that binding sites of TNF to the two types of TNF receptors may be relevant to the safety of the TNF antibody product. GLM is a fully human antibody produced by the transgenic mouse, and is a product with low immunogenicity that can be expected to have efficacy without MTX, and is suitable for patients who have to stop or reduce MTX for some reason such as advanced age or deterioration of liver or kidney function. Finally, I'd like to briefly mention some points to be noted that are relevant to the current situation of the COVID19 pandemic in terms of side effect measures for pneumocystis pneumonia, which have become particularly important after TNFi launch.

LS19

New insights into the roles of TNF-alpha for the pathogenesis of rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid Arthritis is a chronic inflammatory disorder that affects large and small synovial joints and leads to joint destruction and permanent irreversible damage to the joints. During the last 20 years, targeting inflammatory cytokines including TNF-alpha has led to important therapeutic effects in rheumatoid arthritis while these effects are not sufficient. Therefore, further studies will be required to investigate the roles of inflammatory cytokines for the pathogenesis of rheumatoid arthritis. In the present talk, we will summarize the recent studies showing the effects of inflammatory cytokines on the development of rheumatoid arthritis and provide new evidence that targeting TNF-alpha is effective for joint protection.

LS20-1

A major issue in rheumatoid arthritis treatment in Japan -Aging of rheumatoid arthritis patients-

Takao Fujii
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Conflict of interest: Yes

Although rheumatoid arthritis (RA) care has improved, several issues still exist. One of them is the aging of RA patients. The number of RA patients in Japan is estimated to be approximately 825,000 from the National Database of Health Insurance Claims and Specific Health Checkups (Nakajima A, *et al. Int J Rheum Dis,* 2020). By age group, 70-79 year-old patients accounted for the most (28.6%), followed by 60-69 year-old at 26.4%. On the other hand, the proportion of 45-59 year-old is 14.9%, that is lower than the 16.8% of patients over 80 years old. Interestingly, aging of RA patients appears not to be observed in the United States (Myasoedova E, *et al. Ann Rheum Dis,* 2020). According to the RA Clinical Practice Guidelines 2020, the treatment goal is "to improve long-term prognosis, especially maximizing QOL and improving survival by reducing disease activity in RA and inhibiting the progression of joint destruction". T2T strategy should be performed even at an advanced age when there are few complications. In that case, attention should be paid to the reduced potential organ function. Because unexpected infections, dehydration, and bone fractures may rapidly worsen the general condition, side effects of drugs may become apparent. The biggest problem is elderly people with multiple medical diseases such as diabetes mellitus. If patients are more than 75 years with risk factors for infection, shared decision making (SDM) with the patients (and/or family) is important. If SDM is not performed, the "improvement of survival" will not be achieved. At the same time, in the case of elderly RA, it is important to achieve the treatment goal as early as possible. Treatment focused on safety alone leads to irreversible frailty, resulting in an increased risk of infection. Since elderly RA might be a heterogeneous population compared to non-elderly RA. In this presentation, how to maintain the QOL desired by patients and what treatment should be selected, will be discussed.

LS20-2

Role of IL-6 inhibitors for elderly onset rheumatoid arthritis

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Conflict of interest: Yes

With aging of the society, not only "elderly" rheumatoid arthritis (RA) patients but also "elderly onset" RA (EORA) patients are increasing. EORA has unique characters; tends to be seronegative, more affects large joints than small joints, presents with abrupt onset, and shows high inflammatory state compared with young onset RA (YORA). Although previous reports suggested the benign prognosis for joint destruction, recent real-world data revealed more aggressive phenotype of EORA for bone destruction. IL-6 may be involved with that process because IL-6 have a highly inflammatory property with osteoclastogenic capacity. Indeed, in our ANSWER cohort study, the drug retention rates were higher in IL-6 inhibitors than in TNF inhibitors. Elderly patients sometimes develop other rheumatologic conditions, such as polymyalgia rheumatica (PMR), remitting seronegative symmetrical synovitis (RS3PE), or giant cell arthritis (GcA). All these diseases present with common conditions such as high CRP, anemia of chronic disease, high VEGF, and constitutional symptoms. These features may be caused by "senescence-associated cytokines" including IL-6 caused by "inflammaging". In EORA patients, methotrexate (MTX) treatments are often avoided due to renal dysfunction or lung complications, and glucocorticoids (GCs) are frequently used to rapidly relieve symptoms. However, it should be noted that GCs treatment are accompanied by a number of complications such as infection and osteoporosis especially in elderly patients. Because trained rheumatologists can use IL-6 inhibitors safe even in elderly patients, early introduction of IL-6 inhibitors may be much more beneficial for EORA patients if we could reduce the dose of MTX or GCs. In this seminar, pathogenic mechanism of EORA and role of IL-6 inhibitors will be discussed.

LS21

Orthopaedic treatment for rheumatoid arthritis in the new era

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Conflict of interest: Yes

Due to the paradigm shift in the treatment of rheumatoid arthritis (RA), many biologics and JAK inhibitors are now available to control inflammation. However, it is reported that about 75% of cases still fail to achieve remission, partly because of complications and other factors that prevent adequate drug therapy. The total number of surgical treatments for RA has decreased after the paradigm shift. RA surgeries, especially artificial joint surgeries for weight-bearing joints in the lower extremities, have decreased. On the other hand, the number of joint arthroplasties has increased slightly. Deformity of hands and feet progresses even when disease activity is low. The problem of joint instability due to degeneration of soft tissues remains. For this reason, the degree of locomotor dysfunction in RA increases as the duration of disease increases, and drug therapy has increased ADL in rheumatoid arthritis patients, increasing the demand for surgical therapy for small joints. By soft tissue reconstruction while controlling inflammation with drug therapy, the results of artificial joint arthroplasties of small joints, which were difficult in the past, have improved. We have obtained good postoperative results with a combination of tight control by both drug therapy and surgical therapy by a new approach. From 2022, the Japanese Medical Specialty Board have started the "specialist in collagen disease and rheumatoid arthritis". Rheumatologists whose basic field is orthopedics became academically-certified rheumatologists rather than Japanese Medical Specialty Board -certified specialists. In recent years, the number of rheumatologists who specialize in orthopedics has decreased dramatically among the younger generation. RA patients inevitably accompany locomotor disorders as described above when the disease duration is long. Orthopedic surgeons should play a central role in the management and treatment of musculoskeletal disorders.

LS22

Herpes zoster in patients with rheumatoid arthritis and prevention by vaccines. An update

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Conflict of interest: Yes

aricella-zoster virus (VZV) initially infects patients with chickenpox, then latently infects ganglion cells in the cerebrospinal cord, resulting in herpes zoster several years to several decades later. VZV is the only herpesvirus that infects humans epidemically and the only vaccine-preventable virus. The risk of developing herpes zoster is increased by aging, immunosuppressive conditions such as hematologic diseases and SLE. Recently, the risk of herpes zoster has been shown to be higher under the administration of Janus kinase (JAK) inhibitors, which have become available with advances in the treatment of rheumatoid arthritis, ulcerative colitis, psoriatic arthritis, and atopic dermatitis, and is even higher among Japanese and patients with a history of herpes zoster. Early administration of antiviral drugs is the principle treatment for herpes zoster under JAK inhibitor therapy, but vaccine prophylaxis is currently available. There are two types of vaccines that can be used against shingles in Japan: attenuated live varicella vaccine and recombinant herpes zoster vaccine (RZV). The attenuated live varicella vaccine has been widely used as a routine vaccine against varicella since 2014 in children, and the indication was expanded in 2016 for shingles. However, because it is a live vaccine, it cannot be used in patients on immunosuppressive drugs including corticosteroids and JAK inhibitors, such as rheumatoid arthritis, because it may enhance or sustain vaccine virus infection. On the other hand, the recombinant herpes zoster vaccine (RZV), which has been available in Japan since January 2020, is a subunit vaccine containing VZV glycoprotein E as the active ingredient and AS01B as an adjuvant, and is the only herpes zoster vaccine designed for use in patients at high risk of developing herpes zoster due to immunodeficiency or immunosuppression from pre-existing conditions or treatments. This presentation will introduce the survival strategy of VZV from the cycle of initial infection - latent infection - reactivation, and will also outline the characteristics of herpes zoster caused by JAK inhibitors, which has recently attracted attention regarding the disease burden of herpes zoster. The recombinant herpes zoster vaccine (RZV), which is currently the focus of much attention, will be presented, including its preventive efficacy, safety (adverse reactions), and the newly published data on its long-term efficacy of approximately 10 years (follow-up: 81.6%/overall observation period: 89.0%) and on rheumatoid arthritis overseas.

LS23-1

Treatment status and issues of rheumatoid arthritis seen from epidemiological data - Issues of WoCBA-RA generation -

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Conflict of interest: None

Over the last two decades, treatment of rheumatoid arthritis (RA) has improved dramatically owing to biologic disease-modifying antirheumatic drugs (bDMARDs). According to the National Database of Japan (NDB Japan), more than 800,000 people are affected by RA and about 70% of patients visit special institutions for rheumatic diseases at least once in the year. Overall, methotrexate was prescribed to 63% of patients and bDMARDs to 23%. RA can affect peoples called as WoCBA (women of childbearing age). A recent study investigated whether patients and physicians discussed family planning at the beginning of treatment and thereafter. About half of WoCBAs with rheumatic diseases reported that there was a delay in deciding to have children due to fear of passing the disease to their children. These data reaffirm the importance of preconception care. According to NDB Japan in 2017, 28-40% of 28,000 aged 20-39 years and 58,000 aged 40-49 years of RA women with WoCBA generation were treated with bDMARDs. However, NDB Japan lack data on family planning, including the desire to have children, so it is unclear whether this proportion of bDMARD use is appropriate. By validating the use of bDMARDs, we hope that bDMARDs will be economically accessible to RA patients who need them, and that they will be able to live their lives as if they were RA-free.

LS23-2

Treatment strategies for young patients with rheumatoid arthritis considering life stages

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Conflict of interest: Yes

Treatment strategies for young women with rheumatoid arthritis (RA) should account for the long duration of disease and stage of life (i.e., employment, pregnancy, childbirth, childcare, return to work). The Certolizumab- Optimal Prevention of joint damage for Early RA (C-OPERA) study reported that 30% of patients treated with methotrexate using rapid escalation experienced progressive joint destruction. Early joint destruction has an impact on functional disability and persists thereafter. To reduce the progression of early joint destruction, it is important to identify patients who require intensified therapy and to promptly transition them to phase 2. Shared decision making is the foundation of treatment selection; however, if the patient is of childbearing age, placental delivery and lactation effects should also be considered as a factor for beneficial dosing. The pregnancy, gestational age, and postpartum findings is also information that should be shared with RA patients. The importance of early remission induction, as well as maintenance of remission after delivery and into the long term, will be discussed. There are many factors to consider in the treatment of young patients with RA, including the basic concepts of RA treatment, the use of methotrexate, the principles of joint destruction, the introduction of biologic agents, and the maintenance of long-term function. The authors anticipate that this lecture will provide learning opportunities that can be directly applied in clinical practice.

LS24-1

Hypophosphatosis - Challenges from Diagnosis to Treatment

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Conflict of interest: None

Hypophosphatasia (HPP) is an inherited skeletal dysplasia caused by deficiency or dysfunction of tissue-nonspecific alkaline phosphatase. It is currently classified into six clinical forms (perinatal severe, perinatal benign, infantile, pediatric, adult, and odonto-type). In all types, a decrease in serum ALP activity compared with normal values for each age group is the trigger for diagnosis. Currently, the diagnosis of HPP is based on the

"Clinical Practice Guidelines for Hypophosphatasia (2019)" published by the Japanese Society for Pediatric Endocrinology, which is also overviewed here. In Japan, the perinatal form of HPP has been reported most frequently, but recently the adult form has also been reported. The adult form has a wide range of symptoms, including bone fractures, pseudo-fractures, osteomalacia, muscle weakness, myalgia, arthralgia, headache, and dental symptoms such as premature loss of primary teeth and permanent tooth eruption. The severity of symptoms varies from relatively mild to severe. There are limited reports of HPP in Japanese adults in the literature, and it is possible that the disease is underestimated due to lack of awareness of the disease. In particular, it has been reported that the use of bisphosphonates may promote bone fractures in patients with HPP, so it is important to correctly diagnose the disease and to consider the indications for treatment. In this lecture, I will present the diagnosis, treatment, and course of two cases of adult-onset HPP, and discuss the points to be considered in the diagnosis of adult-onset HPP, as well as challenges in the diagnosis and management, including cooperation with other departments and multiple professions, based on experience. The main symptom of this disease is likely to be arthralgia or generalized pain, and it is possible that the patient may visit a rheumatology department. Therefore, it is important to consider the timing of referring the patient to the rheumatology department, in addition to the collaboration system among multiple departments including endocrinology, genetic medicine, orthopedics, oral surgery, and rehabilitation medicine.

LS24-2

Pathogenesis and differential diagnosis of osteoporosis: key points for imaging findings and diagnosing osteomalacia

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Conflict of interest: None

Osteoporosis initially results in bone loss in the trabecular bone area although the total number of basic multicellular units, the smallest unit of bone remodeling, is greater in cortical bone than in trabecular bone. This is because the area of remodeling is larger in trabecular bone. In clinical practice, the imbalance in remodeling can be estimated by measuring markers of bone resorption and bone formation. These markers are osteoclast- and osteoblast-specific proteins and metabolites of type I collagen, which comprise the bulk of the bone matrix, and these markers are useful for determining the early efficacy of pharmacotherapy of osteoporosis. In the diagnosis of osteoporosis, It should be ruled out other diseases that present with low bone mass at first. Imaging findings and blood and biochemical tests are useful for differential diagnosis. When vertebral fractures are seen on imaging, vertebral fractures due to other causes than osteoporosis, such as metastatic spinal tumors or hematopoietic malignancies, should be ruled out first. Although it is often difficult to distinguish these conditions on plain radiographs, vertebral fractures due to neoplastic disease are characterized by a tendency to show neurological symptoms such as paralysis, even though the crushing is mild. The characteristic wrap-around sign observed on CT and MRI is also helpful in the diagnosis of malignant lymphoma of vertebral origin. Among metabolic bone diseases other than osteoporosis that present with low bone mass, hypophosphatemic rickets and osteomalacia should be kept in mind as diseases for which early detection and treatment are desirable. The two main types of FGF23-related hypophosphatemic rickets/osteomalacia are tumor-induced osteomalacia (TIO) and X- linked hypophosphatemic rickets/osteomalacia (XLH). Measurement of serum phosphorus levels is important for the diagnosis of hypophosphatemic rickets/osteomalacia. When the serum phosphorous level is low and find symptoms of rickets/osteomalacia, FGF23 should be measured. Then it is recommended to consult to an endocrinologist promptly if FGF23 is elevated. The first line of therapy for TIO is tumor resection and if it is difficult to resect or find tumors, drug treatment is indicated. In addition to phosphorus replenishment, anti-FGF23 antibodies may be effective.

LS25-1

Importance of T2T in Rheumatoid Arthritis and the Position of TNF Inhibitors in the JCR Guidelines 2020

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Conflict of interest: Yes

A paradigm shift in the treatment of rheumatoid arthritis with biological anti-rheumatic drugs was brought about by the advent of TNF inhibitors. Since then, the treatment of rheumatoid arthritis, once largely ineffective, has been transformed, with the development of a number of molecularly targeted therapies that have enabled many rheumatoid arthritis patients to achieve and maintain clinical remission and limit joint destruction. These changes are not limited to the introduction of new therapeutic agents, but have led to the establishment of the treat-to-target (T2T) strategy, which is based on the clarification of therapeutic targets and the approach to achieving them, and has revolutionized the concept of rheumatoid arthritis treatment. It is noteworthy that the maturation of Evidence-Based Medicine (EBM) played a major role in this remarkable development of rheumatoid arthritis therapeutics, along with new drugs with breakthrough mechanisms. In other words, the cycle of accumulating evidence through high-quality randomized controlled trials (RCTs) with clear endpoints and creating clinical practice guidelines (CPGs) through a bird's-eye view of this evidence via systematic literature search (SLR) has led to the provision of high-quality medical care for many patients. TNF inhibitors are anti-rheumatic drugs that have been developed in line with these trends. On the other hand, TNF inhibitors were the first drugs to be tried as an exit strategy after remission, and ambitious clinical studies such as HIT HARD, HONOR, and HAWK have demonstrated the risk of relapse with dose reduction and withdrawal of TNF inhibitors. These findings may be used in everyday clinical practice. In this seminar, we will review the importance of T2T in rheumatoid arthritis and the position of TNF inhibitors in the JCR Guidelines 2020, focusing on the evidence of adalimumab.

LS25-2

The paradigm shift in treatment of rheumatoid arthritis (RA) and possible involvement of adalimumab

Nobuyuki Miyasaka
Department of Rheumatology, Tokyo Medical and Dental University

Conflict of interest: None

There is no conflict of interest to be disclosed in this lecture. I will discuss the paradigm shift in treatment of rheumatoid arthritis (RA) with possible involvement of TNF-antagonistic biologics such as adalimumab by introducing the results of clinical trials in this lecture. RA is a chronic inflammatory disease affecting joint synovium resulting in permanent joint destruction, and the lungs and many vital organs are often involved. Disturbed quality of life (QOL) in RA patients is therefore frequently encountered in the disease. Elderly-onset RA increased in recent years are often subjected to joint destruction if not treated properly. As a result, life expectancy is approximately 10 years shorter when compared to normal individuals of the same ages. However, with the advent of early diagnosis of the disease and development of efficacious treatments, this situation has no more expected in recent years. Pain-relief is not a goal of RA treatment and remission is highly possible at present. So called 'paradigm shift' in RA treatment has therefore come. I will discuss clinical problems in introducing adalimumab occurred in Japan and representative clinical trials for RA such as CHANGE trial, HOPEFUL-1 trial and PREMIER trial in this lecture. Future problems will be discussed.

LS26-1

Management of the connective tissue disease associated interstitial lung disease in daily clinical practice

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Conflict of interest: Yes

Interstitial lung disease is one of the major manifestations of rheumatoid arthritis or other connective tissue diseases. The management of connective tissue disease-associated interstitial lung disease (CTD-ILD) has crucial role in the daily practice due to its high prevalence and severity.

The “2020 guide for the diagnosis and treatment of interstitial lung disease associated with connective tissue disease” stated that we need to consider both two aspects in CTD-ILD treatment: “improvement of the current situation” and “reduction of future risk”. In considering future risk, it is necessary to understand that progressive fibrosis and declining respiratory function are appear in some CTD-ILDs. These are called progressive fibrosing interstitial lung disease (PF-ILD) and it has been reported to have a poor prognosis, although this varies with the underlying disease. The importance of early detection/diagnosis through screening with physical examination and HRCT imaging, as well as early treatment intervention, has recently been focused. However, there are still many challenges to be found out regarding the appropriate combination of anti-fibrosing therapy and immunosuppressive drugs for the underlying collagen disease. In this lecture, the disease concept and definition of PF-ILD from the design and result of INBUILD study will be reviewed. Second, the best management of interstitial lung diseases and, in the connective tissue diseases including systemic scleroderma, systemic lupus erythematosus, and ANCA-associated vasculitis syndrome will be discussed.

LS26-2

PF-ILD up to date - Focusing on CTD-ILD

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Conflict of interest: Yes

Progressive fibrosing interstitial lung disease (PF-ILD) is a concept that refers to a group of patients who develop progressive lung fibrosis despite appropriate management. PF-ILD has various other names, including progressive fibrosing phenotype of chronic ILD, progressive phenotype of chronic fibrosing ILD, etc. In 2022, ATS/ERS/JRS/ALAT named it progressive pulmonary fibrosis (PPF) and published guidelines. There are a variety of diseases that present with PF-ILD, and each disease has been reported to have slightly different rates of meeting the criteria for PF-ILD and different prognoses. Among them, interstitial lung disease associated with collagen disease (CTD-ILD) is reported to have a slightly better prognosis than other diseases. The reasons for this may include the fact that CTD-ILD is more responsive to anti-inflammatory therapy than other ILDs, that there is a wider range of drug options for background CTD, and that the progression of the disease may decrease after a certain period of time. On the other hand, these factors may pose difficulties in the treatment of CTD-ILD; PF-ILD is a good indication for antifibrotic agents if the primary disease treatment and/or anti-inflammatory therapy are sufficient, if they are not sufficient, antifibrotic may not be fully effective. In this presentation, I will discuss how to detect disease progression in CTD-ILD from the viewpoint of PF-ILD, and the issues and key points in treatment selection.

LS27

Key Revision Points as to CTD-PAH in ESC/ERS Pulmonary Hypertension Guidelines 2022

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Conflict of interest: None

Selective pulmonary vasodilators have been available for the treatment of PAH for almost 20 years, and have had a significant impact on clinical practice by improving symptoms, hemodynamics, exercise capacity, and prognosis. In this context, CTD-PAH, along with other forms of PAH including idiopathic PAH, has been included in clinical trials and registry studies to accumulate evidence, and the World Symposium on Pulmonary Hypertension (WSPH) proceedings and the European Society of Cardiology (ESC)/European Respiratory Society (ERS) guidelines have updated the diagnosis and treatment strategies every few years. In 2022, the ESC/ERS pulmonary hypertension guidelines were revised. Among the many revisions, the definition of pulmonary hypertension, risk assessment, and treatment algorithms have changed significantly. As to the definition of pulmonary hypertension, mean pulmonary arterial pressure at rest was reduced from ≧25 to >20 mmHg in the 2018 WSPH. Subsequently, as to the definition of precapillary pulmonary hypertension, pulmonary vascular resistance was reduced from ≧3 to >2 Wood units. This is largely due to findings in systemic sclerosis. However, since the evidence for therapeutic intervention in this newly diagnosed population has not been established, the current treatment targets are considered appropriate as before. As for treatment algorithms, evidence from PAH clinical trials has been largely reflected, and treatment selection, initial treatment, and treatment intensification have been updated. Among pulmonary vasodilators, riociguat has a unique mechanism of action. In the new treatment algorithm, based on the results of the RESPITE and REPLACE studies, it was incorporated as an option for intensified treatment when efficacy is inadequate. Furthermore, the efficacy of initial combination therapy including riociguat has been reported. In this talk, the latest guidelines will be introduced and the positioning of riociguat will be explained.

LS28

Efficacy and safety of filgotinib in the treatment of rheumatoid arthritis

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Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), clinical, structural and functional remission has become a realistic goal with appropriate early therapeutic intervention with conventional synthetic anti-rheumatic drugs (csDMARDs) such as methotrexate (MTX), and biological anti-rheumatic drugs (bDMARDs). However, only about 60% of patients achieve these goals, and the existence of difficult-to-treat RA (D2TRA), a group of patients who do not achieve remission with current pharmacological therapies, is becoming increasingly clear. Janus kinases (JAKs) are tyrosine kinases that bind permanently to cytokine receptors in cells and are activated by cytokines; JAKs can be divided into four types, JAK1, JAK2, JAK3 and TYK2, which differ in function and mediate the signalling of multiple cytokines. Because of their multi-target effect on innate and acquired immune systems, JAK inhibitors have the potential to meet unmet needs of conventional therapies. Filgotinib has been shown to be effective in MTX-naïve, MTX-inadequate response and bDMARD-inadequate response patients, thus is expected to be effective in D2T RA. FINCH 1 trial showed that filgotinib 200 mg was superior to TNF inhibitors in reducing joint destruction in patients with multiple poor prognostic factors, including high disease activity, positive serology and radiographic bone erosions. In this seminar, we would like to discuss the latest evidence on the efficacy and safety of filgotinib. We will also discuss our experience with filgotinib use and the expectation of this drug in the treatment strategy in RA.

LS29

Considering the transition of ANCA-associated vasculitis treatment and the positioning of TAVNEOS

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Conflict of interest: Yes

ANCA-associated vasculitis (AAV) is a systemic necrotizing vasculitis involving mainly small blood vessels (small arteries, arterioles, capillaries, and venules). AAV is associated with the pathogenesis of anti-neutrophil cytoplasmic antibody (ANCA). Treatment for AAV is predominantly corticosteroids (glucocorticoid: GC) combined with immunosuppressants, but the high relapse rate and treatment-related adverse events, including infection, are problematic. In recent years, the introduction of new drugs, including biologics, is expected to improve therapeutic efficacy as well as reduce adverse events. In addition, recent new comparative studies have demonstrated that it is possible to reduce the dose of GC for remission-induction therapy for AAV. In addition, it has been suggested that avacopan (CCX168), a complement C5a receptor inhibitor, may be able to further reduce the dose of GC, which has been the main therapeutic agent. Avacopan (CCX168), a small molecule with a molecular weight of 581, is an orally available C5a receptor (C5aR) inhibitor of complement C5a. Two

Phase 2 trials were conducted, followed by the ADVOCATE trial, a Phase 3 trial. In this study, patients with new or recurrent AAV were randomized in a double-blind to receive either Avacopan (Avacopan + placebo GC) or control (placebo Avacopan + standard GC) and were given remission induction therapy in combination with standard CY or RTX. Primary endpoint was defined as the percentages of patients achieving or maintaining BVAS remission (BVAS=0 and no PSL in the previous 4 weeks) at 26 and 52 weeks. The primary endpoint was non-inferior in the Avacopan and control groups, with BVAS remission of 72.3% vs. 70.1% at 26 weeks ($p<0.0001$) and superior at 52 weeks (65.7% vs. 54.9%), respectively ($p=0.0066$) (N Eng J Med 384: 599, 2021). In the safety analysis, AEs related to GC were predominantly lower in the avacopan group, and GTI, which evaluates the toxicity of GC, was also predominantly lower in the avacopan group. Sub-analyses demonstrated the evidence of efficacy among AAVs patients with renal involvement. Evidence from the ADVOCATE trial suggests that avacopan may be an alternative to GC for remission-induction therapy of AAV. However, there are no clear guidelines for the use of avacopan in induction remission therapy, nor for its use in maintenance therapy, and this remains an issue for the future. In this seminar, we will review the current status of AAV treatment and discuss the positioning of Avacopan therapy.

LS30

Implementing Treat to Target in Clinical Practice for Systemic Lupus Erythematosus

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Conflict of interest: None

SLE care is multidisciplinary, based on a shared patient-physician decision, and should consider individual, medical and societal costs. Treatment goals include long-term patient survival, prevention of organ damage and optimization of health-related quality of life. Treatment in SLE should aim at remission or low disease activity and prevention of flares in all organs, maintained with the lowest possible dose of glucocorticoids. This strategy reduces damage and improves survival. HCQ is recommended for all patients with SLE, unless contraindicated, at a dose not exceeding 5 mg/kg/real BW. For chronic maintenance treatment, GC should be minimized to less than 7.5 mg/day (prednisone equivalent) and, when possible, withdrawn. Prompt initiation of immunomodulatory agents can expedite the tapering/discontinuation of GC. New biologic agents used as an add on therapy have facilitated the achievement of these treatment goals allowing the tapering of GCs whose chronic use has been associated with damage and poorer outcomes. We have recently proposed quality indicators based on the EULAR recommendations that could serve as a check list to optimize the care of SLE patients. Tapering of prednisone dose to less than 7.5 mg/day was achieved in 93.6% while 73.5% received the recommended hydroxychloroquine dose. Higher adherence to monitoring-related QIs was associated with reduced risk for a composite adverse outcome (flare, hospitalization or damage accrual) during the last year of observation.

LS31

Management and treatment of Glucocorticoid-induced osteoporosis

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Conflict of interest: Yes

Oral steroids are used for various diseases because of their powerful anti-inflammatory and immunosuppressive effects. Glucocorticoid-induced osteoporosis (GIOP) is widely known as a side effect of these drugs. Glucocorticoids increase bone resorption at high doses or at the start of administration and induce apoptosis of osteoblast and osteocyte throughout the administration period. These findings suggest decreased bone formation is mainly attributed to GIOP. There is no safe dosage range that does not increase the risk of osteoporosis. Moreover, fracture risk soars when the prednisolone equivalent exceeds 20 mg per day. Fracture risk increases shortly after initiation; at doses of 5 mg/day or more, the risk increases at 3 months of treatment. In addition, prevalent fractures of the vertebral body have been found to significantly increase the risk of secondary fractures. Based on the above findings, Japanese guidelines for GIOP include patients who are scheduled to receive oral glucocorticoids for at least 3 months, regardless of dose. The guidelines were first published in 2004 and revised in 2014. The 2014 guidelines calculate the fracture risk for each of the following: prevalent fracture, bone mass, age, and glucocorticoid dose. The total risk score is then used to consider treatment. For therapeutic agents, first-line and alternative agents are recommended from among those for which evidence for the treatment of GIOP was available at the time when the guidelines were developed. Since then, new findings have been presented for drugs for which there was no evidence at the time of 2014, as well as for newly launched osteoporosis drugs. As of the end of the year 2022, Japanese Guidelines for the Management and Treatment of Glucocorticoid-Induced Osteoporosis are in the process of revision. This presentation will provide an overview of this latest guideline and present the evidence for the drugs that will be included in the guidelines.

LS32

B cell depletion therapy in systemic sclerosis: which patient is rituximab preferable for?

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Conflict of interest: Yes

Systemic sclerosis (SSc) is characterized by autoimmune activation, microvascular damage, and fibrosis of the skin and visceral organs. Progression in cutaneous thickness occurs most often in the early disease. Over Half of SSc patients developed disease progression including interstitial lung disease (ILD), cardiac involvement, and pulmonary arterial hypertension within 5 years since the first non-Raynaud symptom. The treatment algorithm for SSc-ILD has been provided by the Japanese Respiratory Society and Japan College of Rheumatology. Cyclophosphamide (CYC) or mycophenolate mofetil (MMF) is considered a treatment option for limited disease of ILD with high-risk factors and extensive disease of ILD. Tocilizumab (TCZ) for the early disease of diffuse cutaneous form SSc and nintedanib for progressive fibrosing ILD without end-stage lung disease are also considered. Similarly, the initiation of treatment with CYC, MMF, TCZ, or rituximab (RTX) for clinical SSc-ILD with active disease including skin and/or musculoskeletal manifestations is suggested by expert opinions in the American College of Rheumatology. However, it remained unknown which drug should be introduced as the first-line therapy for SSc-ILD. Those disease-modifying agents except for TCZ regulate the acquired immune system. RTX can bind specifically to CD20 on matured B cells to deplete B cells. B cells play a crucial role in the early stage of SSc and preferentially during severe organ involvement. In addition, B cell depletion ameliorated skin fibrosis in Tight-skin mice. In a clinical trial of the safety and efficacy of RTX in SSc (DESIRES), the absolute change in mRSS at 24 weeks after initiation of study treatment reached statistical significance as the primary endpoint. The progression of ILD was less frequently revealed in the RTX group than in the placebo group. In this session, we would like to talk about patient selection for RTX and careful points in treatment with RTX for SSc patients.

LS33

Diagnosis and management of severe osteoporosis

Taku Saito
Department of Orthopaedic Surgery, Sensory and Motor System Medicine, Graduate School of Medicine, The University of Tokyo

Conflict of interest: Yes

Recently, many kinds of osteoporosis drugs are available, including bisphosphonate, denosumab, teriparatide, and romosozumab. Meanwhile, we should note various pitfalls in diagnosis and management. In this lecture, I introduce molecular mechanisms of these drugs, and issues in diagnosis and management of severe osteoporosis patients.

LS34

Management of rheumatoid arthritis with lung involvement

Kimito Kawahata
Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

Conflict of interest: Yes

Rheumatoid arthritis presents with various complications, among which lung involvement is frequent and affects treatment and prognosis. The cause of its complications is diverse, and it is necessary to pay attention not only to interstitial pneumonia and airway disease due to rheumatoid arthritis, but also to drugs, infections, and tumors. With respect to interstitial pneumonia associated with rheumatoid arthritis, knowledge is being accumulated on the immunopathology, prognostic factors, and the effects of anti-rheumatic drugs and anti-fibrotic drugs. As a result, its management is facing a different phase than before. On the other hand, there are still many issues such as patient stratification based on prognosis and treatment response, appropriate treatment selection, and acute exacerbation management. In this presentation, the latest findings from immunopathology to treatment will be overviewed, focusing on rheumatoid arthritis complicated with interstitial lung disease and airway disease.

LS35-1

Integrated medical guidance and communication in daily practice to prevent D2T-RA

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

Conflict of interest: Yes

The biggest problem for RA patients is irreversible deterioration of quality of life due to joint destruction, but thanks to recent advances in RA treatment, more than 10 years have passed since the “Non-Erosive Era”, an era in which joint destruction does not occur. The treatment of RA has been widely recognized as T2T (Treating RA to Target), with the recommendation to consider biologics if target (remission) cannot be achieved with pharmacological therapy centered on MTX follow by bio- or ts-DMARDs. Several clinical trials including etanercept have shown that drug-free remission, or “cure”, is possible in about 15% of patients. We would also like to introduce the new Etanercept device, which was designed from the patient’s perspective and introduced last year, as well as patient support services. On the other hand, in Japan, a total of nine bo-DMARDs including TNFα inhibitors, IL-6 receptor inhibitors, and T-cell co-stimulation modulator, are available for use. However, not all patients can benefit from them due to high medical costs, selection of patients with complications (interstitial pneumonia, renal and hepatic dysfunction, elderly patients), problems with side effects (especially infections), and the safety of long-term use has not been established. Recently, the concept of difficult-to-treat RA (D2T RA) was proposed for the first time in the 2019 EULAR Treatment Recommendations as the greatest unmet need, and various measures are being considered. In the second half of the session, we will discuss the integrated guideline for RA presented at ACR2022 and communication methods that can be used in daily practice from the perspective of D2T RA prevention.

LS35-2

The management of rheumatoid arthritis based on evidence

Yuko Kaneko
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has changed dramatically with the establishment of low-dose intermittent methotrexate and the advent of biologic agents. Although the efficacy of biologics in RA has already been proven, the current approach is to maximize the efficacy of the drugs, taking into consideration the pathophysiology and background of each patient, to ensure their use and safety in the short and long term, as well as their efficacy and safety in the economic and social aspects. However, there is now a need to maximize the efficacy of drugs and ensure their short- and long-term safety and efficacy while taking into consideration the pathophysiology and background of individual patients. Each therapeutic agent is unique in terms of target molecule, structure, and half-life. The choice of which drug is best suited for a patient depends on the patient’s background, the combination of anti-rheumatic drugs, and the method of use. Etanercept (ETN), a TNF inhibitor, has been used in Japan for more than 18 years since it became available. There have been no reports of Neutralizing Antibodies for ETN, and stable efficacy with few secondary invalidations, and high clinical continuation rate. In addition, new ETN device was launched in February 2022 to meet the unmet needs of RA patients. In addition, knowledge is accumulating regarding optimal therapy, such as targeted use to achieve remission, ETN dose reduction after remission is achieved, or discontinuation of concomitant MTX. In this seminar, we will consider treatment strategies for induction and maintenance of remission in RA based on the current evidence including new ETN device.

LS36-1

Collaboration between collagen disease physicians and lung cancer physicians, for the optimal patient selection and controlling immune related adverse events

Takehito Shukuya
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Conflict of interest: Yes

Immune checkpoint inhibitors (ICIs) such as PD-1/PD-L1 inhibitors have been available for the treatment of unresectable advanced or recurrent non-small cell lung cancer (NSCLC) since 2015, making a major paradigm shift in the treatment of lung cancer. Today, ICIs have become an important key drug for lung cancer treatment, with indications expanding to the perioperative period in addition to first-line treatment, second-line treatment, and maintenance therapy after chemoradiotherapy for patients with NSCLC. This drug’s mechanism of action is to promote the elimination of tumor cells by immune cells by suppressing the function of molecules that negatively regulate the tumor immunity. However, it is known that immune-related adverse events (irAEs) similar to collagen diseases can occur as characteristic adverse events and can be fatal in severe cases. irAEs cannot be predicted when and which organs will be affected, but when they appear, they should be treated promptly and appropriately. Although the use of oral corticosteroids and immunosuppressive agents as a basic treatment for irAE has been indicated in domestic and international guidelines, patients with collagen disease are often excluded from clinical trials evaluating ICI, and it is difficult to determine which patients with lung cancer complicated with collagen disease should be treated with ICI and how to deal with irAE and exacerbations of collagen disease that may occur when ICI is used. Therefore, it is important for lung cancer physicians and collagen disease physicians to collaborate in patient selection and management of irAEs and exacerbations of collagen disease. In this lecture, We would like to discuss the basic concepts of ICI and irAE, and the necessity for collaboration between lung cancer doctors and collagen disease physicians, in order to achieve optimal patient selection and medical care in the event of irAE or collagen disease exacerbation.

LS36-2

The use of immune checkpoint inhibitors in cancer patients with Pre-Existing Rheumatic Diseases: Evidence, experience of use at our hospital

Keita Kudo
Department of Medical Oncology, NHO Osaka Minami Medical Center, Osaka, Japan

Conflict of interest: None

Patients with rheumatoid arthritis (RA) have a risk of contracting lung cancer, and it has been reported that the RA complication rate in lung cancer patients is 5.9%. Lung cancer specialists are more likely than oncologist who specialize in other cancers. There is a possibility that there are many opportunities to come into contact with RA concomitant cases. In recent years, immune checkpoint inhibitors (ICIs) have appeared in lung

cancer treatment and have become central drugs in lung cancer drug therapy. As a result, long-term prognosis can be expected in patients with advanced lung cancer. For this reason, the use of ICI is very important when considering drug therapy for lung cancer patients with Pre-Existing RA. However, most clinical trials have excluded the efficacy and safety of ICI for lung cancer patients with Pre-Existing autoimmune diseases including RA. There are concerns such as exacerbation of autoimmune diseases and the risk of irAE due to the use of ICIs, the indications for ICI treatment are being considered based on the individual judgment of clinicians without clear criteria in practice. Our hospital is maintained as a central facility of the National Hospital Organization Kinki Group for immunological disorders. About 2,500 patients are treated annually for rheumatoid arthritis (RA). For this reason, there are relatively many opportunities to treat lung cancer patients with Pre-Existing autoimmune diseases, including RA. At our hospital, medical oncologist and rheumatologist discuss the indications for ICI therapy. In this seminar, we believe that it is meaningful to organize the limited evidence on the use of ICI in cancer patients with Pre-Existing RA in clinical practice and share the experience widely as a case series. We will review the exacerbation of RA, the relationship between immunosuppressive therapy and ICI effects, and introduce our experience with RA-complicated lung cancer and collaboration with the Department of Collagen Disease and Rheumatology.

LS37-1

Promotion of Early Diagnosis and Treatment of non SSc-PH ~For the Better Patients Life~

Hideyuki Okada
Department of General Internal Medicine and Rheumatology, Gifu Prefectural General Medical Center

Conflict of interest: None

For rheumatologists, pulmonary hypertension (PH) should be a common disease. Because PH is present where there is connective tissue disease (CTD). That is, similar to interstitial pneumoniae (IP) and nephrotic syndrome (NS), PH also exists as one of the organ disorders associated with CTD. We should be exposed to PH as well as SLE and IIM every day, but still few patients of CTD-PH. The reason for this may be that there are many cases of CTD-PH is not noticed due to diagnostic difficulties specific to CTD-PH. For example, complexity of disease, depend on the pathology of each disease, it may take various form, Group 1: pulmonary artery hypertension (PAH), Group 2: PH associated with left heart disease, Group 3: PH associated with lung disease, Group 4: PH associated with pulmonary artery obstructions. Of note, one SLE patient may have all type of PH. However, in any case there must be initial symptoms. According to 2022 ESC/ERS Guidelines, dyspnea on exertion or when bending forward, fatigue, palpitations, hemoptysis, exercise-induced abdominal distension and nausea, weight gain due to fluid retention and syncope has been described as earlier symptoms of PH. On the other hand, shortness of breath, wheezing, cough, chest pain and hoarseness as later symptoms. Among the flashy CTD symptoms such as high fever up to 40°C and severe rash, we are aware of the symptoms that indicate the existence of PH, could this be the first step in diagnosing the disease? When we treat patients with CTD, we suspect that they may have PH from the beginning, it is also characteristic of CTD-PH that we can diagnose it at an earlier stage compared to IPAH. Recently, various therapeutic agents for PAH have become available, so the prognosis of PAH has improved dramatically. However, CTD-PH still has poor. One way to improve the prognosis of CTD-PH is to detect and diagnosis as early as possible. As rheumatologists, we must strive every day to improve the lives of all patients with CTD-PH.

LS37-2

Early diagnosis and therapeutic options of Non SSc-PAH as considered by a cardiologist

Kohtaro Abe
Department of Cardiovascular Medicine, Kyushu University Hospital

Conflict of interest: None

The treatments for pulmonary hypertension have been advanced dramatically over the past two decades. In particular, the prognosis of idiopathic pulmonary arterial hypertension (IPAH) has been improved dramatically with upfront combination therapy with PGI2, endothelin receptor antagonists, PDE5 inhibitors, or soluble guanylate cyclase stimulators. Currently, the goal of treatment of PAH focuses on the improvement of quality of life through early diagnosis and treatments. On the other hand, because pulmonary hypertension related to collagen disease involves not only PAH (group 1) but also left heart disease (group 2) and lung disease (group 3), appropriate diagnosis and therapeutic options according to the pathology of each patient are required. I will present the diagnosis and treatment of pulmonary hypertension based on the newly revised ESC/ERS guideline 2022, as well as the diagnosis and treatment of pulmonary hypertension related to collagen diseases, including non SSc such as SLE and Sjogren's syndrome, from a cardiologist's perspective.

LS38

From diagnosis to treatment of CTD-PAH

Masaru Kato
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Conflict of interest: Yes

Connective tissue diseases (CTD) cause inflammation and fibrosis in organs throughout the body. Pulmonary arterial hypertension (PAH) is one of the most serious organ lesions, and its screeningand early treatment are important because it has a significant impact on the prognosis of patientswith CTD, depending on the timing and severity of its detection. In the treatment of CTD-PAH, the use of appropriate selective pulmonary vasodilators, along with treatment of the underlyingdisease, is expected to improve the prognosis and quality of life of the patients. In this seminar, we will discuss the diagnostic follow-up and treatment options of CTD consideringthe assessment of PAH.

LS39-1

Imaging in ankylosing spondylitis: pearls and pitfalls

Taiki Nozaki
Department of Radiology, St. Luke's International Hospital, Tokyo, Japan

Conflict of interest: None

Axial spondyloarthritis includes radiographic axial SpA, and non-radiographic axial SpA that does not meet the modified New York criteria. According to the ASAS classification criteria proposed in 2009, imaging findings of sacroiliitis are one of the important basis. However, it is sometimes experienced to be difficult to diagnose, especially in young to middle-aged women. Diagnosis of sacroiliitis using imaging modalities may seem easy, but it is actually quite difficult. Plain radiographs are not highly reliable among observers, and if the findings are subtle, detailed examinations such as MRI and CT are required. There is some debate as to which imaging modality is best, but MRI is currently recommended since there is no radiation exposure. In diagnostic imaging of sacroiliitis, it is necessary to consider "active/inflammatory lesions" and "structural abnormalities/destruction" separately. Imaging evaluation focusing only on the findings of bone marrow edema, which is representative of the active lesions, may lead to erroneous diagnosis. In addition, there are many subjective elements in diagnosing these imaging findings, and training and empirical values are required. We must keep in mind. In this lecture, in addition to the basic anatomical knowledge, the basic concept of plain radiograph, the how to order MR including sequences and imaging planes, and the picking up of imaging findings for the diagnosis of axial spondyloarthritis. I would like to present the images that should be differentiated and excluded while discussing the current status and problems of diagnostic imaging.

LS39-2

Treatment of ankylosing spondylitis based on its clinical condition and pathogenesis

Naoto Tamura
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Conflict of interest: Yes

Ankylosing spondylitis (AS) is a disease of spondyloarthritides, and

mainly affects the sacroiliac joints, spine, and hip joints. Although strongly correlated with the *HLA-B27* gene, it affects about 5% of the carriers. It has been considered that intestinal flora, bacterial infection, and mechanical stress to the enthesis are related to the onset. It develops in young people with inflammatory low back pain, which is often very severe, followed by bone erosion and subsequent new bone formation and ankylosis that cause characteristic physical dysfunction. Residential innate immune cells at the enthesis are thought to be involved in the pathogenic process, and TNF and IL-17 are main cytokines that cause chronic inflammation and bone destruction. IL-17 and IL-22 are also thought to be involved in new bone formation. Recent report indicated that the expression of membranous TNF was high in spondyloarthritis synovia, and AS-like new ankylosis was observed in mice with high expression of membranous TNF, suggesting its involvement in new bone formation in AS. The main aim of AS treatment is to suppress inflammation and improve pain, but it has also been reported that the more inflammation was suppressed, the less progression of bone lesions. Recently, a treat-to-target strategy has been advocated in treatment for AS, and it is recommended to correct treatment with the goal of low disease activity below an ankylosing spondylitis disease activity score (ASDAS) of less than 2.1. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first choice and are highly effective for AS pain. If the maximum tolerated NSAID dose does not meet the goal in 2-4 weeks, switch to another NSAID and reassess. If the response is inadequate, start either a biologic TNF inhibitor or an IL-17 inhibitor. TNF inhibitors of choice if recurrent uveitis or inflammatory bowel disease is present. If the effect is insufficient, biologics are switched, and JAK inhibitor upadacitinib is also a new option after considering the patient's background. In this seminar, we will outline pathogenesis and treatment of AS with clinical trial data.

LS40

Expectations for Belimumab in the Treatment of Lupus Nephritis

Hiroko Kanda
Immune-Mediated Diseases Therapy Center, The University of Tokyo

Conflict of interest: Yes

Lupus nephritis (LN) is one of the major organ failures associated with systemic lupus erythematosus (SLE) and is observed in approximately 60% of all cases during the course of the disease. SLE is an autoimmune disease that is triggered by environmental factors on a genetic background, resulting in a variety of immune abnormalities that lea to the production of immune complexes, organ deposition, and complement activation. Since SLE often develops in young women and relapses repeatedly, not only induction therapy but also maintenance therapy to prevent organ damage is being emphasized as a treatment method. In the latest national and international guidelines, the induction therapy for active LN is a combination of steroids and mycophenolate mofetil (MMF) or intermittent intravenous cyclophosphamide therapy (IVCY). If remission is not achieved, multi-target therapy (concomitant use of calcineurin inhibitors) is administered. Maintenance therapy is continuation of MMF. However, there are problems that the dosage of MMF has not been established, or that it cannot be administered in sufficient doses due to side effects, and there are many cases of relapse. Recently, the anti-BlyS antibody, belimumab, was reported to be effective in LN in phase III (BLISS-LN). Furthermore, in a post-hoc analysis, concomitant administration of belimumab with MMF suppressed proteinuria in subnephrotic proteinuria and proliferative LN without membranous nephropathy, compared with conventional therapy. Significantly higher efficacy and renal function preserving efficacy were also reported. In this luncheon seminar, I would like to review these results again and consider the positioning of belimumab for LN treatment, including our own experience.

LS41

An update on systemic sclerosis

Dinesh Khanna
University of Michigan, Ann Arbor, USA

Conflict of interest: Yes

Systemic sclerosis is a multi system autoimmune disease associated with inflammation, fibrosis, and vasculopathy. The lecture will cover recent advances in the management of systemic sclerosis, including review of the trials in interstitial lung disease. I will discuss the role of immunosuppressive and biological therapies in SSc, including mycophenolate mofetil, rituximab, tocilizumab, and stem cell transplant. I will also discuss the role of anti-fibrotic therapies in the management of interstitial lung disease.

Evening Seminar

ES1-1

Role of Abatacept in the era of molecular targeted therapies

Motomu Hashimoto
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Conflict of interest: Yes

Currently, total 13 biologics or JAK inhibitors are available in the clinical practice of rheumatoid arthritis (RA) in JAPAN. While 12 therapies target inflammatory cytokines or cytokine signaling, abatacept is the only drug that specifically target T cells. Abatacept may have the following unique characteristics. First, Abatacept is a biologics that utilize CTLA4, an essential molecule of regulatory T cells (Treg). Recent single cell analyses revealed the importance of Treg in the pathogenesis of RA. Treg cannot control the activation of effector T cells in the presence of TNF or IL-6 in RA. However, CTLA4-Ig fusion protein can exert the suppressive function even in the presence of these inflammatory cytokines. Second, Abatacept suppress B cell autoantibody production via inhibition of Tfh and Tph. It is well known that ACPA positive RA has a poor prognosis, but Abatacept showed higher efficacy in ACPA positive RA than in ACPA negative RA in clinical trials. It is a unique character of Abatacept, not observed with other cytokine signal inhibitors. Third, Abatacept suppresses acquired immunity, but does not suppress innate immunity. It may be one of the reasons why Abatacept causes relatively few serious infections. It is of particular importance for the treatment of elderly RA or RA patients with lung complications who have higher risks of infection. Indeed, Abatacept showed high retention rate in elderly RA patients over 65 years old in our real-world database, the ANSWER cohort. In this seminar, significance and advantages of Abatacept in the era of molecular targeted therapies will be discussed.

ES1-2

Further development beyond RA and beyond biologicals

Thomas Huizinga
Leiden University Medical School, The Netherlands

Conflict of interest: None

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 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.

ES2-1

Treatment of rheumatoid arthritis patients in the pre-senior generation (age of 50-60s)

Nobunori Takahashi
Department of Orthopaedic Surgery, Aichi Medical University

Conflict of interest: Yes

Drug therapy for RA has advanced dramatically with the advent of methotrexate (MTX) and molecular-targeted therapies. Today, many patients can achieve good arthritis control if they follow the standard of care, which is a combination of sufficient doses of MTX and molecularly-targeted therapies. There are certain points that need to be considered for each generation when implementing standard drug therapy for RA. In the elderly, the risk of kidney, liver, and other organ damage, respiratory complications, and other problems often preclude the use of sufficient doses of MTX, and cognitive decline can also make drug adherence management problematic. Conversely, younger patients require a very long-term treatment strategy. In addition, women need to adjust the use of teratogenic MTX for life events such as pregnancy and childbirth, as well as adjusting medications during pregnancy and lactation while balancing the control of disease activity in RA. The pre-senior generation (50s to 60s), which is sandwiched between these two generations, has been considered as a generation that is more likely to practice standard treatment because they have relatively few organ failures, are still physically strong, and are often financially able to afford it. However, when affected by RA, they are the generation that can easily suffer from functional decline if disease activity is controlled slowly, and in the long term, as elderly people, they will have problems with organ damage and will need to adjust their medication, including discontinuation of MTX. In the long term, they may experience organ damage, which may require drug adjustment, including discontinuation of MTX. In this presentation, I would like to discuss the drug treatment strategy especially in the pre-senior generation with you.

ES2-2

Treatment of rheumatoid arthritis with TNF inhibitors -distinguishing between induction and maintenance therapy-

Kensuke Oryoji
Center for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by polyarthritis. In the EULAR recommendation and the Japanese guidelines for the treatment of rheumatoid arthritis 2020, methotrexate (MTX) should be started as soon as RA is diagnosed unless there are contraindications. On the other hand, the c-OPERA study of anti-CCP antibody-positive RA patients in Japan showed that the percentage of patients who achieved SDAI remission with MTX alone at the maximum dose was about 30%, while the percentage was nearly 60% with MTX plus a TNF inhibitor. This means that 30% of patients who test positive for anti-CCP antibodies, one of the poor prognostic factors in RA, require TNF inhibition in addition to MTX from the early stages of the disease. When we treat patients in the early stages of disease onset, we need to quickly determine the response to MTX and consider the use of TNF inhibitors early on in patients who need them. One of the problems in the remission maintenance phase is the aging of rheumatoid arthritis patients in Japan, with more than 45% of patients over the age of 70, according to the National Database (NDB Japan) in 2017. In the Rheumatoid Arthritis Practice Guidelines 2020, Treatment Principle D states, "Patients require access to multiple drugs with different modes of action to address the heterogeneity of RA; they may require multiple successive therapies throughout life". As patients with RA age, they should carefully consider whether to continue MTX at the same dose as at onset. In this session, I would like to discuss the position of TNF inhibitors in the actual clinical practice of RA in cases of poor initial response to MTX and drug adjustment during the remission maintenance period in a way that is relevant to Japan.

ES3-1

Role of hydroxychloroquine in the treatment of SLE

Hajime Kono
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Tokyo, Japan

Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is an autoimmune disease with various organ involvement. Control of the disease has been shown to prevent long-term damage. Glucocorticoids (GC) have dramatically improved the life outcome of SLE, and GC has been the mainstay of drug therapy. However, the accumulation of damage in SLE is due more to the side effects of GCs than disease activity. GCs should be discontinued or administered at the lowest possible dose. While the appropriate use of immunosuppressive and molecularly targeted drugs is essential, the antimalarial drug hydroxychloroquine (HCQ) is recommended for use in all cases of SLE. HCQ accumulates in lysosomes and increases their pH, which may contribute to Toll receptor signaling and antigen presentation associated with SLE pathogenesis and the production of interferon and inflammatory cytokines. Clinically, there is evidence that using HCQ in SLE improves life expectancy, prevents organ damage, decreases the risk of relapse, and prevents antiphospholipid antibody-related thrombosis while contributing to a reduction in glucocorticoid dosage. It is particularly effective for skin rashes and joint symptoms. HCQ is generally a safe drug and can be prescribed to pregnant women. However, long-term use of HCQ can lead to retinopathy, a severe complication, with a prevalence of retinal abnormalities exceeding 10% after 20 years of continuous use. Major risk factors for retinopathy include advanced age, length of treatment, dose, chronic kidney disease, liver dysfunction, and pre-existing retinal disease. The EULAR guidelines recommend a dose of 5 mg/kg/day or less, which has a low risk of toxicity. Since retinopathy is rarely a clinical problem if detected early, performing regular ophthalmologic examinations at least once a year is crucial, following JCR guidelines.

ES3-2

Basics of Hydroxychloroquine Retinopathy and Cooperation with Ophthalmologists

Mineo Kondo
Ophthalmology, Mie University

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. However, an 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. Seven 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. I hope that this lecture will provide an opportunity for prescribing physicians to consider the ideal form of collaboration with ophthalmologists.

ES4

Future perspectives: JAK inhibitors in the treatment of Rheumatoid Arthritis

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Conflict of interest: None

Rheumatoid arthritis (RA) is a chronic, progressive, systemic inflammatory autoimmune disease that affects about 1% of the population worldwide. RA can be associated with substantial morbidity and accelerated mortality, and exerts a tremendous economic toll on affected patients, their families, and society. Recent years have witnessed tremendous progress in the therapeutic approach to RA. The developments have been driven largely by 3 factors: 1) an ever growing appreciation of the potential severity of RA, highlighting the crucial need to optimize outcomes for as many patients as possible, with both newer treatment approaches and novel therapeutic agents 2) increased understanding of the complex immunopathophysiology of the disease, highlighting potential new targets within the dysregulated immune response that initiates and sustains the chronic systemic inflammation characteristic of the disease, and 3) advances in biotechnology, allowing specific targeting of cell types, mediators, and their relevant molecular interaction. Many therapies, with different mechanisms of action, have become available in recent years for the treatment of RA, with additional treatments available each year. Categories of potential therapies for RA include 1) the conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs). 2) biologic agents, and 3) targeted synthetic DMARDs (tsDMARDs). Prominent among tsDMARDs are jakinibs. These agents inhibit enzymes in the Janus kinase family (JAK1, JAK2, JAK3, Tyk 2). Worldwide, there are currently 5 jakinibs approved for RA: tofacitinib, baricitinib, upadacitinib, pefcitinib and filgotinib. Growing experience with these agents has established their efficacy in RA. A recent consideration that has received attention lately relates to the safety and tolerability of jakinibs in RA. As with any immune modulating medication, there is potential concern for infection, particularly Herpes Zoster. More recently, concerns about an increased risk for major adverse cardiac events (MACE) and treatment related malignancies have been raised. Close attention to relevant data indicates that much can be understood about the patients at greatest risk for such adverse effects; that should allow optimization of treatment approaches that can benefit many RA patients.

ES5-1

Safety of JAK inhibitors in treatment of rheumatoid arthritis: Evidence from real-world clinical data

Shunsuke Mori
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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an immune-mediated inflammatory disease and its pathogenesis involves a complex network of various cytokines. The JAK (Janus kinase)-STAT (signal transducer and activator of transcription) signaling pathway transduces extracellular cytokine signals from cell surface receptors to the nucleus. There are four JAK isoforms and seven STAT proteins. Various combinations of these molecules contribute to the induction of a wide range of cytokine activities. JAK inhibitors are the latest drug class of disease-modifying antirheumatic drugs (DMARDs) to emerge for RA treatment. In Japan, five JAK inhibitors are approved. Unlike existing biological DMARDs (bDMARDs), JAK inhibitors can prevent the signaling pathway of multiple cytokines. Through comparison studies between JAK inhibitors and bDMARDs, we can determine the optimal position of JAK inhibitors in the treatment algorithm for RA. Recent clinical trials showed that JAK inhibitors had clinical efficacy in RA patients with an inadequate response to methotrexate (MTX) or bDMARD. Additionally, JAK inhibitors in combination with MTX exhibited similar therapeutic efficacy compared with adalimumab plus MTX therapy. In our multicenter cohort study using ongoing real-world registries, tofacitinib was more likely to induce the reduction in clinical disease activity in clinical disease activity during the 12-month treatment compared with tocilizumab in bDMARD-naïve patients with MTX-refractory active RA, but these differences were not observed in the treatment of previous bDMARD-failure patients. Despite the positive therapeutic impacts, concerns have been raised regarding the risk of venous thromboembolism (VTE). We experienced a case of massive pulmonary embolism during JAK inhibitor treatment for multiple bDMARD-resistant RA. In this seminar, we focus on the VTE risk during JAK inhibitor treatment for RA and discuss the safety of JAK inhibitors based on our real-world clinical data.

ES5-2

Infection control and prevention of pneumonia in rheumatoid arthritis patients

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Conflict of interest: None

It is widely known that rheumatoid arthritis (RA) patients are at high

risk for infections. RA patients are often complicated by infectious diseases due to their own immune abnormalities, and they are also exposed to serious infectious disease risk due to immunosuppressive therapy. In Japan, the Ministry of Health, Labour and Welfare (MHLW) is planning to announce the "Phase 2: Action Plan for Antimicrobial Resistance (AMR) Control" to comprehensively address the drug resistance problem. Pneumonia is the most frequent infection in RA patients, and S. pneumoniae is the most frequently isolated organism. One of the measures to prevent pneumonia caused by S. pneumoniae is the pneumococcal vaccine. The American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) recommend pneumococcal vaccination along with influenza vaccine for adult patients with immunosuppressed conditions such as RA. In Japan, the Japan College of Rheumatology (JCR) recommends pneumococcal vaccination in the MTX treatment guidelines. Currently, two types of pneumococcal vaccines are available in Japan for adults (65 years and older): 13-valent pneumococcal conjugate vaccine (PCV13: Prevenar 13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23). In January 2015, the Joint Committee of the Japanese Respiratory Society (JRS) and the Japanese Association for Infectious Diseases (JAID) issued a statement on pneumococcal vaccination of adults aged 65 years and older. In this presentation, the importance of pneumonia prevention and the risk of infection will be discussed, citing current infectious disease topics and issues, and introducing RA therapies such as biologic agents.

ES6

Pursuit implementing Rheumatoid Arthritis Treatment for the Next Decade (Go above and beyond)

Yoshiya Tanaka[1], Tsutomu Takeuchi[2,3], Josef Smolen[4], Gerd R Burmester[5], Ryoji Noritake[6], Mieko Hasegawa[7], Satoshi Kubo[8], Yuko Kaneko[9], Sonosuke Yukawa[10], Sakae Tanaka[11], Kiyoshi Kurokawa[6]
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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has made great strides based on the spread of Treat to Target (T2T) treatment strategies and the development of therapeutic agents such as MTX and biologic agents. In particular, structural remission as assessed by X-rays is now achievable in many patients, making RA one of the diseases with relatively high treatment satisfaction among both physicians and patients. On the other hand, there are some remaining challenges, which will be discussed especially following 3 points in this seminar. The first is the increasing number of elderly patients with RA, along with the aging of the patient population. The presence of multiple complications, in addition to the impairment of physiological functions of the liver, kidneys, lungs, heart, metabolism, musculoskeletal system, and immune system, makes the condition difficult to treat according to guidelines. The other is difficult-to-treat RA (D2T RA), meaning patients who have difficulty controlling disease activity even with the use of two or more biologic agents (bDMARDs) or JAK inhibitors (tsDMARDs) with different mechanisms of action. Third, even after achieving clinical remission, there are a certain number of patients with residual joint pain and fatigue. In daily practice, objective indicators from the perspective of the medical staff are not only considered important, but also patient-reported outcomes (PROs), including subjective symptoms from the viewpoint of the patient's quality of life, and reflecting them in treatment has become an issue. Under the theme of "Pursuit implementing Rheumatoid Arthritis Treatment for the Next Decade (Go above and beyond)" this year's seminar will be held on consisting of three sessions of discussions on how to solve the unmet needs of rheumatoid arthritis treatment, along with an organization of the unmet needs of rheumatoid arthritis treatment. In the first session, national and international experts in RA will summarize "the development of rheumatoid arthritis treatment and its achievements" and "remaining challenges". In the next session, the next generation of experts will discuss their vision for the next 10 years, including health care policy. The final session will consolidate the discussions and present messages from the entire session of this seminar. We hope that this seminar will provide you with an opportunity to reconsider the original goal of T2T treatment, which is to maximize the patient's long-term quality of life, and that it will serve as a reference for your future research and practice.

ES7-1

Symposium for rheumatoid hand in JCR2023~challenges for difficult to treat RA~

Takuji Iwamoto
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Conflict of interest: Yes

More than 10 years have passed since a paradigm shift in the treatment of RA occurred with the introduction of biological agents. Formerly, joint replacement surgery and arthrodesis were the mainstays of RA treatment, but nowadays there is a demand for functional reconstruction with joint preserving surgery and for aesthetic reconstruction. On the other hand, it is important to recognize that there are patients with difficult-to-treat RA (D2T-RA), defined as RA that is refractory to several types of biologic or targeted synthetic DMARDs. Although the main principle of current RA treatment is to control RA with pharmacotherapy, it is necessary to consider the effectiveness of surgery based on a total assessment of the patient's age, occupation, hobbies, and disease activity when considering the improvement of the quality of life of patients. In the special lecture, Dr. Keiichiro Nishida will discuss the role of orthopedic surgeons and hand surgeons in a lecture titled " Treatment approaches for D2T-RA - Evidence for tocilizumab and the role of hand surgery". He will discuss the importance of pharmacotherapy and timely surgical intervention, based on his experience as a two-faced physician - rheumatologist and rheumatology surgeon. The theme for the panel discussion is "Reconsidering wrist surgery for RA". Total wrist arthroplasty is recently available in Japan and has become a new alternative for wrist surgery. With advances in pharmacotherapy, it is necessary to determine the indication for surgery by considering the balance between maintaining range of motion and stability. Dr. Yuuichiro Matsui will share his experience with the original developer of the wrist prosthesis. Dr. Shousuke Akita and Dr. Yoshitaka Hamada will present the indications for wrist surgery based on their case experience in situations where new options have been added, and we would like to reconsider wrist surgery for RA patients together with the participants.

ES7-2

Treatment approaches for D2T-RA - Evidence for tocilizumab and the role of hand surgery -

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Conflict of interest: Yes

Difficult-to-treat rheumatoid arthritis (D2T RA) refers to patients with refractory RA whose symptoms do not improve despite the several different treatments and who have a high patients' and financial burden. The European League Against Rheumatism (EULAR) defined D2T RA as having a history of (1) treatment failure, (2) active/symptomatic features and (3) clinical recognition by the rheumatologist and/or patient. Several factors complicate and make treatment more difficult in D2T RA, including resistance to DMARDs, limited medical treatment options due to side effects, comorbidities that preclude the use of DMARDs and non-adherence to treatment. In general, the efficacy of b/tsDMARDs is reduced in patients who have been treated unsuccessfully with multiple bDMARDs, and b/tsDMARDs with a different mode of action (MOA) are more effective. On the other hand, in D2T RA, longer time required for the search of more effective drugs may lead to progressive joint destruction and, ultimately, functional impairment and deformity. The item of "active/symptomatic characteristic" includes "having symptoms that reduce quality of life de-

spite well-controlled disease", which means that patients cannot depart from D2T-RA if severe hand deformity or pain persists. In our department, 20 patients with D2T RA underwent hand surgery under the control of JAK inhibitors, with 4.2 previous b/tsDMARDs. The preoperative DAS28-CRP was 1.94, of which 13 patients had moderate disease activity or higher. Surgeries included four total elbow arthroplasties, seven wrist operations, six on MCP joints, three on thumb CM joints, two on PIP joints and four tendon graft/transfer (including duplicates). Perioperative drug discontinuation was done in 6 cases, and no delayed wound healing or surgical site infection was observed. This presentation will review these cases and discuss the role of hand surgery in D2T RA.

ES8-1

Anti-ganglionic nicotinic acetylcholine receptor antibodies in systemic lupus erythematosus

Michihito Kono
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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is an autoimmune disease that involves the kidney, the central nervous system, the skin, and the gastrointestinal tract. Anti-ganglionic nicotinic acetylcholine receptor (gAChR) antibodies (Abs) were detected in the sera of patients with autoimmune autonomic ganglionopathy. Recently some papers reported that patients with connective tissue diseases, including SLE and systemic sclerosis, have serum anti-gAhR Abs. We measured anti-gAhR Abs for 144 patients with SLE, and these antibodies were detected in 29 patients. Lupus enteritis was more frequently seen in anti-gAChRα3 Ab-positive patients than negative patients. The rate of lupus enteritis development or relapse from the time of sera collection was higher in anti-gAChRα3 Ab-positive patients than in negative patients. In this seminar, I would like to discuss the significance of anti-gAhR Ab measurement in SLE.

ES8-2

Autonomic dysfunction in autoimmune diseases including RA, SLE, SS, and SSc

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Conflict of interest: None

Do the patients with autoimmune diseases suffer from autonomic dysfunction? Autoantibodies (AAbs) against the ganglionic nicotinic acetylcholine receptor (gAChR), which exists in the autonomic ganglion, a synapse of the autonomic nervous system, were discovered in 1998 in United States. We established the first assay system for gAChR AAbs in Japan in 2012. The gAChR AAbs have a pathogenic potential to interrupt the synaptic transmission in autonomic ganglia and has been confirmed in the serum from patients with autoimmune autonomic ganglionopathy (AAG). AAG patients demonstrate various autonomic manifestations, as well as extra-autonomic manifestations such as CNS involvement and sensory disturbance. In 2020, we reported the analysis of AAG cases in Japan and found that approximately 30% of AAG patients had autoimmune diseases. Actually, we previously reported that gAChR AAbs were found in approximately 10-20% of patients with autoimmune rheumatic diseases. Based on these results, we started a multicenter study on the prevalence of autonomic dysfunction and gAChR AAbs in autoimmune diseases including RA, SLE, SS, and SSc. At present, the answer to the first question is: "Autonomic dysfunction occurs in patients with autoimmune diseases". Autonomic dysfunction may be involved in Raynaud's phenomenon, gastrointestinal dysmotility, as well as nervous system complications in patients with autoimmune rheumatic diseases. From the viewpoint of the correlation between the immune system and the autonomic nervous system, vagus nerve stimulation for rheumatoid arthritis has recently attracted attention. Until now, the autonomic nervous system has been regarded as an immune target, but it is necessary to pay more attention to the concept of the autonomic nervous system controlling the immune system in the future. This presentation will also introduce recent findings on the correlation between the immune system and the autonomic nervous system.

ES9-1

Diagnosis and treatment of psoriatic arthritis from the perspective of enthesitis

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Conflict of interest: Yes

Psoriasis is characterized by erythematous plaques with silvery-white scales and is associated with polyarthritis in 10-40% of cases and is called psoriatic arthritis. PsA develops in people in their 30s and 40s, and the number of patients in Japan is estimated to be 100,000 to 200,000. PsA develops as enthesitis of tendons, ligaments, etc., associated with immunological abnormalities, and various clinical symptoms such as peripheral arthritis, spondyloarthritis, nail lesions, and dactylitis develop as the inflammation spreads. PsA causes progressive damage to the joints and spine of the whole body and often significantly interferes with daily life. In addition, uveitis and lifestyle-related diseases occur at a high rate, increasing cardiovascular events. In psoriatic arthritis, there are cases of psoriatic arthritis that present with symmetrical arthritis from the onset and cases of psoriatic arthritis in which distal finger joint lesions or nail lesions are not evident. Since it exists, it is essential to differentiate it comprehensively from other diseases. Psoriatic arthritis sometimes presents clinical symptoms similar to rheumatoid arthritis and synovitis. This is thought because synovitis occurs secondarily by affecting the Enthesis organ (synovio-enthseal complex). Since the pathology of psoriatic arthritis is mainly enthesitis, in distinguishing it from rheumatoid arthritis, evaluating not only skin lesions, the presence of rheumatoid factor and anti-CCP antibodies, but also the presence of various symptoms caused by enthesitis, such as distal phalangeal joint lesions, spine lesions, enthesitis of the Achilles tendon, dactylitis, and nail lesions, is essential and valuable in differentiating from rheumatoid arthritis. Recently, various biologic agents have become available for psoriatic arthritis, and with proper treatment, both skin symptoms and spondyloarthritis can be controlled. The importance of diagnosis and differential diagnosis is increasing for early and accurate therapeutic intervention.

ES9-2

Diagnosis, Differential Disease and Treatment Strategies for Psoriatic Arthritis

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Conflict of interest: Yes

Treatments for psoriasis and psoriatic arthritis have made dramatic progress in the last decade. Especially with the advent of biologics and molecular-targeted drugs, such as JAK inhibitors, the goal is PASI90 or PASI clear for the skin and MDA (minimal disease activity) for arthritis. It has become possible to aim for disease activity. Currently, there are many options, such as TNF inhibitors, IL-17 inhibitors, IL-23 inhibitors, and JAK inhibitors. It is necessary to consider to which domain is the treatment targeted, and what kinds of complications and comorbidities exist in the background. In psoriatic arthritis, there are various lesions (domains), such as cutaneous lesions of skin and nails, peripheral lesions, axial lesions, enthesitis, dactylitis, and extra-articular symptoms (uveitis, inflammatory bowel disease, etc.). It is also called a psoriatic disease because it causes disorders and has a high risk of cardiovascular events caused by metabolic syndrome, and hence its systemic management is important. It is necessary to correctly evaluate the activity and severity of each domain, and at that time, it is possible to obtain a lot of information not only from the patient's own symptoms, but also from imaging tests such as joint echocardiography and MRI. Furthermore, depending on the presence or absence of comorbidities, organ damage caused by them (renal dysfunction due to diabetes, liver dysfunction due to obesity, heart function, etc.), and extra-articular symptoms, it is necessary to adjust the dosage of the drug and change the drug options. Currently, EULAR2019 and GRAPPA2021 recommendations are widely used mainly for the treatment of psoriatic arthritis, and these treatment strategies will be explained in this seminar.

ES10-1

An overview of the benefit/risk and safety profile of JAK inhibitors in 2023

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Conflict of interest: Yes

In the 10 years since tofacitinib's approval, multiple new JAK inhibitors have been developed and approved for rheumatoid arthritis, psoriatic arthritis, inflammatory bowel disease, and other auto-immune conditions. While collectively these JAK inhibitors differ in their selectivity for the four JAK kinases (JAK 1-3, TYK-2), largely uniform dose-dependent adverse events have been observed for these compounds. While these agents raise the risk of serious bacterial infections and likely other opportunistic infections similar to TNF inhibitors, their propensity for reactivating some latent viruses (e.g. varicella zoster) sets them apart from other Disease Modifying Anti-Rheumatic Drugs (DMARDS). Aside from infections, important questions have been raised from the recent ORAL Surveillance study of tofacitinib conducted in patients >50 years old with cardiovascular risk factors. Most notably, this data suggested an increased risk of some types of malignancies, particularly among certain sub-groups of patients. While this study led to label changes from regulatory agencies, and the perception by regulatory authorities that all approved JAKi compounds have similar risks, there exist mechanistic differences and other potential explanations as to why some of these compounds might carry differential risk with regards to some Adverse Events of Special Interest like malignancy, infection, venous thromboembolism, and others. This presentation will review the latest safety profile as understood for each JAK inhibitor, including the recently approved TYK-2 inhibitor, and highlight the use of JAK inhibitors from the standpoint of maximizing their benefit and minimizing risk. In addition, the presentation will give practical advice regarding screening, suppressive therapy, and the use of vaccination to prevent infectious adverse events.

ES10-2

What we learned from ORAL Surveillance and how JAK inhibitors can help patients to reach treatment goals

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Conflict of interest: Yes

The development of Janus Kinase inhibitors (JAKi) as orally available small molecules offers novel treatment options for rheumatic diseases. JAKi interfere with signal transduction of the Janus Kinase-Signal transducer and activator of transcription (JAK-STAT) pathway causing effective suppression of downstream cytokine signaling. They act as competitive antagonists at activation sites for Janus kinases and as such interrupt downstream signals along the JAK-STAT pathway, effectively leading to suppression of cytokine production. The JAK-STAT pathway includes several kinases and JAKi can be grouped by their kinase-specific effects. Several drugs have been developed and been approved for the treatment of autoimmune and inflammatory conditions, with each expressing a certain specificity towards Janus kinases. A recent review carried out by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency included the results from an open-label clinical trial (ORAL Surveillance study) 1 of the JAK inhibitor tofacitinib in patients with rheumatoid arthritis and cardiovascular risk factors which found a higher risk of these events with tofacitinib than with TNF-alpha inhibitors. EMA concluded that the identified risks apply to all JAK inhibitors approved for the treatment of chronic inflammatory disorders and stated that these drugs should only be used in the following patients if no suitable treatment alternatives are available: those aged 65 years or above, those who are current or past long-time smokers, those with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors, or those with other malignancy risk factors. It will now be important in clinical practice to carefully analyze the risk (see factors above)/benefit ratio in our patients. The benefits include oral administration, high efficacy even in resistant cases, the possibility of monotherapy without methotrexate and the short half-life which may be important upon infections, surgery, and pregnancy planning. In many settings, JAKi will remain an important part of our treatment armamentarium.

ES11-1

The role of anifrolumab in the treatment of systemic lupus erythematosus

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease leading to significant morbidity and shortened lifespan. Treatment of SLE is challenging because of the limited efficacy and poor tolerability of standard therapy. The therapeutic target is remission without any systemic symptoms or organ disorders, and the realistic therapeutic goal was lupus low disease active state (LLDAS) to avoid relapse or organ disorders. As glucocorticoids and immunosuppressive drugs are non-specific therapeutic agents that cause organ damage, the development of drugs aiming to control specific abnormal immune network is anticipated. Type I interferon (IFN) pathway plays a central role in SLE pathogenesis. Anifrolumab is a human monoclonal antibody to the type I IFN receptor subunit 1, which blocks the action of type I IFNs. Two phase 3 studies (TULIP-1 and TULIP-2) and a phase 2b study (MUSE) provide substantial evidence for the efficacy and safety of anifrolumab for moderately to severely active SLE. In TULIP-2 study, anifrolumab demonstrated a statistically significant benefit in overall disease activity (as defined by BICLA response rate at Week 52), as well as its steroid-sparing effect, the improvements in SLE skin manifestations, and a strong trend in flare reduction. Concerning the percentage of high interferon gene signature, anifrolumab might be a good choice for moderately to severely active SLE in Japan, but patient number is limited in the clinical trial, we need further more data from real world evidence to re-check both efficacy and safety for Japanese patient. We have experienced that anifrolumab is effective in patients who cannot achieve or maintain LLDAS due to minor flares and in those who achieve LLDAS and seek to reduce glucocorticoids and achieve remission. In this seminar, we would like to discuss the role of anifrolumab in long-term therapeutic strategies for SLE.

ES11-2

New therapeutic strategies in Systemic Lupus Erythematosus

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Conflict of interest: Yes

Patients with systemic lupus erythematosus (SLE, lupus), the archetypal multisystem autoimmune disease, have poor outcomes in morbidity, quality of life, and mortality that have changed little in the last 20 years. This contrasts to dramatic improvements in outcomes in diseases such as rheumatoid arthritis (RA). Learning from the RA experience suggests a multi-pronged approach is needed to improve outcomes for SLE patients.

ES12

Reviewing physician-patient communication: How to get the most from a time-pressured office visit

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Conflict of interest: Yes

*Limiting the intended audience of physicians to 48, this evening seminar shall be conducted in a workshop including a lecture, discussions, and role-play. While many rheumatologists feel that physician-patient communication significantly influences the treatment outcomes, they have limited time to devote to the diagnosis and treatment of rheumatism owing to the increasing complexity of treatment and practice-related paperwork. CONVERSATIONS in MOTION (CIM) was created to address this reality. CIM is a communication technique program designed to help physicians make the most effective use of time-pressured outpatient visits. CIM was developed collaboratively by linguistic and communication experts, and rheumatologists in Japan and other countries. The effectiveness of each technique in CIM has been scientifically verified. CIM is comprised of four modules: (I) Shared Decision Making, (II) Empathy and Trust, (III) Practice Efficiency, and (IV) Medication Adherence. This seminar focuses on Module II: Empathy and Trust. Physicians and patients work together to find a therapeutic goal, which will enhance empathy and trust, and positively influence physician-patient communication. Such interactions allow physicians and patients to share high-quality information, have a positive effect on patient satisfaction and adherence, and provide support for forging a physician-patient partnership to achieve clinical objectives. In this workshop, "empathy" is defined as a physician's capacity and level of understanding of how patients may think and feel physically and emotionally, and "trust" is the patient's level of faith in the physicians' attitude toward understanding the patients and their medical conditions on top of the physicians' experience and knowledge in providing the best advice and treatment practices for their patients. The workshop will present three communication techniques focusing on enhancing empathy and trust. Through group discussions and role-playing activities, the participants will be provided tips to enhance their empathy and trust that can be applied into medical practice immediately after the workshop.

ES13-1

Therapeutic targets for Rheumatoid Arthritis: Focus on IL-6 inhibitors

Tsutomu Takeuchi
Saitama Medical University/Keio University

Conflict of interest: None

The treatment for rheumatoid arthritis (RA) has achieved great improvements recently. Especially, standardization of RA including from early diagnosis, treat to target, and to clinical, structural, and functional remission, has been widely established during 10 years from 2010. In addition to the publication and regular revision of recommendations and guidelines which indicate appropriate treatment for anti-rheumatic drugs by major global academic societies, progressions in therapeutic drugs such as bDMARDs have made it possible to standardize RA treatment. RA treatment recommendations of EULAR are revised every three years, and thought leaders in RA, primarily in Europe and around the world, are engaged in developing the consensus. The usage of glucocorticoids and b/ts DMARDs was revised based on the latest evidence in 2022. Also, RA Clinical Practice Guidelines 2020 has been announced by JCR, and revision work is currently conducting. In parallel with these advances in therapeutic strategies, elucidation of the pathogenesis of RA, which is a heterogeneous disease presenting diverse pathologies, has progressed. While new pathological cells and molecules such as Tph cells, AtoM cells, tissue-localized macrophages, and aggressive fibroblasts have been identified in addition to molecular pathological analysis by single cell analysis, our understanding of the network of inflammatory cytokines including IL-6 and TNFα, is also increasing. So far, we have demonstrated not only clinical research data, but also comprehensive molecular and cellular data using blood samples. Moreover, we have also been investigating factors that affect clinical efficacy, the relationship between cytokines and bone destruction with RA, and various cell dynamics at the molecular level. Thus, we will highlight the significance of IL-6 inhibition associated with RA pathogenesis and the current RA treatment from the latest evidence and state-of-the-art EULAR recommendations.

ES13-2

The key role of Interleukin-6 on inflammation, bone loss and bone repair in rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is autoimmune disease that is associated with a reduced quality of life by systemic inflammation and disability by progressive local and systemic bone destruction. The appropriate identification and monitoring of bone erosions is of crucial because erosions are the central sign of progressive destructive arthritis and are associated with an impaired functional outcome. High Resolution-peripheral Quantitative Computer Tomography enables evaluation of peripheral bone microarchitecture and accuracy in assessing bone changes in RA. Inflammation leads to an imbalance of bone metabolism by proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) in RA. This imbalance between bone resorption and bone formation causes progressive bone destruction based on increased osteoclasts and decreased osteoblasts. Current data have supported a key role of IL-6 in bone loss in RA, suggesting that IL-6 suppresses repair of damage bone in RA. This concept is based on findings that suggest that treatment with the anti-IL-6 receptor antibody tocilizumab (TCZ) achieves more pronounced repair of bone erosions than inhibition of TNF-alpha with respective therapeutic antibodies in patients with RA. These findings point to a homeostatic role of IL-6 in bone, which is also supported by findings that show that treatment with TCZ increases systemic markers of bone formation indicating repair such as osteocalcin. Thus, apart from the anti-inflammatory action of IL-6 targeted therapies in RA, such approach also seems to restore bone homeostasis. Therapeutic strategies that inhibit IL-6 may be prioritized to aim at repairing inflammatory bone damage in RA. In this symposium, I will focus on new possibilities related to IL-6 for tissue regeneration in inflammatory diseases including RA.

ES14-1

Emerging learnings in PsA: From clinical trials to clinical practice

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Conflict of interest: Yes

Psoriatic arthritis (PsA) is a chronic, progressive form of inflammatory arthritis that can cause swelling, stiffness and pain in and around the joints, entheses, and spine and leads to impaired physical function. It is caused by dysregulation of the immune system yielding excess pro-inflammatory cell cytokine activity. This results in tissue inflammation and destruction in the joints, tendon insertions, spine, skin and nails. With recent therapeutic advances in development of biologics and targeted synthetic disease modifying drugs, we are able to achieve states of remission or low disease activity. One target of treatment, endorsed by multiple professional organizations, is known as Minimal Disease Activity (MDA) - achievement of five of seven low states of musculoskeletal and skin disease activity. Ixekizumab is a monoclonal antibody that selectively binds with interleukin 17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Ixekizumab demonstrated rapid and sustained efficacy across different clinical domains of PsA, including MDA, regardless of whether it was used with or without MTX, and an acceptable safety profile in PsA clinical trials. Citrate-free formulation of ixekizumab, designed to reduce injection site pain, was approved in 2022. I'll provide up-to-date information related to PsA and ixekizumab.

ES14-2

Challenges in the treatment of RA and the role of JAK inhibitors

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Conflict of interest: Yes

Unlike biologics that inhibit single cytokines such as IL-6 or TNF-α, JAK inhibitors simultaneously suppress multiple cytokine signals via inhibition of intracellular kinases, and a wide variety of cytokine signals are involved in JAKs, some of which play important roles in RA pathogenesis but are not covered by existing therapies. For example, IFN-α (signal transmitted via JAK1/ TYK2) is an important cytokine in the pathogenesis of RA. Because IFN-α and TNF-α productions are cross-regulated in our body, IFN-α signature can be upregulated in patients treated by TNF inhibitor that could lead to treatment resistance or development of lupus-like phenomenon. Importance of IFN-γ (signal transmitted via JAK1/JAK2) was also suggested by a recent single cell analysis of RA synovial tissues. Our multi-omics analysis for factors associated with failure of TNF inhibitors treatment revealed that the high IFN-α signature at baseline and upregulation of IFN-γ signature early after treatment were associated with treatment failure of TNF inhibitors. Further, GM-CSF (signal transmitted via JAK2) is a common effector cytokine secreted by both Th1 and Th17 cells. GM-CSF is also involved with the perception of pain in RA. Thus, JAK inhibitors suppress multiple cytokine signaling involved with RA pathogenesis and can be an important therapeutic option for RA, including so to say "difficult to treat RA". In this seminar, the challenges and opportunities in the current RA treatment and role of JAK inhibitors will be discussed. Recent results of long term clinical trials with a JAK inhibitor, Baricitinib, will be also presented.

ES15-1

Structure and profile of ozoralizumab, a next-generation antibody

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Conflict of interest: Yes

Antibody drugs have made a great contribution to medical care since their advent. A number of antibody drugs have been launched mainly in the oncology and immunology areas. It is not uncommon that the antibody drugs show superior therapeutic effects in various diseases against the conventional drugs. However, it has been suggested in recent years that target antigens for antibody drugs have been depleted. To break through this situation, research and development of next-generation antibody drugs with new functions added to natural antibody molecules have been advanced. A next-generation antibody is an antibody drug for which attempts are made to add new functions such as an action on another target or a function as a delivery carrier through protein engineering, e.g., adding low-molecular compounds and/or mixing multiple types of partial structures of general IgG antibodies. VHH antibody is attracting attention as one of them. VHH is the variable region of the naturally occurring heavy chain antibody of camelids and is characteristically able to bind specifically to a target in a single domain. As a drug modality, however, VHH antibody has some issues such as short blood retention and low target affinity due to the smaller binding surface than usual IgG. Ut has advantages, however, such as high tissue infiltration, epitope structure different from IgG, and feasible protein engineering. In addition, from viewpoints of molecular recognition, it has ideal characteristics as a drug modality due to its structural properties between antibody and small molecule. VHH antibody is called nanobody®. A novel TNF inhibitor, ozoralizumab, was launched on December 1, 2022, as the first manufacturing and marketing approval in Japan. Ozoralizumab is a trimer of two anti-human TNFα nanobodies® and one anti-human serum albumin nanobody® with a molecular size of approximately a quarter of conventional IgG antibodies. In this seminar, we will outline the molecular structure and physical properties of VHH and ozoralizumab, a next-generation antibody as an example of drug application. NANOBODY® is a registered trademark of Ablynx. Ablynx originally discovered and performed initial development of the NANOBODY® compound ozoralizumab. Ablynx is an affiliate of Sanofi.

ES15-2

Safety and Efficacy of a New TNF Inhibitor, Ozoralizumab

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Conflict of interest: Yes

Treatment for rheumatoid arthritis (RA) has dramatically evolved in the last 20 years. In the past, symptomatic therapy with drugs such as NSAIDs and steroids, was predominant. However, the advent of antirheumatic biologics and Janus kinase (JAK) inhibitors that have shown breakthrough therapeutic effects has greatly expanded the drug treatment options. With this progress in therapeutic drugs, the treatment for RA has led to the establishment of a treat-to-target treatment strategy. TNF inhibitors, the first approved antirheumatic biological drug, have made a great contribution to this breakthrough. The effects of TNFα on inflammation and bone metabolism in the pathology of RA are widely known, and its inhibition is very important in the treatment of RA. Approximately 20 years have passed since the introduction of TNF inhibitors, but many studies are still being conducted on them, and new evidence has been reported. Recently, ozoralizumab, a TNF inhibitor with a new structure, has been launched as a next-generation antibody. Ozoralizumab has a trimer structure consisting of two anti-human TNFα Nanobodies® and one anti-human serum albumin Nanobody® which has no Fc region and whose molecular weight is approximately one-fourth the weight of a typical IgG antibody. Nanobody® is a low molecular weight antibody in which the variable region of an antibody, called the heavy chain antibody (composed of only heavy chains), naturally produced by camelid animals is fragmented and humanized. It can bind to antigens specifically in a single domain. The safety, efficacy, and pharmacokinetics of ozoralizumab were evaluated in the phase II/III clinical study in patients with RA which inadequately responded to methotrexate (MTX) treatments (OHZORA study) and the phase III clinical study in patients with RA without MTX (NATSUZORA study). As the results, manufacturing and marketing approval was granted for the indication of rheumatoid arthritis, which is inadequately managed by the current available treatments on September 26, 2022. In this seminar, we will outline the positioning of TNF inhibitors in drug therapy for RA and present the characteristic structure and study results of ozoralizumab, a new TNF inhibitor launched on December 1, 2022. NANOBODY® is a registered trademark of Ablynx. Ablynx originally discovered and performed initial development of the NANOBODY® compound ozoralizumab. Ablynx is an affiliate of Sanofi.

ES16-1

Reconsideration of the Potential of the JAK Inhibitor Upadacitinib: From the viewpoint of efficacy

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Conflict of interest: Yes

The Treat-to-Target strategy has been prevailing in the management of rheumatoid arthritis (RA) and spondyloarthritides (SpA), and the treatment goal is to maximize the patients' quality of life through the early remission induction and its long-term maintenance. The first-line drugs for RA/SpA include methotrexate and non-steroidal anti-inflammatory drugs from the viewpoint of drug costs, although biological agents or Janus kinase (JAK) inhibitors such as upadacitinib are indicated for refractory patients. In addition, upadacitinib has demonstrated short-term and long-term efficacy in patients including those who had experienced biological agents by the SELECT series of clinical trials without considerable effects of concomitant drugs. Future treatment strategy beyond RA/SpA remission by JAK inhibitors may include their tapered and long-term use, the switching to biological agents, especially biosimilars, in addition to the discontinuation of JAK inhibitors from the viewpoints of risk-benefit-cost balance.

ES16-2

Reconsideration of the Potential of the JAK Inhibitor Upadacitinib: From the viewpoint of safety

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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has made dramatic progress with the advent of biologics targeting inflammatory cytokines, and the spread of "Treat to Target (T2T)" to clarify the treatment goal of clinical remission and optimize the treatment to achieve the goal has revolutionized the treatment of rheumatoid arthritis. Furthermore, the advent of JAK inhibitors, which target JAK, has expanded treatment options for achieving treatment goals. Currently, there are 5 JAK inhibitors indicated for RA in Japan. Upadacitinib potently inhibits JAK1 and exerts anti-inflammatory effects by inhibiting cytokine signaling associated with RA pathology. The Phase III SELECT study evaluated the efficacy and safety of upadacitinib in RA patients with diverse background characteristics and demonstrated the usefulness of upadacitinib in combination with csDMARDs including MTX or as monotherapy. In this lecture, I'd like to discuss the safety profile of upadacitinib based on the results of the long-term integrated safety analysis in the Phase 3 studies and the results of the interim analysis of the special use-results survey (PMS) in Japanese subjects.

ES17

The precious track-history of Tofacitinib during the 1 decade~The door to a better future for Rheumatology based on the evidence~

Kenta Misaki
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Conflict of interest: Yes

Tofacitinib (TOF) appeared in the world of the region of rheumatoid arthritis (RA) in 2013 after just 1 decade when the first biologics (Bio) was approved in Japan in 2003. TOF is one of the JAK inhibitors (JAKi) focused on various cytokines led to severe inflammation of RA unlike the mechanism of Bio: just targeted to one cytokine. The approvement 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 prescribed TOF to the Bio-IR of RA patients cuz 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 conditionally elected in Phase II of the 2020 Japanese guideline as well as those of abroad. Additionally, TOF is also approved to inflammatory bowel diseases under the medical insurance in Japan. Just 1 decade 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 10 years, on the other hand we faced on so many issues at the same time. The first, a novel-concept of difficult to treat (D2T) was proposed contrary to the concept of RA-treat to target. Another, adverse cardiovascular events or malignancies under the treatment of TOF was published as the data of Oral Surveillance (OS) trial. OS trial brings attention the issue of pre-screening of RA patients before administration not only TOF but also Bio. Especially, we Rheumatologists have a wide viewpoint about OS trial in various aspects. I'll introduce the novel track-history of TOF during the 1 decade including the provisions of RA treatment led to the future one based on the current state of D2T and OS trial in this session.

ES18

Basic Seminar for Spondyloarthritis 2023To understand the current diagnosis and treatment of spondyloarthritis

Masahiro Yamamura[1], Tetsuya Tomita[2], Satoshi Kawaai[3], Tadashi Okano[4], Yoshinori Taniguchi[5]
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Conflict of interest: Yes

Spondyloarthritis (SpA) is a group of inflammatory rheumatic diseases comprising ankylosing spondyritis (AS), psoriatic arthritis (PsA), reactive arthritis, SpA-associated with inflammatory bowel diseases, and undifferentiated SpA. More recently, axial and peripheral SpA (axSpA and pSpA) have been classified by the Assessment of SpondyloArthritis international Society (ASAS). In addition, axSpA is divided into radiographic and non-radiographic axSpA (r-axSpA/nr-axSpA) with or without definite X-ray evidence of sacroiliitis. These interrelated disorders share clinical features such as axial and peripheral arthritis, uveitis, enteritis, and skin lesions, and disease onset and severity are associated with MHC class I molecules, in particular HLA-B27. Activation of the IL-23/IL-17 pathway and the TNF-a proinflammatory cascade plays an important role in the pathogenesis. At present, inhibitors against TNFa, IL-17, IL-23, and PDE4 are currently available, and the disease activity of SpA has been demonstrated to be controlled by these effective drugs. However, the delay in diagnosis and treatment initiation can lead to irreversible joint damage and disability. For correctly diagnosing SpA and implementing appropriate treatment, SpA routine evaluations, such as history taking, joint examination, and blood examinations, will be required. In the seminar, speakers will focus on the current diagnosis and treatment of SpA.

ES19

Clinical features and management of glucocorticoid-induced osteoporosis

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Soen Orthopaedics, Osteoporosis and Rheumatology Clinic

Conflict of interest: Yes

Oral glucocorticoids (GC) are used for various diseases, and the most common adverse effects of GC are osteoporosis and fragility fractures. Fracture risk is associated with mean daily GC dose. There is no safe margin of GC dose for fracture risk, and the risk of non-vertebral fractures increases sharply when the daily dose exceeds 20 mg prednisolone equivalent. It has been shown that the risk of fracture is maximized 3 to 6 months after the start of GC, suggesting that primary prevention is important. In addition, it has been clarified that fractures occur even with high bone mineral density in GC-administered patients, and it is possible that male patients have a higher risk of fractures. Since the American College of Rheumatology issued recommendations for GIO in 1996, recommendations and guidelines have been published and revised in various countries. In Japan, the Japanese Society for Bone and Mineral Research issued its first management and treatment guideline for GIO in 2005, and it was revised in 2014. Patients who are using oral GC for more than 3 months or who are planning to use oral GC for more than 3 months, totaling the scores for each item of prevalent fractures, age, average daily GC dose, and lumbar bone mineral density, and scoring 3 points or more are eligible for treatment. Alendronate and risedronate, which have been shown to be effective in preventing vertebral fractures in both primary and secondary prevention, are the first-choice drugs. Recombinant teriparatide, ibandronate, alfacalcidol, and calcitriol, for which evidence was inconsistent, were considered alternatives. In recent years, controlled trials of zoledronic acid and denosumab compared with risedronate have been conducted overseas, and clinical trials of minodronic acid, eldecalcitol, and teriparatide acetate have also been conducted in Japan. And, the Japanese guidelines are currently in the process of being revised.

ES20-1

Why SDM is necessary for rheumatoid arthritis practice

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Conflict of interest: Yes

Rheumatoid arthritis (RA) practice has seen a dramatic development in therapeutics since the end of the 20th century: MTX, biologics, JAK inhibitors, etc. Remission and low disease activity have become realistic goals, and patient outcomes have improved dramatically. On the other hand, the treatment has become more prolonged due to the increase in superior therapies. Multimorbidity and polypharmacy are also real problems for RA patients, and drug interactions and poor adherence are common. Patients range in age from young to elderly. It is becoming increasingly difficult to achieve satisfactory results with uniform treatment for patients of different ages, values, comorbidities, and number of treatments. Shared

Decision Making (SDM) is attracting attention for effective and stable implementation of complex RA treatment. In this lecture, we will introduce SDM as one of the ideas to facilitate various RA treatments, and hope that it will provide some hints for the treatment of RA.

ES20-2

Preconception care for the patients with Rheumatoid Arthritis

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Conflict of interest: None

Preconception care (PCC) is a new concept that is defined as the health care and education for women of childbearing age and their partners to prepare them for future pregnancies. However, this care is not intended to "get the patient pregnant as soon as possible". It is about supporting women of childbearing age and their partners in reassessing their physical and mental health for a better life in the future. PCC in rheumatoid arthritis (RA) care begins at the time of diagnosis. It might be difficult, especially for male physicians, to discuss pregnancy and childbirth with young female patients. However, because methotrexate, a key drug in RA practice, is clearly a teratogenic drug, it is essential to check for pregnancy and provide contraceptive guidance prior to its introduction. In this context, it would be advisable to interview the patient about her feelings about future life planning and family planning. There are three key points in practicing PCC. First, providers should actively seek to provide information about pregnancy and childbirth to all patients of childbearing age and their families, even if they do not specifically ask for it. Second, it is also important that the patient and her partner fully understand that pregnancy is ideally achieved when the patient is in remission or maintaining low disease activity while using stable medications that are acceptable for use during pregnancy. To this end, patients' concerns about drug use during pregnancy should be taken seriously, and SDM should be practiced after carefully explaining the benefits of controlling disease activity during pregnancy. Finally, it is also important to share the points discussed at the PCC with all the professions involved with the patient. It is advisable to practice PCC as a team, utilizing the strengths of medical staff such as nurses and midwives.

ES20-3

Reconsidering immunological features of WoCBA-RA and their therapy for remission induction and maintenance

Isao Matsumoto
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Conflict of interest: Yes

The treatment strategy mainly focusing on the pregnancy and delivery management are highlighted on older age of the pregnancy in the rheumatoid arthritis (RA). It is reported that it tends to be hard to become pregnant within high disease activity in RA. In RA, there are many reports that symptoms are generally alleviated during pregnancy and tend to be exacerbated after childbirth. There is the teratogenicity in methotrexate which is anchor drug of the treatment, and the JAK inhibitor is contraindicated in a pregnant woman. Thus, it is necessary to consider discontinuation of these drugs after remission induction, or start with other treatment without using them. Beneficial cast with biologics, shared decision making is necessary for the benefit to give biologics during the pregnancy exceed a disadvantage. In addition, the TNF inhibitor shifts to a fetus to a child born, and attention is necessary at inoculation time of the live vaccine. In this seminar, we will summarize the immunological findings of RA pathology during pregnancy, the history of the collagen disease-complicated pregnancy outpatient clinic opened at our facility in 2022, the characteristics of biologics via compact MRI, and the results in local joints.

ES21-1

The position of Benlysta in the Evidence-Based Treatment of SLE/LN

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Conflict of interest: Yes

SLE is a lifelong and burdensome disease associated with poor quality of life, uncertainty around disease activity, and often insufficient treatment. As a chronic disease, a key challenge is minimising the long-term effects of disease activity and treatment toxicity; in particular, the accumulation of organ damage. To minimise organ damage accrual, control of disease activity must coincide with the avoidance of excessive glucocorticoid (GC) use. Organ involvement in the form of lupus nephritis (LN) is a serious complication of SLE that has a particularly high incidence in Asian patients with SLE compared with the global average. Treatment of LN requires urgent and decisive action to preserve kidney function; however, this is often not achieved with standard immunosuppressive therapy, with 20% of patients with LN progressing to end-stage kidney disease within 10 years of diagnosis. Benlysta (belimumab) is a biologic therapy with an established position in treatment guidelines as an add on therapy for uncontrolled SLE. Importantly, in addition to improving disease activity, and decreasing the risk of new severe flares and the need for GC, it has demonstrated the ability to slow organ damage progression compared with standard therapy alone, and earlier use has been attributed to better outcomes. However, its use in LN is less clear since formal guidelines have not yet been updated to include newer therapies. Two-year data from the BLISS-LN trial have demonstrated a significant reduction in kidney disease activity and risk of renal flare, as well as greater preservation of eGFR, in those receiving Benlysta plus standard therapy compared with standard therapy alone. The addition of Benlysta also supports the reduction of GC use in those with LN. Therefore, the evidence supports the addition of Benlysta to standard therapy used in induction and maintenance therapy for LN, providing clinicians with a treatment that can enhance short- and long-term outcomes in both SLE and LN.

ES21-2

SLE patient suitable for belimumab inferred from real world data

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) treatment involves glucocorticoid (GC) therapy with various immunosuppressive drugs. The initial GC dose and selection of immunosuppressive drugs are based on several factors, including SLE disease activity, presence or absence of major organ involvement, and complications. However, these drugs are nonspecific, and their long-term use can increase the risk of organ damage and adversely affect the quality of life and prognosis of patients. In other words, molecular-targeted drugs that are more specific to the pathology are needed to improve the quality of life and prognosis of SLE patients. Belimumab (BEL) is a fully human monoclonal antibody against B-cell activating factor, which is a member of the tumor necrosis factor family (BAFF), and was the first biologic approved for SLE treatment. In fact, various clinical trials have confirmed the efficacy and safety of BEL, as well as its ability to suppress organ damage. The BLISS-NEA trial confirmed the efficacy and long-term safety of BEL in patients with SLE in North East Asia (NEA), including Japanese patients. The BLISS-LN trial also showed that early BEL combined with induction therapy after remission induction therapy for lupus nephritis with high disease activity improves renal prognosis at two years. In other words, clinical trials have demonstrated the efficacy and safety of BEL in SLE patients with intermediate to high disease activity. However, the long-term efficacy and safety of BEL in real clinical settings with diverse patient backgrounds remain to be fully investigated. According to the treat-to-target strategy for SLE, 'lupus maintenance treatment should aim for the lowest GC dosage needed to control disease, and if possible, GCs should be withdrawn completely'. In real-world clinical practice, reducing or discontinuing drugs in patients with SLE can be challenging. From the LOOPS registry, a database of SLE patients in our department, we will analyze the long-term efficacy and safety of BEL in clinical practice. In addition, we will determine which SLE patients have the potential for GC dose reduction or discontinuation and investigate the optimal patient profile for BEL in the treatment of SLE.

AUTHORS' INDEX

PL .... **Presidential Lecture**

SL .... **Special Lecture**

S .... **Symposium**

SS .... **Special 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**

Bold Abstract No. ..... **Presenting Author**

E

F

G

H

I

J

L

M

N

O

P

Q

R

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U

Z

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