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JAPAN COLLEGE OF RHEUMATOLOGY ABSTRACT SUPPLEMENT

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ABSTRACTS

Presidential Lecture

PL

Rheumatoid Arthritis: New challenges

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Conflict of interest: Yes

Some 30 years ago, it was the dawn of new era for rheumatoid arthritis (RA) treatment. Methotrexate has approved in the united states in 1988. In 1994, break through news about the evolutionary effect of anti-TNF biological agents went thorough around the world. The clinical development for biological agents were extremely rapid, that we have never seen before. In addition to TNF, we obtained biologics targeting on IL-6 receptor, T cells, and B cells. Most recently, the fifth target JAK is attracting the big attention. By patting the back by the evolutional progress in disease-modifying anti-rheumatic drugs, as well as the standardized clinical measurements, new classification criteria, new remission criteria, treat to target strategy, repeated revisions of recommendations/guidelines, and new imaging modality are generated. Thus, the RA treatment strategy is established as the present form, which was not unexpected at all in 1990. At present, clinical remission is the realistic goal and most of the patients are aiming at inhibition of progression of structural damage and maintaining the activity of daily living. 100% achievement of clinical remission at 6 months after new treatment is not possible. There is no new drug for preventing pre-RA progressing to full blown RA. There still exist a gap between clinical remission and patient satisfaction. The gap also exists among imaging modalities for structural damage. The recent epidemiological and clinical observations show us that the onset of RA is moving toward the aged population and the sero-positivity is gradually down during three decades in Minnesota county, despite the proportion of the patients with early radiographic progression is increased. I would like to share our experiences with multi-omics profiling of molecular signatures in peripheral blood of RA patients with the different targeted treatment and the recent publications from the world leading laboratories for the single cell analysis of untreated active RA synovium and fate mapping in the model animals. Now, we should aim to induce the normalization of the ADL of RA patients, backing to life in the pre-disease status, hopefully even by drug- free. Challenging toward such an ideal target should be required in the next stage. Finally, I would like to ask every young rheumatologists to step forward, not stopping, and challenge toward the big breakthrough with ultimate goal and ambition.

Representative Session

RS

PMDA's efforts to promote medical innovation

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Pharmaceuticals and Medical Devices Agency (PMDA)

Conflict of interest: None

The Pharmaceuticals and Medical Devices Agency (PMDA) plays three key roles-relief services for persons injured by adverse reactions to drugs and regenerative medical products, product reviews, and safety measures. To provide patients and healthcare professionals with rapid access to safer, more effective drugs, medical devices, and regenerative medical products, the PMDA is engaged in ensuring quality, efficacy, and safety from development to post-market stages. Since its inception in 2004, the PMDA has steadily improved its outcomes based on regulatory science. Those include significantly diminishing its review time frame for new products. With the emergence of innovative products, an increasing number of cases will have no precedents to refer to, propelling the PMDA to be the first in the world to make regulatory decisions. Quality at the PMDA will be even more important. Especially, as specific efforts to address innovative technologies and products, we have introduced regulatory schemes such as "SAKIGAKE Designation", "Conditional Early Approval for Pharmaceuticals", "Conditional and Time-limited Approval for Regenerative Medical Products", etc. for early practical application of new medical products. In addition, to further advance regulatory science, PMDA established the Regulatory Science Center in April 2018, and has started various initiatives including the "Science Board", "Horizon Scanning", etc. in order to address products utilizing emerging technology. In this lecture, I would like to introduce PMDA's activities for faster access to safer and more effective medical products.

Special Symposium

SS1-1

Managing difficult to treat RA in the real world

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Conflict of interest: None

Managing difficult to treat RA (dttRA) is a real problem for daily practice. However, not everybody uses the same definition / concept of difficult to treat RA. Therefore, an EULAR Task Force started to formulate a definition, that is now published in ARD. Following this definition, a systematic literature search was started and many factors were identified that may lead to dttRA, such as wrong diagnosis, lack of compliance, complaints more based on damage than on inflammation, one or more co-morbidities and others. It is very difficult to distill from literature what drug-treatment would be best for the individual dttRA patient. The complete RA history needs to be taken into account, but also psychological and social factors. No definite advise can be given, but some leads will be discussed.

SS1-2

Challenges in PsA - the EULAR updated view?

Daniel Aletaha
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Conflict of interest: None

Psoriatic arthritis is a very heterogeneous disease. While EULAR recommends the use of conventional synthetic disease modifying drugs (csDMARDs) first line in polyarticular disease, the initial therapy for oligoarticular PsA, predominant enthesitis or axial disease continues to ne no-steroidal antirheumatics (NSAIDs). The first choice of biological therapy in the EULAR 2020 recommendations is TNFi, or IL17i in axial disease, with the additional options of IL-12/23i when arthritis or enthesitis predominates. Whenever skin involvement is relevant, there is a preference of IL-17i over TNFi. When these modalities fail, arthritis and enthesitis may potentially also benefit from targeted synthetic (ts) DMARDs initial treatment option. The updated view also includes statements about consideration of treatment reduction in case of well controlled disease. The EULAR recommendations are worded in a quite general way, but cover most clinical situations while providing a simple flowchart that allows clinicians the best option for their patients.

SS1-3

When treating malignancy becomes a rheumatologic problem (Checkpoint inhibitors)

Iain B McInnes
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Conflict of interest: None

The advent of immune checkpoint inhibitors has revolutionised the approach to the treatment of a range of tumours. Rheumatic and musculoskeletal immune-related adverse events (irAEs) are observed in about 10% of patients with cancer receiving checkpoint inhibitors. Given the recent emergence of these events and the lack of guidance for rheumatologists addressing them, a European League Against Rheumatism task force was convened to harmonise expert opinion regarding their identification and management. In this lecture I will summarise the key findings of this taskforce and apply them to the management of this increasingly common referral into rheumatology clinical practice.

SS2-1

Using genetics and genomics to define molecular mechanisms for rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis is a highly heritable autoimmune disease affecting up to 1% of the general population. Immune mediated destruction of the joints leads to inflammation, pain, and eventually to disability. Here we discuss recent progress in the application of genetics and genomics to define pathogenic genes, pathways and cell-types in rheumatoid arthritis. First, we will discuss genetic studies of rheumatoid arthritis. Second, we will discuss the HLA and efforts to fine-map that locus to define key driving alleles. Third, we will discuss non-HLA loci, and present data demonstrating how functional alleles alter gene regulation in CD4+ T cells. Finally, we will present recent data using single cell technologies examining the different cell-types in the inflamed joint, to define the cellular landscape of pathogenic cell-types.

SS2-2

Mechanisms underlying joint damage and pain in osteoarthritis reveal new targets

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Conflict of interest: Yes

Osteoarthritis (OA) is a chronic progressive, painful disease of synovial joints, affecting mainly the knees, hips, hands, and small joints in the spine. OA is the most common form of arthritis, and one of the major causes of chronic pain worldwide. Joint pain is the main symptom that drives OA patients to seek medical help, but current strategies for pain management are inadequate. No available treatments slow or halt the progressive degeneration of the joint characteristic of OA. Ultimately, patients with knee and hip OA often end up undergoing total joint replacements. Cartilage degradation, subchondral bone remodeling, and osteophyte formation are the hallmarks of OA, and there is low-grade synovitis. There is a strong mechanical component in OA pathogenesis, but it is now also widely appreciated that the interplay between mechanical factors and low-grade inflammation is a key driver for disease. While a discordance between radiographic OA and the presence of pain can be observed, strong clinical evidence suggests that ongoing peripheral input from the affected joint drives pain in OA. The seminar will summarize current understanding of mechanisms of pain associated with progressive joint damage in OA, highlighting findings in patient cohorts and in newly developed animal models of OA. It will be discussed how these insights can lead to novel mechanism-based approaches to target OA pain, both at the level of the joint and in the nervous system. Emerging new treatments which target the neurotrophin nerve growth factor (NGF) will be discussed in more detail. In addition, novel potential disease-modifying drugs for OA (DMOADs) will be discussed.

Symposium

S1-1

Type I Interferon Targeting in SLE

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Conflict of interest: Yes

Developing new treatments for systemic lupus erythematosus (SLE) is difficult because of its clinical and biological heterogeneity, as well as issues with study and endpoints design. Preclinical validation of multiple therapeutic targets in mouse studies has not been followed by clinical trial success. Therefore, validation first in human SLE has arisen as a new paradigm. The first such target to be supported by clinical trials is type I interferon (IFN). Autoimmunity to nuclear antigens in SLE results in activation of innate immune mechanisms which evolved to support responses to viral infection, mediated by production of IFN. Evidence of IFN activation in SLE includes the highly reproducible finding of IFN signature gene (ISG) expression in blood and affected tissues, associated with markers of disease severity. Even though it is not primarily pathogenic in classic murine lupus models, IFN exacerbates murine models of SLE and IFN treatment of other human diseases can induce SLE-like phenotypes. Together, these data supported trialling IFN-targeting treatments in SLE. Recently, multiple clinical trials of IFN targeting agents have confirmed the role of IFN in SLE. Studies of antibodies to IFNalpha, and of a vaccine inducing neutralizing IFN antibodies, yielded mixed but overall supportive results. Importantly, three randomized trials of an antibody to the type I IFN receptor, which may cause greater suppression of ISG than other agents, showed reproducible efficacy across composite outcome measures, skin disease, and glucocorticoid tapering. However, the primary outcome was not met in one of these trials, potentially reflecting issues with endpoints per se. Safety issues identified include increased rates of herpes zoster, in line with expectations based on the mechanism of action. These findings provide support for the role of IFN in the pathogenesis of SLE, and for the potential benefit of treatments targeting this pathway for patients.

S1-2

Role of IL-12 and IL-23 in the pathophysiology of systemic lupus erythematosus and their utility as therapeutic targets

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Conflict of interest: Yes

IL-12 and IL-23 are cytokines that share the subunit p40, and induce Th1 and Th17 cells, respectively. The diseases associated with genetic polymorphisms of IL-12, IL-23, and their receptors include ankylosing spondylitis, psoriasis (PsO), psoriatic arthritis (PsA), Behçet disease, Crohn's disease (CD), ulcerative colitis, and Takayasu arteritis. They are characterized by the association with HLA class I. Although the role of IL-12 and IL-23 in the pathophysiology of systemic lupus erythematosus (SLE) has not been fully understood, genomic analysis has revealed the association of *STAT4* and *IL12A* genes with SLE susceptibility (Julia, Arthritis Res Ther, 2018). It has also been reported that p40 is highly expressed in SLE patients and correlates with disease activity (Lauwerys, Lupus, 2012). Although type I interferons (IFN) have been spotlighted recently as pivotal factors of the pathogenesis, IL-12 (p70) and type II IFN may also be involved as triggers of the pathophysiology. The selection of primary endpoint and dosage is critically important for the success of phase 3 randomized controlled trials (RCT). However, the issue is how we can create a useful disease activity indices, because SLE has a variety of organ symptoms. Recent clinical trials have used composite measures such as SRI-4 and BICLA. Ustekinumab (UST) is a monoclonal antibody that inhibits p40. UST showed its dramatic effects on PsO (Leonardi, Lancet, 2008), but only marginal effects on PsA (Gottlieb, Lancet, 2009) and CD (Sandborn, Gastroenterology, 2008). In phase 2 RCT of UST for SLE (van Vollenhoven, Lancet, 2018), the UST group showed a significantly better response in SRI-4 at 24 weeks ($p = 0.006$). Next, phase 3 RCT (LOTUS study) was performed, but it was discontinued because of poor results in the interim analysis. The safety of UST was confirmed. One problem should be that the dose of UST is set low. Better results may be obtained by modifying the dosage of UST.

S1-3

Type I and type II anti-CD20

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a prototypic systemic autoimmune disease that affects various organs, and unmet needs particularly remain in the management of lupus nephritis (LN). The pathogenesis of SLE is characterized by B cell hyperactivation and autoantibody production. CD20 is highly expressed from pre-B to memory B cell stage, but its expression subsides at plasma cell stage. Thus, anti-CD20 mAbs mainly target pathogenic B cells at an intermediate stage of development without affecting Ab levels. Rituximab (RTX), a type I anti-CD20 mAb, was shown to be effective in several observational open-label trials, while two randomized controlled trials, EXPLORER and LUNAR, failed to meet primary endpoints. However, a large number of subjects in the RTX arms of both studies achieved remission and serological improvement. Despite these controversies, ACR and EULAR guidelines recommend consideration of RTX for treatment of refractory SLE, including LN. Obinutuzumab (OBZ), an Fc-engineered type II anti-CD20 mAb, exhibits more direct B-cell-killing effects and relies less on complement-dependent cytotoxicity as compared with RTX. A recent study showed that OBZ is more effective than RTX at depleting B cells and ameliorating glomerulonephritis in murine lupus model. In humans, OBZ and MMF or placebo was evaluated in NOBILITY, a phase II trial that enrolled active LN patients (class III and IV). Two OBZ pulses were initiated along with induction therapy and were repeated after 6 months. Complete renal response (CRR) was shown to be greater with OBZ than placebo at week 52 (35% vs. 23%, $P = 0.115$), week 76 (40% vs. 18%, $P = 0.007$) and week 104 (41% vs. 23%, $P = 0.026$), implying the longevity of its effect. No serious adverse events were noted in the OBZ group. The phase III trial of OBZ in LN is currently ongoing. These findings reinforce the idea that B cells play pathological roles in SLE, probably by exerting Ab-dependent and -independent functions.

S1-4

Targeting the JAK in the treatment of SLE

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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. As glucocorticoids and immunosuppressive drugs are non-specific therapeutic agents that cause many adverse reactions, the development of molecular target therapy with balanced effectiveness and safety is anticipated in the treatment of SLE. Whole-genome association analysis revealed that many of disease-susceptibility genes for SLE are present in lymphocytes, while they are also present in dendritic cells in innate immune system. Thus, there are high expectations for the development of therapeutic agents targeting "bridging cytokines" such as BAFF, IFNs, and IL-12/23 produced by dendritic cells, which connect the innate and acquired immune systems. Janus kinase (JAK), which constitutively binds to cytokine receptors, plays an important role in cytokine signaling. JAK is comprised of JAK1, JAK2, JAK3, and TYK2. Activation of cytokines involved in the pathogenesis of SLE depends on the JAK signal, *i.e.* type I IFN signals via JAK1/TYK2, and IL-12 and IL-23 transmit signals via JAK2/TYK2. JAK inhibitor can inhibit and fine-tune the activity of one or more of JAK signal. Considering the regulations of both immunity and inflammation by JAK inhibitors, their application to SLE is expected. Tofacitinib, baricitinib, filgotinib, upadacitinib and several new JAK inhibitors such as TYK2 inhibitor (BMS-986165) and JAK1/TYK2 inhibitor (PF-06700841) are now being tested in clinical trials. Increasing

evidence points to immunological heterogeneity of SLE. Therefore, it is expected that different JAK inhibitors will be used to apply therapeutic strategies, such as precision medicine, by classification of patients according to their immunological conditions, and to set a therapeutic goal of the discontinuation of glucocorticoids in the future.

S1-5

Efficacy of Low-Dose Interleukin-2 for Primary Sjögren's Syndrome-A Randomized Double-blind, Placebo-controlled Clinical Trial

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Conflict of interest: None

Background The use of low dose IL-2 in the treatment of autoimmune diseases is promising in previous studies, but the efficacy and safety in SS are still to be confirmed by randomized, double-blinded, and placebo-controlled trials. **Objective** To investigate the efficacy and safety of low-dose IL-2 in treatment of pSS patients. **Methods** A double-blind, placebo-controlled randomized clinical trial was conducted from June 2015 to August 2017. Sixty patients with active disease were recruited from Peking University People's Hospital. Patients were treated with low-dose IL-2 or placebo for 3-month and accompanied by 3-month follow-up. The primary endpoint was defined as improvement in the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI) score at week 24. Secondary endpoints comprised of improvements in immunological parameters. Efficacy analyses were based on the intention-to-treat principle. **Results** A total of 66 patients with active disease of pSS were screened and 60 of them were randomly assigned to receive either low-dose IL-2 (n=30) or placebo (n=30). A higher percentage of IL-2 group patients (66.7%) achieved ESSDAI reduction (≧3 points) than the placebo patients (26.7%) at week 24 (P = 0.004). Resolutions of eye dryness, pain, and fatigue were greater in IL-2 group than placebo group (P = 0.001, P=0.026, P=0.012, respectively). Parotid gland swelling was also significant improved (P<0.05). No severe adverse event was found in this trial, but less infections were noticed in low-dose IL-2 group of patients. Immunological analyses revealed that low-dose IL-2 led to expansions of CD25highCD127low regulatory T cells and CD24highCD27+ regulatory B cells, while pro-inflammatory cytokines including IL-17A and IFN-α were reduced with low-dose IL-2 treatment. **Conclusion** This trial suggests that low-dose IL-2 therapy was tolerated and effective in active SS (ClinicalTrials. gov number: NCT02464319).

S2-1

Current genomics of autoimmune diseases: towards precision medicine

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Conflict of interest: None

Genome-wide association studies (GWAS) have identified many disease susceptibility loci for autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. Although more than 100 genetic loci have been identified for these diseases, these only partially explain the genetic components of diseases, suggesting that there are still unidentified genetic factors. In addition, to understand the pathological mechanism of diseases, it is essential to identify the causative variants in these loci and clarify how these genetic variants affect the functions of neighboring genes. Furthermore, in order to realize genomic precision medicine using individual genomic information, it is necessary to evaluate how the accumulation of these genetic factors is involved in the pathological condition of individual patients. The current topics in the genomic research of autoimmune diseases are the followings: 1) identification of more susceptibility loci by GWAS meta-analysis at the world level, 2) identification of rare variants, which GWAS had not mainly targeted, by whole genome sequencing, 3) identification of repetitive-sequence variants and structural variants involved in diseases by long read sequencing, 4) functional analysis of genetic variants by expression quantitative trait locus (eQTL) analysis using transcriptome data of immune cell subsets, 5) application of genomic information to precision medicine using polygenic risk score (PRS). In this presentation, these topics will be outlined through our own research experience.

S2-2

Multi-omics approach to autoimmune diseases

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Conflict of interest: Yes

Genome-wide association studies (GWAS) have revealed many variants associated with autoimmune diseases. Majority of those variants are located in non-coding genomic regions and have gene-regulatory functions. As the gene-regulatory functions are significantly diversified among cell types and environment, multi-omics approach with multiple layers of data should be informative for elucidating genetic functions. As an example, we performed epigenomic analysis of synovial fibroblasts from rheumatoid arthritis (RA) patients and unveiled the dynamic change of super-enhancers under cytokine stimulation. Super enhancers under multiple cytokine-stimulation condition showed significant overlap with RA associated GWAS risk loci and explained the functions of these loci. Moreover, we constructed functional genomics dataset (ImmuNexUT database) which consist of RNA-seq and whole-genome sequence data of 28 kinds of immune cells from more than 400 cases who were diagnosed as 10 kinds of immune diseases. We performed expression quantitative trait loci (eQTL) analysis and constructed eQTL database from more than 9000 immune cell samples. Our analysis revealed cell type specificity of immune cell eQTLs. These cell type-specific eQTLs explained the functions of some immune disease-associated variants. As patient-derived our cohort can be considered as physiologic stimulatory conditions of immune cells, we analyzed the interaction of eQTL effects and environmental factors and revealed the physiological diversity of eQTL effects in immune cells. These context-dependent eQTLs showed significant enrichment in immune disease-associated GWAS variants. In summary, multi-omics analysis with patient-derived samples is useful for understanding the pathogenesis of immune-associated diseases. In this session, we report the analysis results from our database and discuss the utility of multi-omics dataset for disease studies.

S2-3

Our progress in genetic analysis of gout/hyperuricemia and gout with international collaborations

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Conflict of interest: None

Recent molecular epidemiological analyses have shown that gout/hyperuricemia have strong genetic factors. Because only a part of hyperuricemia cases develops gout attacks, and the reason, we consider, is that there are two steps in the development of gout; at the first step, the serum uric acid (SUA) levels of normouricemic individuals elevate without gout attacks; and at the second step, such asymptomatic hyperuricemia (AHUA) individuals develop gout attacks due to innate immunity. So far, we reported *ABCG2* as a urate transporter gene and that its variants markedly increase gout risk (Matsuo et al, ***Sci Transl Med***, 2009). We also proposed a new classification of hyperuricemia from the viewpoint of extra-renal urate excretion (Ichida et al, ***Nat Commun***, 2012). Moreover, we also showed that a genetic factor (ABCG2 dysfunction) have stronger effects on the development of hyperuricemia than environmental factors (Na-

kayama et al, ***Sci Rep***, 2014). Two genome-wide association studies (GWASs) with clinically-defined gout cases identified multiple gout risk loci (Matsuo et al, ***Ann Rheum Dis***, 2016 and Nakayama et al, ***Ann Rheum Dis***, 2017). We additionally conducted the first-ever GWAS with clinically defined gout cases and AHUA controls and found the individual genetic differences on the second step, which could relate to innate immunity and inflammation (Kawamura et al, ***Ann Rheum Dis***, 2019). Recently, the largest GWAS of SUA in Asia and the trans-ethnic meta-analysis along with European data displayed multiple genetic loci (Nakatochi et al, ***Commun Biol***, 2019). We also conducted GWASs of 4 differentiated subtypes of gout and identified multiple subtype-specific gout loci (Nakayama et al, ***Ann Rheum Dis***, 2020). We held the Asia-Pacific Gout Consortium (APGC 2019) in Tokyo and have also made efforts on international collaborations in gout researches. Our challenges will contribute to develop the individualized medicine/prevention for gout/hyperuricemia.

S2-4

Understanding of human disease biology using organoid technology

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Conflict of interest: None

In homeostatic adult tissues, niche factors regulate long-term self-renewal and multiple differentiation capacity of tissue stem cells. By reconstructing niche factors in vitro, tissue stem cells form a stereotypic organoid structure and self-renew for the long-term. Recent studies have identified tissue-specific niche factors, which enabled the propagation of organoids from a variety of adult tissues. This knowledge revealed that niche factor signaling coincides with oncogenic driver signaling in the original tissues, and suggested the linkage between niche factor dependency and disease pathogenesis. However, it remains elusive how niche dependency of stem cells alters during tumorigenesis and other gastrointestinal disease pathogenesis. We established intestinal epithelial organoids from various gastrointestinal diseased tissues and characterized their niche dependency in association with genetic alterations. On the other hand, clonal expansion of organoids and their deep-sequencing analysis revealed the accumulation of genetic mutations in normal tissue stem cells along with aging. These mutations include cancer driver genes, suggesting an insidious expansion of precancerous lesions in normal tissues. We also identified frequent genetic mutations in epithelium from patients with inflammatory bowel disease. The recurrent somatic mutations are associated with inflammatory signaling, and render the mutant clones resistant to the inflammatory cytokine-induced cytotoxicity, and thereby leading to the selective expansion of the mutant clones. CRISPR-Cas9 genome editing reconstructed various somatic mutations in normal organoids, and validated genotype-phenotype association; cancer driver gene mutations vs. niche independency, and cytokine signal mutations vs. inflammation resistant phenotype. Therefore, the establishment of disease tissue organoids and their genetic reconstruction provides new biological insights into disease pathogenesis. In this symposium, I would like to talk about how we can use organoid technology to understand human gastrointestinal disease biology with our recent progress.

S2-5

A Genomics Study of Behçet's Disease

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Conflict of interest: Yes

Behcet's disease is an intractable disease characterized by oral ulcers, skin lesions, genital ulcers, and uveitis, as well as inflammation of joints, blood vessels, central nervous system, and intestinal tract. Several genome-wide association analyses have been performed over the past 10 years, and in addition to HLA-B*51, important genetic predispositions such as HLA-A*26, *ERAP1*, and *IL23R* have been discovered, and Behçet's disease has been found to be an "MHC Class I-o-pathy" similar to psoriasis and ankylosing spondylitis. However, previous GWASs have not focused on severe lesions such as intestinal types, and it is difficult to apply this genetic information immediately to clinical practice at this time. A recent cluster analysis we performed based on clinical information showed that the complete and enteric types are subtypes with different clinical manifestations, and differences in HLA-B*51 prevalence and prognosis in each cluster were confirmed (Soejima et al, submitted). The Behçet's disease registry study based on the Platform for Incurable Diseases is currently being conducted under the auspices of AMED and the Ministry of Health, Labour, and Welfare to identify further clinical subtypes of Behçet's disease that are directly related to prognosis. In addition to detailed clinical information on Behçet's disease, including clinical symptoms, medication, disease activity index, and prognosis, the study will integrate genetic information such as cytokines and genomics information such as GWAS and RNA seq. We will prospectively accumulate information on more than 2000 cases of Behçet's disease patients from more than 50 participating centers in Japan. We will use this accumulated information to obtain genomic information related to the prognosis and severity of Behcet's disease to contribute to the development of optimized medicine. In this talk, I will present the progress of the Behçet disease registry study and its future prospects.

S3-1

Current status and challenges of T2T in rheumatic diseases

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Conflict of interest: Yes

The principle of the management of rheumatoid arthritis (RA) is to set numerical target values and estimated arrival times and aggressively intervene from an early stage (Treat to Target; T2T), similarly to representative chronic diseases such as hypertension, dyslipidemia and diabetes. T2T strategy not only reduces the current burden of illness such as joint pain and stiffness, but also avoids future events such as irreversible dysfunction due to joint destruction and shortened life prognosis due to chronic inflammation. The T2T principle has spread to other rheumatic diseases such as systemic lupus erythematosus and spondyloarthritides, and has greatly contributed to improving the quality of life (QOL) of patients. However, many issues have been pointed out in the clinical evaluation of RA and the quantification of evaluation results, and the drug treatment costs as a percentage of total medical costs is acceleratingly increasing. The amount of information that patients should share with healthcare professionals is also increasing, and there are many concerns about the safety profiles of treatment in a super-aged society. In these circumstances, the role of nurses in connecting physicians and patients and practicing the best rheumatology care is more and more crucial. Sufficient medical knowledge and communication skills are essential for promoting and facilitating two-way information transmission, such as concisely communicating information obtained from patients to doctors and helping patients understand the doctor's idea and treatment choice correctly. Ideally, the treatment policy could be modified if necessary and explained to both the physician and the patient to accept the proposal. As with the treatment of cancer, the expectations of patients and doctors for nurses are rising in the treatment of rheumatic diseases, which makes it a very rewarding professional.

S3-2

The 2018 revision of EULAR recommendations for the role of nurses and their implementation

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Conflict of interest: None

The EULAR recommendations for the role of the nurse in the management of patients with chronic inflammatory arthritis, including rheumatoid arthritis was published in 2012 and has been disseminated all over the world. However, it has been reported that the implementation of these recommendations is not sufficient although the level of agreement on them is high. The 2018 updated version that includes new evidence has been published[1]. In this revised version, 3 overarching principles have been added: (1) Rheumatology nurses are part of the healthcare team, (2) Rheumatology nurses provide evidence-based care, and (3) Rheumatology nursing is

based on shared decision-making with the patient. This version consists of 8 recommendations. The first three recommendations are stated from the patient's point of view, such that patients should consult with a nurse according to their needs. The remaining 5 recommendations describe a wider range of roles from the standpoint of nurses as follows: nurses' participation in comprehensive disease management, self-management support, improvement of self-efficacy, support including psychosocial aspects, and continuous improvement of nurses' own knowledge and skills using a specialized education. In this lecture, I would like to introduce the 2018 updated version, which serves as a guideline for a wide range of rheumatology nursing, and consider how they should be put into practice in Japan including issues. Reference: 1) Bech B, et al: 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. Ann Rheum Dis 2020: 79:61-68.

S3-3

The role of nurses expected by rheumatologists

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Conflict of interest: Yes

Advances in therapeutic agents have made it possible to achieve remission, which is the goal of rheumatoid arthritis treatment, and the concept of "Treat to Target (T2T)" has become implemented in Japan. However, even with effective medications, adherence to treatment is often reduced for a variety of reasons such as infections that prevent patients from continuing treatment, self discontinuation due to fear of side effects, and forgetting the date or time of medication. The role of the nurse is also important in improving adherence to maximize the effects of the medication, improving the disease and the physical condition of the patient. Nursed are also expected to provide psychological support by communicating with patients to reduce their anxiety and to obtain information from patients and their families about life and work at home and provide social support according to their needs. Furthermore, in order to realize "shared decision-making" between healthcare providers and patients, which is the most important aspect of medical care, it is necessary to convey correct knowledge and information to patients in words they can understand, and nurses are expected to support patients in improving their health literacy. Nurses are also expected to support patients to increase their self-efficacy and support self-management. In addition, nurses, as the closest presence to patients, also play a role of connecting patients and healthcare providers. I would like to consider the role of the nurse expected by physicians, based on both aspects of the clinical situation and rheumatology nursing.

S3-4

Rheumatoid care nurse activities and challenges

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Conflict of interest: None

University hospitals have a mission not only to provide medical care but also to promote research for the next generation. I believe that this is the mission of all university hospital staff, including nurses, as well as doctors. In the last 20 years, new drugs have been introduced in rheumatic diseases and many patients have benefited from the dramatic changes. Evidence-based care and patient education is now required in the field of nursing as well. In collaboration with orthopedic surgeons, we have conducted a variety of nursing research studies mainly on patients with rheumatoid arthritis. The first of these studies was a survey of rheumatoid arthritis patients' self-injection practices. These learnings have led to the creation of a checklist to review the teaching methods and continuous involvement during the introduction of the procedure. Also, in the last few years, pen and auto-injector type self-injection products have been introduced for the treatment of rheumatoid arthritis. A total of more than 400 rheumatology patients have been surveyed and researched on these products on three occasions between 2017 and 2019. We have been able to use the information we have gained from this research to help us guide rheumatology patients. We have found that there are many questions that arise in our daily work and interactions with patients, such as: Is this really the right way to go? You may have questions about how to care for your rheumatoid arthritis patients. It is important to conduct surveys and statistical analyses of rheumatology patients and to discuss the results with other professionals in order to improve nursing care. In addition, quantified and scientifically validated data can be useful for mutual understanding of rheumatology. In this symposium, we will discuss how we have conducted nursing research and introduce some of the background, methods, results, and challenges.

S3-5

The Role and Challenges of Nurses in Rheumatology Clinics

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Conflict of interest: None

RA nursing at PS Clinic (Fukukoka, Japan) is based on the EULAR Recommendations for people with inflammatory arthritis. The basic principles of these guidlines are that rheumatology nurses (1) are part of the health care team, (2) provide evidence-based care, and (3) base their rheumatology nursing on Shared Decision Making (SDM) with patients. The basic principles of treat-to-target also indicate the need for SDM between physicians and patients, but this can only be achieved if successful communication between physicians and patients is strengthened. Therefore, the rheumatology nurse acts as an intermediary between the physician and the patient, acting as a "bridge," listening and explaining to the physician what the patient has difficulty telling to the physician. However, it is not enough for the rheumatology nurse to help facilitate communication between physican and patient; it is also important to conduct an assessment of the information heard from the patient and provide the necessary nursing care. Clinics have a team approach to Health care, but because we do not have other there are not other specialists on staff like at larger hospitals, the nurses must cover the knowledge and skill-sets of other specialists as well. These specific skill-set demands therefore limit rheumatology nurses' ability to teach in other specialties. In addition, with the significant aging of RA patients, there is a need for RA treatment guidance and education, as well as community involvement and knowledge of care and welfare. Although there are various problems regarding nursing education, such as a lack of time to learn technical knowledge, the use of web-based learning being utilized during the current COVID-19 pandemic may be useful as a new way for nurses to gain better on-the-job training at clinics. Because clinics do not have physician transfers and nurse rotations like in hospitals, patients are likely to stay with the same physicians and nurses longer, thus developing stronger relationships all around. Nurses in clinics share a close and accessible environment with patients, which allows them to better understand the mental and social changes in patients, precise and timely nursing care.

S4-1

Current topics of shoulder joint in RA patients

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Conflict of interest: None

Before the introduction of biologic and JAK inhibitors, treatment of shoulder conditions in rheumatoid artritis (RA) consisted of treating inflammation, concomitant synovitis and secondary lesions to the shoulder joint. Treatment options consisted of injections with local agents, physical therapy and surgical interventions: often synovectomy, rotator cuff repair and shoulder arthroplasty. Since the revolution in systemic therapy, the lesions in joint conditions in rheumatoid patient resemble more those observed in osteo-artritis (OA). However, the number and type of complications and failure rates of surgical interventions are still different from non-rheumatic conditions. Not all patients respond well to systemic treatment, resulting in a small group of patients still showing traditional RA deformities. Although the functional outcome of interventions in RA is inferior to OA, pain relief is usually comparable. The current surgical treatment strategies for shoulder lesions are: Rotator-cuff repair (subscapularis repair or pectoralis major transfer in anterosuperior tears, tendon transfer of latissimus dorsi or teres major in posterosuperior rotator-cuff tears), (reverse) shoulder arthroplasty and rarely synovectomy. In the last decade reversed shoulder arthroplasty has become more popular and

more widely used in RA patients, but complications are serious (eg infection or instability). In younger patients an anatomical shoulder arthroplasty combined with tendon transfers might be a viable and safer alternative and is currently under investigation.

S4-2

Evolution of elbow surgery for rheumatoid arthritis in biologic and JAK inhibitor era

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Conflict of interest: None

The elbow is frequently affected joint in patients with rheumatoid arthritis (RA), and estimated to be involved in 20 to 65% of patients. Several reports indicate that involvement of elbow joints compromises quality of life of RA patients. The recent advancement of antirheumatic drugs and treatment strategy aiming at remission have changed the surgery for RA. Our study from the Japanese nationwide cohort database indicates that the incidence of orthopedic surgeries consistently decreased, and the greatest reduction was found in hip and knee arthroplasty, whereas there was no significant change in elbow arthroplasty. Surgery is considered for patients with persistent symptoms despite an adequate nonoperative treatment such as use of elbow braces and steroid injection. Synovectomy and elbow arthroplasty are two major surgeries for rheumatoid elbow. Synovectomy is the procedure of choice for persistent swelling and pain in elbows without severe destructive changes in spite of appropriate therapy by antirheumatic drugs. Although it provides pain relief and functional improvements, recurrence of symptoms is reported to be up to 50% by 5 years. On the other hand, total elbow arthroplasty (TEA) is a very successful surgical option for rheumatoid elbow with advanced joint destruction. Recent improvement of implant design and surgical techniques provide good implant survivorship. Our data showed that survival rate of Kudo type-5 prosthesis at ten years was 77.6%, which is similar to those of previous reports. Nowadays, RA patients with multiple joint destruction decreased and they live more active lifestyle, and therefore have higher expectations for surgery. Further development of implant design and surgical technique will be needed to meet these expectations.

S4-3

Rheumatoid hand surgery today

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Conflict of interest: None

Even with good medical control of the disease, symptoms may appear or progress in the hand and wrist in rheumatoid patients due to mechanical wear of soft tissues and joints secondary to lesions induced by the disease at its onset. Tendon imbalances, osteochondral erosions and articular malalignment lead to pain, joint instability or stiffness and segmental deformities. Good pain control obtained with current therapies, can also favour overuse and osteochondral wear of the affected segments since the antalgic reduction of physical activities is lower. In addition, a percentage of patients may be in a non-responder condition, be intolerant to biologics or have a recurrence of disease. Surgery is therefore indicated to preserve or restore function, correct deformities and to reduce pain. The aesthetic value of surgical correction is also important for today's patients. Soft tissue operations concern the capsular, ligamentous and tendinous structures. Joint surgery consists of biological arthroplasties, implant reconstructions or arthrodesis. Given the efficacy of present biological therapy, synovectomies are seldom performed as isolated surgery, and these are generally part of more complex reparative procedures. Tendon surgery consists of tendon realignments, aiming to restore the right dynamic balance and joint stability, and reparative procedures for tendon ruptures, which today are among the most frequent indications in rheumatoid hand surgery. Osteoarticular surgery aims to restore joint biomechanics in the absence of pain: current options include motion sparing procedures, such as limited carpal fusions, biological arthroplasties and prosthetic replacements of the wrist and finger joints; total joint fusions keep anyhow their indications in today surgery. Proper rehabilitation should alwayssupport surgery in order to implement the patient's functional recovery.

S4-4

Progress in surgery for forefoot deformities in patients with rheumatoid arthritis

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Conflict of interest: None

Along with a progress in the pharmacological treatment for rheumatoid arthritis (RA), trends is surgeries for RA have been changed over two decades. The rates of small joint surgery for patients with RA have been decreased in both UK (Nikiphorou at al AR2014) and US (Richter et al Arthritis Care Res 2018), however increased in Japan (Momohara et al Mod Rheumatol 2011). This difference in a trend for rheumatoid surgery may result from the presence of "orthopaedic rheumatologists" in Japan, who have developed and modified so-called "joint-preserving surgeries" for rheumatoid forefoot deformities, for which resection arthroplasty had been applied as a standard treatment. There have been several procedures of MTP joint-preserving surgery for rheumatoid forefoot deformity. Most of the procedures combine corrective osteotomy of the first metatarsal and shortening osteotomy of the lesser toes. We have been performed biplane interlocking osteotomy for hallux valgus, and Weil osteotomy for lesser toe deformities. The clinical outcomes of our joint-preserving procedures were better than the outcomes achieved by resection arthroplasty with regard to the function of hallux and alignment of the lesser toes. Although satisfactory results have been reported with a number of different procedures, the followings are major concerns remaining unsolved during the joint-preserving surgeries for rheumatoid forefoot deformities. 1. The recurrence of hallux valgus. 2. The stiffness of lesser toes. 3. Delayed wound healing. These issues will be discussed in this presentation based on the recent available evidence.

S4-5

Evolution of the treatment for osteoporosis associated with rheumatic diseases

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is associated with increased bone turnover and early bone loss, which lead to increased fracture risk and progressive joint destruction. Pro-inflammatory cytokines, such as IL (interleukin)-17, TNF-α (tumor necrosis factor alpha), IL-1, and IL-6 induce the expression of RANKL (receptor activation of nuclear factor κB ligand) from synovial fibroblasts. RANKL promotes osteoclasts differentiation and activation. According to the arrival of various new osteoporosis therapeutic agents (anti-bone resorption, bone anabolic, and dual effect agents), it is of great interest to investigate effective osteoporosis treatment strategy to prevent both fracture and joint destruction progression. In this symposium, I would like to review the recent evidences and evolution of the treatment for osteoporosis associated with rheumatic diseases.

S5-1

Giant cell arteritis basic research update 2021

Ryu Watanabe
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Conflict of interest: Yes

Giant cell arteritis (GCA) is an inflammatory disease that causes granulomatous inflammation of large- and medium-sized blood vessels, causing blindness, cerebral infarction, and aortic aneurysm. Glucocorticosteroids remain the mainstay of treatment, but in 2017, tocilizumab (TCZ) was approved in Japan. However, there have been several case reports in which vascular lesions progress even under TCZ therapy. Therefore, deeper elucidation of the pathophysiology is essential. Since the involvement of HLA in GCA has been reported, and CD4+ T cells and macrophages are

mainly observed in granulomatous inflammation, CD4+ T cells have been considered to be the central player of the pathophysiology. In fact, CD4+ T cells present in vascular lesions produce not only Interferon-γ and IL-17 but also various cytokines such as IL-9, IL-21 and IL-22. A research group at Stanford University (Prof. Cornelia M. Weyand), where the speaker was enrolled, suspected that activated T cells might be caused by the disruption of the regulatory immune system in the periphery. We have demonstrated that dendritic cells present in vascular lesions have the reduced expression of the checkpoint molecule (PD-L1) and CD8+ regulatory T cells (CD8+ Treg) are deficient in GCA. In addition, we have revealed that mTORC1 expression is increased in CD4+ T cells via CD28-Akt axis and NOTCH1-HES1 axis, contributing to various cytokine production and vascular remodeling, and that the invasion of CD4+ T cells into vascular lesions is regulated by proteolytic enzymes such as MMP-9 from macrophages. Furthermore, it has been reported that the JAK-STAT pathway is enhanced in CD4+ T cells derived from GCA patients. JAK inhibitors not only suppressed cytokine production in CD4+ T cells, but also suppressed antigen presentation by monocytes and macrophages, suggesting that they may be effective against GCA. In this seminar, I will explain the role of various immune cells involved in the pathology of GCA.

S5-2

Significance of autoantibodies in Takayasu's arteritis

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Conflict of interest: Yes

Takayasu's arteritis and giant cell arteritis are both inflammatory diseases classified as idiopathic large vessel vasculitis (LVV). In recent years, research on these two diseases has progressed, and their treatment methods have also advanced. Although this has improved the prognosis of both diseases, many problems are still encountered in clinical practice with regard to their diagnosis and the selection of a treatment method. One of the biggest problems in terms of diagnosis is the difficulty in suspecting the disease. First, in the early stages, when vascular lesions have not progressed, there are few specific, clear physical symptoms and findings. Dullness, dizziness, staggering, and chest discomfort, which are common in this disease, are considered indefinite complaints, and it is not uncommon to find them as irreversible changes due to the progression of the vascular lesions. Recently, the relatively early diagnosis has become possible by performing imaging examinations such as contrast CT and PET, triggered by the detection of chronic inflammatory findings. However, it is still a disease that cannot be diagnosed without expensive and invasive imaging tests such as radiation exposure, which are performed in well-equipped facilities. In addition, when the disease is suspected, new biomarkers can be used as an indicator of whether or not to proceed with the diagnostic imaging. From a therapeutic point of view, advances in the treatment methods for LVV using biologics have become a recent topic of interest. Conventionally, drugs other than steroids have not been sufficiently effective for LVV. The efficacy of tocilizumab, an IL6 receptor antibody, was demonstrated, and it was approved as a therapeutic drug both for Takayasu's arteritis and giant cell arteritis. On the other hand, the drug for which a clear difference in efficacy has been confirmed between the two diseases is abatacept. This indicates that there are LVV subtypes that appear to be comparable on imaging findings when a targeted treatment is performed. It also indicates that treatment methods need to be prepared separately for each, and that there is also a need for the presence of biomarkers that divide the LVV diagnosed using imaging findings into their subtypes. Utilization of autoantibodies expressed in Takayasu's arteritis is expected to be a candidate biomarker that may be useful in these situations.

S5-3

A prospective cohort study of patients with ANCA-associated vasculitis treated with rituximab (RemIRIT)

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Conflict of interest: None

Objective: Information on rituxaimab (RTX) for treating Japanese ANCA-associated vasculitis (AAV) patient is insufficient due to lack of clinical trials targeting Japanese patients. This prospective cohort study was conducted by the Research Committee on Intractable Vasculitides on a strategic study group, to establish evidence for treatment guidelines on intractable vasculitis. **Methods**: Treatment strategy for each patient was decided by the attending physician. All AAV patients treated with RTX have been enrolled from each institution and will be followed-up for 2 years. Data on demographic characteristics, symptoms, test results, treatment content, efficacy and safety were collected and those up to 6 months analyzed. **Results**: From January 2016 to the end of December 2017, 79 cases (30 granulomatosis with polyangiitis; GPA, 49 microscopic polyangiitis; MPA) were registered. There were 27 males and 52 females and the mean age was 67.6 years-old. According to BVAS, the frequency of kidney (59.5%) and respiratory (45.6%) manifestations were high, with an average BVAS of 12.0 at the time of enrollment. In addition, 25 patients (31.7%) had respiratory diseases other than vasculitis such as COPD. At the time of enrollment, the average creatinine concentration was 1.41 mg / dL, the mean prednisolone (PSL) dose was 32.3 mg / day, and 10 patients (12.7%) also were treated with glucocorticoid pulse. RTX was administered as induction therapy (BVAS> 0 at enrollment) in 75 patients, and 29 patients received RTX within 2 weeks after the start of initial treatment for MPA and GPA. By 6 months, 54 of 75 (72%) patients achieved remission, but 2 had relapsed by 6 months. The mean PSL dose at 6 months was 10.0 mg / day. Serious adverse events (SAE) occurred in 20 patients (26.7%), deaths occurred in 9 (12%), and either SAE or death was observed in 20 (26.7%). In induction therapy, 21 of 75 patients (28%) did not achieve remission, but 11 of these patients had SAE or death, which was considered to be an important inhibitor of remission. Therefore, factors associated with the occurrence of SAE or death in induction-treated patients were examined, suggesting that higher doses of PSL at the beginning of RTX and older age were associated. On the other hand, 4 patients who received RTX as remission maintenance treatment (BVAS = 0 at enrollment) maintained remission during 6 months with no SAE or death. **Conclusion**: The effectiveness and safety of RTX for GPA and MPA up to 6 months in Japan was clarified.

S5-4

Novel Treatment of AAV with Avacopan

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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. Avacopan (CCX168), a small molecule with a molecular weight of 581, is an orally available C5a receptor (C5aR) inhibitor of complement C5a. Histologically, significant inhibition of glomerulonephritis was observed with avacopan treatment in a mouse model. 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 PSL) or control (placebo Avacopan + standard PSL) 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. Results were reported at the 2020 EULAR Congress (Session:

Opening Plenary abstract session, OP0011). 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). There was no significant difference between the two groups as for safety profile. This result showed that Avacopan is a promising alternative to GC in remission induction therapy for AAV.

S5-5

Kawasaki Disease - The Late Dr. Tomisaku Kawasaki's Achievements and Prospects for the Future

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Conflict of interest: Yes

Kawasaki disease, first described by Dr. Tomisaku Kawasaki in 1967, is a medium-sized vasculitis that is common in infants. Japan is the country with the highest incidence of Kawasaki disease in the world. Despite the rapid decline in birthrates, the number of cases continues to rise, with approximately 16,000 new cases occurring each year, affecting one in 100 infants. Dr. Kawasaki experienced his first case in 1961, and I am amazed at his clinical ability to quickly identify a new disease based on its characteristic clinical features at a time when patients were still rare. In the 1970s, when no treatment was available, 10% of patients had coronary artery disease and 1% died; since the middle 1980s, the introduction of immunoglobulins has markedly improved both coronary and life outcomes. Subsequently, steroids, infliximab, cyclosporine, and plasma exchange further improved prognosis, but 2.6% of patients still have coronary artery aneurysms. Meanwhile, no drug has been developed yet that is capable of stopping the progression of coronary aneurysms that have begun to spread Even though Dr. Kawasaki was over 90 years old, he still attended the Kawasaki Disease Conference every year and always took a front-row seat. He always said, "I want to see the cause of Kawasaki disease discovered". He passed away last year but the cause of the disease is still unknown. Recently, pediatric multisystem inflammatory syndrome (MIS-C), in which SARS-CoV2 infection is followed by the development of Kawasaki disease-like symptoms, including coronary artery aneurysms, has been reported in Europe and the United States. MIS-C is a very interesting disease when considering the pathogenesis of Kawasaki disease. Uncovering the true cause of Kawasaki disease is still the biggest theme. Thus, Kawasaki disease is one of the most common but most enigmatic diseases that is clinically fascinating and rich in research topics. In this talk, I would like to share the story of the discovery of Kawasaki disease and discuss the future prospects.

S6-1

Development and future tasks for TNK ankle as a total ankle implant

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Conflict of interest: None

Degenerative change in the midfoot and hindfoot are usually shown in patient with rheumatoid arthritis. Alignment failure causes to the deformity and consecutive skin ulcer as well as the joint pain, that leads the treatment to be refractory. In the small joints between the tarsal bones, arthrodesis is a useful option, however it is ideal to preserve the joint mobility in the ankle. In our institute, total ankle implant was developed in 1975 using the stainless steel as its material. In 1980, the material was changed to the alumina ceramic, and since 1991, cement beads were mounted on the surface of the implant and screw hall was set to obtain the rigid fixation. Design concept of two components and semi-constrain type of implant is consistently employed as TNK ankle®, and different curvature in tibial and talar components brought to the favorable ankle motion. Application of calcium phosphate and putting the bone marrow on the surface of tibial component assist to the rigid fixation. Favorable clinical results are obtained by TNK ankle®, however the talus is short bone covered with articular cartilage, so it has a potential risk for subsidence of talar component. A customized artificial talus is applied for the failure of the talar component, and nowadays a total ankle arthroplasty combined with the artificial talus is applied for the patient with severe deformity or large cystic lesion in the talus. In this symposium session, development and future tasks for TNK ankle® would be presented.

S6-2

FINE total ankle system

Makoto Hirao[1], Kosuke Ebina[1], Yuki Etani[1], Hideki Tsuboi[2], Takaaki Noguchi[3], Gensuke Okamura[2], Shigeyoshi Tsuji[3], Yasuo Kunugiza[4], Koichiro Takahi[5], Seiji Okada[1], Jun Hashimoto[3]
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Conflict of interest: None

To obtain the successful outcomes after total ankle arthroplasty, augmentation of the bone, controlling the soft tissue balance including Achilles tendon are very important. Furthermore, cementing technique and design of implant-bone and/or implant-insert interface are also stasks which should be resolved.

S6-3

Outcomes and challenges associated with transfibular total ankle arthroplasty

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Conflict of interest: None

The Trabecular Metal™ Total Ankle (TM ankle) introduced by Zimmer-Biomet in August 2018 shows the following features: (1) it utilizes a lateral approach to expose the ankle joint after fibular cutting, (2) it enables accurate bone cutting owing to fixation of the ankle to the frame, (3) the round design is useful to implant on a high bone density area and, (4) it is composed of trabecular metal and highly crosslinked polyethylene. Since its launch in 2018, we have performed 55 total ankle arthroplasties using this device. Compared with other prostheses, the TM ankle was associated with a longer mean operative time (approximately 170 min). The use of the TM ankle is associated with a learning curve to acquire the skills to effectively perform all procedures. However, we could successfully use the TM ankle even in patients with severe malalignment after skill acquisition and experience in all the necessary techniques. Following are the complications associated with the implant: (a) Delayed wound healing-we used lateral curved skin incisions before; however, most instances of delayed wound healing occurred at the curved sites. Therefore, we altered our strategy and used straight incisions, and the bone was cut more proximally, which significantly reduced the rate of delayed wound healing. (b) Although a few perioperative medial malleolar fractures were observed, satisfactory bone union occurred in all patients without postoperative protocol delays. (c) Gradual lateral displacement of the tibial component occurred in one patient. (d) Deep infection occurred in a patient; however, the prosthesis was preserved, following thorough joint irrigation and insert replacement. The TM ankle was launched in western countries in 2012. The longest follow-up duration reported by studies that investigated the outcomes of the TM ankle is <4 years. Mid- and long-term outcomes remain unclear; therefore, further studies are warranted for a better understanding regarding outcomes.

S7-1

What is known about the long-term prognosis of articular type of juvenile idiopathic arthritis (JIA)?

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Conflict of interest: Yes

Biologics has significantly improved the outcome of articular JIA. However, the period since their approval in Japan (2009) is not long, and information on long-term prognosis and adverse events is limited. On the other hand, it has been approved one after another in other countries since 1999, and long-term results have begun to be reported. In a cohort study from Norway (Arthritis Res Ther. 2018), 410 (97%) of 423 JIA patients, excluding systemic JIA, achieved remission (Wallace's criteria) after 8 years. Of these, 166 (40.5%) were in remission without medication and 38 (9.3%) in remission on medication. On the other hand, physical function evaluation (CHAQ) showed some dysfunction in 32.7% of cases. A cohort study from Greece (Rheumatology. 2017) also followed 102 JIA patients for 17 years, achieving remission without medication in 47.6% and having dysfunction in 30.3%. The prognosis was different depending on the type of JIA, and that of the oligoarticular type was better. In Japan, there has been no large-scale, long-term observable JIA cohort study as described above, and the long-term prognosis of Japanese JIA patients is unclear. Therefore, we extracted patients (adult JIA) registered as articular JIA in the large-scale rheumatoid arthritis (RA) database "NinJa" and compared them with RA patients with the same background to determine the prognosis retrospectively (Mod Rheumatol. 2020). As a result, adult JIA patients had a higher rate of biologics use and lower disease activity than RA patients of the same disease duration, but had similar degrees of joint destruction and more dysfunction. However, there are many other limitations in this study, so further studies are necessary in the future. Patients with articular JIA use biologics at a high rate during the transition period. Therefore, it is necessary to verify the long-term merits and demerits and how long it should be used in the adulthood in collaboration with perdiatrician and adult rheumatologists.

S7-2

Difference in evaluation index between juvenile idiopathic arthritis and rheumatoid arthritis

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Conflict of interest: None

Oligoarthritis, rheumatoid factor negative and positive polyarthritis Juvenile idiopathic arthritis (aJIA) mainly develops synovitis, and this disease state and treatment for synovitis are relatively common to rheumatoid arthritis (RA). In recent years, JIA in adolescence and adulthood is increasingly being treated in the adult department, and it is expected that the necessity of clinical research for both diseases will increase in the future. The disease activity index used in JIA clinical practice and clinical research is JADAS, and indices such as DAS 28, SDAI, CDAI and Boolean remission which are disease activity indexes of RA are not generally used. Furthermore, HAQ is used as an objective evaluation of physical dysfunction in RA, while CHAQ (Childhood Health Assessment Questionnaire) is used in JIA. In the examination in aJIA using large-scale JIA database CoNinJa (Children's version of National Database of Rheumatic Diseases in Japan), there was absolute and relative correlation between JADAS -27 and each disease activity index of RA. However, there is a discrepancy between the JADAS -27 remission standard and the remission standard for each RA disease activity index ($\kappa = 0.55$ -0.78) (Reported in JCR 2020). In order to improve the convenience of disease activity indicators in the adolescent and adult JIA and RA clinical practice sections, and in order to conduct clinical studies including disease activity indicators smoothly, it is necessary to consider cut-off values for remission criteria and calculation parameters for scores. This section discusses differences in disease activity indices between JIA and RA and measures to improve compatibility.

S7-3

What is the difference between the pathophysiology and treatment target of juvenile idiopathic arthritis and rheumatoid arthritis?

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Conflict of interest: None

Articular-type JIA is defined as chronic arthritis of unknown cause that develops before the age of 16 and lasts for at least 6 weeks. Similar to RA, it causes irreversible joint destruction and requires early sedation of inflammation. JIA is classified into 7 types, "systemic type" which is similar to adult-onset Still's disease, "psoriatic arthritis" associated with psoriasis, and "adhesion-related arthritis" associated with ankylosing spondylitis. Furthermore, the type of disease differs depending on the number of affected joints and the presence or absence of rheumatoid factor (RF). Systemic JIA, which is based on abnormal innate immunity, mainly has systemic inflammatory conditions such as fever and erythema, while the pathological conditions of arthritis called arthritis and RF positive/negative arthritis are similar to RA. It is thought to be an autoimmune disease caused by abnormal acquired immunity, but it is unclear whether this is the same mechanism as RA. Oligoarthritis, which is defined as having 4 or less affected joints, often affects large joints such as knee joints, ankle joints, and elbow joints, but polyarthritis also affects small joints such as finger joints and toe joints. The most common form of joint destruction is RF-positive polyarthritis. Persistent lower limb arthritis in growing children may cause laterality in lower limb length, most often with oligoarthritis. The positive rate of RF and anti-CCP antibodies is not as high as that of adult RA, but positive individuals are often refractory to treatment. Uveitis is a characteristic extra-articular complication of JIA. In Japan, it is found in about 6% of JIA, and the risk factors for its onset are oligoarthritis, early onset of arthritis, and positive antinuclear antibody. Regular ophthalmic examination is required because it is generally asymptomatic, not parallel to arthritis activity, and can develop before the onset of arthritis and after the end of arthritis treatment. Currently, in JIA treatment algorithms other than systemic type in Japan, MTX oral administration is started early for the "high risk group" such as RF or anti-CCP antibody positive. Although various biologics are indicated for MTX-resistant patients, articular-type JIA that transitions to adulthood is often intractable, and the proportion of biologics used is high. In addition, for patients with uveitis, the therapeutic agent varies depending on the severity of the disease, but among the biologics indicated for JIA, adalimumab is effective against uveitis.

S7-4

Long term prognosis of Sjögren's syndrome in children

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Conflict of interest: None

Sjögren's syndrome (SS) is a systemic autoimmune inflammatory disease characterized by disorders of the systemic exocrine glands, mainly the lacrimal and salivary glands. Inflammation of the exocrine glands as well as various extra-glandular organ damage can occur. Life prognosis depends on concomitant extra-glandular organ damage, malignant lymphoma is the most relevant to prognosis in adult SS. In pediatric SS, only a few cases of malignant lymphoma have been reported including oversea cases. One death was reported in a nationwide survey in 1995, but the details were unknown. In childhood, the prognosis for life is not bad. However, cases of extra-glandular organ damage, such as myocarditis, nephritis, and autoimmune hepatitis, require treatment with glucocorticoids and immunosuppressive drugs, and organ damage itself and side effects of treatment have a prognostic impact. Subjective symptoms of dryness are rare at the time of initial diagnosis. However, over time, the glandular lesions progress and subjective symptoms of dryness become more apparent. The timing of appearance and severity of both extra-glandular organ damage and glandular symptoms vary greatly among individuals, making it difficult to determine the beginning of therapeutic intervention.

S7-5

Evaluation indexes for child-onset and adult-onset Sjogren's syndrome

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Conflict of interest: None

Sjogren's syndrome (SS) usually presents in middle-aged women with

sicca symptoms, whereas about only 30% of child-onset SS cases present with dry symptoms. Children with primary SS (pSS) frequently develop fever, erythema, and parotid gland swelling at onset. In Japan, based on characteristics of children with pSS, diagnosis of SS by results of blood tests and exocrine gland disorder examination has been proposed. There is no pediatric evaluation of dryness and disease activity as indicators used in adults. The EULAR Sjogren Syndrome Disease Activity Index (ESSDAI) has been reported as a disease activity evaluation method for systemic symptoms of SS. Although validation was completed for adult patients, it has not been validated in children. Therefore, the Japan Pediatric SS Study Group evaluated whether ESSDAI is useful in children with pSS. Subjects comprised 31 children with pSS treated at medical facilities of pediatric rheumatism specialists. Data of symptoms at first visit, initial ESSDAI score, and treatment regimens, were retrospectively collected. Associations among ESSDAI scores and treatment regimens were analyzed. Prednisolone (PSL) dose was significantly associated with ESSDAI score. Median ESSDAI score was significantly higher in patients treated with high/medium- than with no/low-dose PSL (16.5 vs 5.0). Eight (66.7 %) of 12 patients administered medium/high-dose PSL and one (5.3%) of 19 administered no/low-dose PSL had high disease activity on ESSDAI. ESSDAI score did not influence treatment choice by attending physicians as treatment was decided prior to ESSDAI assessment. Nevertheless, disease activity assessed by ESSDAI tended to be consistent with disease activity assessed by pediatric rheumatologists in determining treatment regimens. These results suggest ESSDAI is useful to assess disease activity in Japanese children with pSS. It will be necessary to evaluate ESSDAI and treatment over time, leading to more seamless

S7-6

Differences in the pathology and therapeutic targets between childhood SS and adult SS

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Conflict of interest: None

Sjogren's syndrome (SS) is a systemic inflammatory autoimmune disease. It mainly involves disorders caused by the inflammation of exocrine glands such as the salivary glands and lacrimal glands, along with a variety of extraglandular organ disorders. The natural history of SS in childhood is still unclear. It is believed that the symptoms of dryness are rare in childhood, that exocrine gland disorders progress with aging, and that the symptoms of dryness become apparent in adulthood. Therefore, unlike adult SS, treatment for glandular symptoms may be unnecessary in many cases. On the other hand, childhood SS more frequently exhibits extraglandular symptoms than adult SS. The cause for this remains unclear. One possible cause is the difference in the pathologies of childhood SS and adulthood SS. Alternatively, extraglandular symptoms are possibly more frequently diagnosed because the symptoms of dryness are rare in childhood SS. In any event, it should be noted that the assessment and treatment of extraglandular symptoms are important in terms of medical care for childhood SS. In the treatment for extraglandular symptoms of childhood SS, similar to adult SS, non-steroidal anti-inflammatory drugs, glucocorticoids, immunosuppressive drugs, gamma globulin agents, etc. are used in accordance with symptoms and organ disorders. However, the long-term administration of glucocorticoids and immunosuppressants to children causes side effects such as growth disorders. Therefore, desirable treatments should more safely target the molecules involved in pathogenesis. Biological drugs are therapeutic agents synthesized by organisms and targeting specific cytokines, receptors, etc. Biological drugs targeting molecules such as immune cells and cytokines involved in the pathogenesis of SS are expected to be especially effective against childhood SS, which is thought to be closer to the early stages of the disease. A clinical study on biological drugs targeting adult SS has shown that rituximab is a chimeric antibody against CD20, abatacept (CTLA4 Ig), and berimumab as a monoclonal antibody against B cell activating factor (BAFF), possibly having effects on both glandular and extraglandular lesions. Examination of the effects and safety of biological agents on childhood SS is an important issue going forward. Unlike clinical studies on adult SS, in which exocrine gland disorders have already progressed, clinical studies that set outcomes based on long-term prognosis are expected.

S8-1

Systemic lupus erythematosus (SLE)

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Conflict of interest: Yes

SLE is a representative autoimmune disease characterized by multiple organ manifestations and involved by activation of autoreactive T cells and production of autoantibodies by B cells. Because SLE is molecularly and clinically heterogeneous which makes managing the disease control difficult, innovative approaches using biologics targeting molecules involved in the pathogenesis of SLE have been emerging. However, many biologicals such as CD20 antibodies targeting B cells have appeared promising but did not yield favorable results. In contrast, an anti-BAFF antibody belimumab was first approved for SLE because of moderate efficacy and good tolerability. Soluble BAFF is secreted by dendritic cells and regulate class switch and differentiation of B cells. IFN-stimulated genes, IFN signatures, are upregulated notably in SLE and one phase III clinical trial (TULIP-2) of anifrolumab, an anti-IFN-alpha receptor antibody, met the primary endpoint. Anifrolumab was more efficacious in patients with high IFN gene signatures than those with low ones. Recent GWASs have shown that multiple genetic loci play roles in the pathogenesis of SLE and many of the risk alleles are related to innate immunity as well as acquired immunity. Thus, successful treatments with biologicals targeting "bridging cytokines" such as BAFF and IFN, which are produced by dendritic cells and activate B cells and T cells and form a bridge between the innate and acquired and autoimmune systems, is of particular interest. Furthermore, baricitinib, an orally available JAK1/2 inhibitor, which is involved in signaling via IFN, significantly improved the signs and symptoms of active SLE in a phase IIb trial. In addition, precision medicine via the strategic selection of different biologics based on different clinical and/or molecular characteristics in each individual could be warranted for the treatment of SLE, which resulting in setting a therapeutic goal of the discontinuation of glucocorticoids.

S8-2

Management of Systemic Sclerosis-Associated Lung Fibrosis—Perspective from a US Scleroderma Center

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Conflict of interest: Yes

Systemic sclerosis associated ILD (SSc-ILD) occurs in 70-80% of patients and is associated with significant morbidity and mortality. Screening, early diagnosis and treatment of SSc-ILD is important as up to 33% of SSc-related deaths are attributed to ILD and initiating treatment early in the course of the disease has been shown to slow the progression of ILD. The lecture will summarize the best practices for diagnosis and treatment of SSc-ILD, including the recent approvals of nintedanib and tocilizumab.

S8-3

Lessons Learned from Myositis Clinical Trials

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Conflict of interest: Yes

Less than 20 years ago, most published studies in myositis were from single referral centers reporting retrospectively on small numbers of patients often followed for brief periods of time. Problems included different myositis classification criteria, a lack of uniformity in inclusion/exclusion criteria, and, most importantly, a lack of uniformity in outcome assessment. The establishment of the International Myositis Assessment and Clinical Studies (IMACS) Group changed this. This multidisciplinary adult and pediatric consortium of specialists with an expertise in myositis care paved the way for the "birth" of clinical trials in myositis. Critical factors included agreed upon core set measures (CSM) assessing the domains of disease activity, muscle strength, physical function, laboratory and extramuscular assessment. Clinically meaningful improvement pa-

rameters were agreed upon by consensus and a preliminary definition of improvement was developed and published; i.e. 3 of any 6 CSM improving by ≧20% with no more than 2 CSM worsening by ≧25%. Consensus guidelines for the conduct of myositis clinical trials and the development of tools for myositis disease activity and damage led to the largest clinical trial in adult and pediatric myositis - the Rituximab in Myositis Trial. Much has been learned since the RIM Trial and many other smaller clinical trials have been conducted. More recently, new myositis classification criteria have been developed and published as well as new myositis response criteria which will lead to more efficient and meaningful clinical trials. Nevertheless, the conduct of clinical trials continues to be a dynamic process that will require revision and refinement of the assessment tools as the current assessment tools suffer from subjectivity and a lack of meaningful objective quantification.

S8-4

Treatment strategies in axial spondyloarthritis

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Conflict of interest: Yes

According to the Treat-to-Target recommendations for spondyloarthritis (SpA), the main treatment target is defined as remission / absence of clinical and serological activity of musculoskeletal manifestations of the disease taking extra-musculoskeletal manifestations into account. The recent TICOSPA study showed, however, only a marginal benefit of a tight control strategy using the ASDAS <2.1 as an ultimate goal. At the same time, such a tight control strategy might have socio-economics and safety implications. As of today, only two classes of biological disease modifying anti-rheumatic drugs had shown clinical efficacy in randomized controlled trials and have been approved for axial SpA patients not responding to nonsteroidal anti-inflammatory drugs (NSAIDs): tumor necrosis factor (TNF) and interleukin (IL)-17 inhibitors. Despite similar clinical efficacy in terms of reduction of inflammatory activity in the axial skeleton and in peripheral joints, there are differences in efficacy against extra-articular manifestations of SpA (psoriasis, inflammatory bowel diseases, uveitis) that should be considered while making individual treatment decisions. Surprisingly, IL-23 blockade and phosphodiestherase-4 blockade that showed efficacy in psoriasis and psoriasis arthritis, failed to show clinical benefit in randomized controlled trials in axial SpA. There are positive results of phase II and III studies with Janus kinase inhibitors. Retardation of structural damage progression in the spine is an important long-term treatment aim in axSpA. Early and effective suppression of inflammation is associated with retardation radiographic spinal progression. There are new data indicating a time-shifted effect of TNF inhibitors on radiographic spinal progression. A specific effect of IL-17 inhibition and of a combination of TNF inhibitor with an NSAID on radiographic spinal progression are being currently investigated in prospective trials.

S8-5

Translational research to clinical trial in FMF

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Conflict of interest: None

Familial Mediterranean fever (FMF) is a typical hereditary autoinflammatory disease characterized by recurrent attacks of fever with arthritis, abdominal pain, skin rash and/or serositis. The *Mediterranean Fever (MEFV)* gene, coding pyrin that acts as a major regulatory component of the inflammasome, is important as a disease susceptibility gene. We have been investigating the pathogenetic role of candidate genes including *MEFV* gene, cytokines/chemokines and related molecules expression, inflammasome by cell-free reconstruction systems and clinical trial for patients with FMF. These projects have been supported by AMED. In this session, we are going to show the genetic analysis, cytokines/chemokines profile and clinical trial for FMF. Two hundred SNPs in the whole region of *MEFV* gene including promoter regions and intron regions were genotyped using next generation sequencer and the most significant two SNPs (rs28940578; M694I in exon 10, Odds ratio [OR]=153, $p=2.47\times10^{-21}$ and rs3743930; E148Q in exon 2, OR=1.65, $p<0.0005$) were identified. In addition, our recent data identify the possession of exon 2 or exon 3 variants in the *MEFV* gene promotes inflammasome activation in Japanese patients with FMF with a heterozygous exon 10 mutation. For cytokines/chemokines profiling in sera of FMF patients, our study identified that IL-6 had the best performance for distinguishing FMF in attack from healthy controls or FMF in remission. Our data also showed the difference between FMF and RA in cytokines/chemokines profile in sera. Additionally, we identified that microRNA-204-3p, expression of which suppressed in disease flare of FMF, inhibits lipopolysaccharide-induced cytokines production including IL-6 in FMF via the phosphoinositide 3-kinase γ pathway, indicating that IL-6 as a major inflammatory cytokine in FMF and promising target in this disease. Accordingly, we have been investing the efficacy and safety of anti-human IL-6 receptor monoclonal antibody, tocilizumab, in patients with FMF refractory or intolerant to colchicine through investigator-initiated clinical trial supported by AMED. Enrollment of the patients are successfully finished and the results have been finalized in 2020. In this symposium, we are going to discuss the ongoing roadmap of translational research of FMF and related autoinflammatory diseases.

S9-1

Transcriptomic and epigenomic features of synovial fibroblasts in RA

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Conflict of interest: Yes

Synovial fibroblasts (SFs) are one of the major source of the inflammatory mediators in the joint of rheumatoid arthritis (RA). Many cytokines and chemokines produced in the joints are thought to have a significant effect on synovial fibroblast function. For a detailed analysis of the association between chromatin remodeling and RA susceptibility polymorphisms in stimulated synovial fibroblasts, we evaluated transcriptome and epigenome of SFs from RA and osteoarthritis (OA) patients stimulated with 8 different cytokines (IFN-α, IFN-γ, TNF-α, IL-1β, IL-6/sIL-6R, IL-17, TGF-β1, IL-18) or a combination of all 8 (8-mix). Integrative analyses including mRNA expression, histone modifications (H3K27ac, H3K4me1, H3K4me3), 3D genome architecture (Hi-C) and genetic variations of SNPs were performed. Although unstimulated RASFs differed markedly from OASFs in the transcriptome and epigenome, most of the responses to stimulations were shared between the diseases. Notably, activated SFs expressed pathogenic genes, including CD40 whose induction by IFN-γ was significantly affected by a RA risk SNP (rs6074022). Upon chromatin remodeling in activated SFs, RA risk loci were enriched in clusters of super-enhancers (SEs) induced by synergistic proinflammatory cytokines. A RA risk SNP (rs28411362), located in a SE under synergistically acting cytokines, formed three-dimensional contact with the promoter of *MTF1* gene, whose binding motif showed significant enrichment in stimulation specific-SEs. Consistent with a hypothesis that MTF1 contributes to the SE formation in stimulated SFs, inhibition of MTF1 suppressed cytokine and chemokine production from SFs and ameliorated mice model of arthritis. Our findings elucidated the dynamic landscape of activated SFs and revealed potential therapeutic targets associated with genetic risk of RA.

S9-2

Identification of a novel arthritis-associated osteoclast precursor macrophage

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Conflict of interest: Yes

Osteoclasts have a unique bone-destroying capacity, playing key roles in steady-state bone remodelling and arthritic bone erosion. Whether these two populations of osteoclasts in different tissue settings arise from the same precursor states of monocytoid cells is presently unknown. Here, we show that osteoclasts in pannus originate exclusively from circulating bone marrow-derived cells and not from locally resident macrophages. We identify CX3CR1hiLy6CintF4/80+I-A/I-E+ macrophages (termed "arthritis-associated osteoclastogenic macrophages [AtoMs]") as the osteoclast precursor (OP)-containing population in the inflamed synovium, comprising a subset distinct from conventional OPs in homeostatic bone remodelling. Tamoxifen-inducible FoxM1 deletion suppressed the capacity of AtoMs to differentiate into osteoclasts in vitro and in vivo. Furthermore, synovial samples from human rheumatoid arthritis (RA) patients contained CX3CR1+HLA-DRhiCD11c+CD80-CD86+ cells that corresponded to human AtoMs, and osteoclastogenesis was inhibited by the FoxM1 inhibitor, thiostrepton, constituting a potential target for RA treatment.

S9-3

Functional genomics of immune cells and fibroblasts

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Conflict of interest: Yes

We will discuss the use of genetics and functional genomics to define mechanisms of rheumatoid arthritis and other immune-mediated diseases. We will focus on the discovery of key alleles driving rheumatoid arthritis susceptibility inside and outside of the MHC locus. Then we will explore how these alleles act in immune and stromal cells. We will focus on the immune and stromal cells that have been discovered using high dimensional appraoches, such as single cell RNA-seq, as applied to the inflammed synovium of rheumatoid arthritis patients.

S9-4

Local priming of joints for susceptibility to arthritis

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Conflict of interest: None

Clinical observations indicate that arthritis preferentially recurs at sites that have been previously affected by inflammation, suggesting the existence of a certain form of "inflammatory tissue priming". Such local priming of tissue may explain the site-specific re-appearance of arthritis and the presence of susceptible spots in the body that are particularly prone to inflammation based om "primed" tissue. How, such priming may work has been unclear to date. We found that re-exposure of joints to inflammatory stimuli caused positional prolonged and aggravated clinical signs of experimental arthritis as well as higher levels of local inflammation and tissue damage. Tissue priming developed locally and was independent of the adaptive immune system. Fibroblasts isolated from paws repeatedly exposed to inflammatory stimuli ("primed fibroblasts") exhibited enhanced metabolic activity leading to functional changes with higher migration, invasiveness and osteoclastogenic potential. Human fibroblasts derived from established arthritis exhibited a similar primed functional phenotype as compared to fibroblasts from very early arthritis or non-inflamed joints. Transcriptomic and epigenomic analyses revealed upregulation of the complement system and confirmed metabolic reprogramming in primed fibroblasts. Genetic and pharmacological targeting of complement factor C3, its receptor C3a, downstream mTOR and HIF1α as well as NLRP3 reversed this priming, induced an exhausted phenotype in fibroblasts and abrogated inflammatory tissue priming *in vitro* and *in vivo.* Our results suggest that inflammatory tissue priming is a process that leads to intracellular complement C3/C3aR activation and mTOR/HIF-1α-mediated metabolic activation of fibroblasts that trigger enhanced NLRP3 inflammasome activity and in consequence facilitates local tissue sensitivity to inflammation.

S9-5

Osteoimmune interactions in arthritis

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Conflict of interest: Yes

Rheumatoid arthritis is caused by autoimmune reactions, which result in synovitis and joint damage. To develop future therapeutic strategies, it is vitally important to identify the mechanisms underlying the prolonged inflammation and tissue destruction. We have been working on the hypothesis that autoimmune inflammation induced by Th17 cells stimulates synovial fibroblasts to express osteoclast differentiation factor RANKL. Here I will discuss the recent advances on understanding the pathogenesis of arthritis focusing on the interactions among immunity, synoviocytes and bone.

S10-1

Progress in established therapies

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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 available 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. Because they can be less costly than originator agents, these agents 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 There has been great progress in the use of established therapies in Rheumatoid Arthritis. Some critical topics include: 1) earlier intervention, 2) treat to target, 3) consideration of non-inflammatory pain, 4) optimizing safety considerations 5) the optimal introduction of biosimilar agents 6) predictors of response to individual agents, 7) combination therapy. With greater understanding, we may finally be approaching the era of 'personalized medicine' in the treatment of RA.

S10-2

Message from post-marketing surveillance subcommittee of Japan College of Rheumatology

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Conflict of interest: None

Post-marketing surveillance (PMS) of pharmaceutical drugs is to monitor the safety and efficacy and refine the proper use after their release to the clinical setting. PMS system includes the report on side effects and infections, re-review of approval, and re-assessment. Drug information is limited at the beginning, due to the property of clinical trials, which involve healthy volunteers and patients of relatively small numbers. They normally do not have other medical conditions, which may exist in the general population. The major restricting factors are age, comorbidity,

concomitant medication, short periods of medication and observation, and patient-management under experts in the trials. PMS can further refine, and confirm or deny, the safety and efficacy of drugs after they are used in patients who have a wide variety of medical conditions, including child, elderly, expectant and nursing mothers, the patients with dysfunction of liver or kidney. PMS is indispensable. PMS subcommittee of JCR has handled 18 drugs; biologics (IFX, ETN, TCZ, ADA, ABT and GLM for RA, IFX and ADA for AS, canakinumab for FMF and hyper-IgD syndrome, belimumab for SLE and the juvenile type, and mepolizumab for EGPA), JAK inhibitors for RA (tofacitinib, baricitinib, peficitinib, upadacitinib and filgotinib), csDMARDs (LEF, TAC and IGU), and mycophenolate mofetil for lupus nephritis. The important task of the PMS subcommittee of JCR is to give suggestions and/or recommendations on the plan, conduct and result of surveys to the pharmaceutical companies. Special attention has been paid to safety, including serious adverse events identified in the trial, but also potential risks. The subcommittee collaborates with the Guideline committee to develop the guide for drugs. Contribution to publication and presentation has often been asked. The members are held to a high standard of ethics according to COI. PMS subcommittee of JCR is now actively supporting pharmacovigilance of rheumatic diseases.

S10-3

New molecule therapeutics for rheumatoid arthritis

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Conflict of interest: None

The treatment of rheumatoid arthritis has changed dramatically over the past 30 years with the widespread use of effective conventional synthetic disease modifying drugs (csDMARDs) in addition to utilization of the Treat -To - Target strategy. Further advancements were accomplished with the introduction of multiple biologic DMARDs (bDMARD) with multiple mechanisms of action targeting specific pathways in the pathogenesis of RA. In recent years, targeted synthetic DMARDs (tsDMARD) have been introduced with the most recent additions of two molecules, upadacitinib and filgotinib, which are engineered to inhibit JAK1 preferentially. This discussion will discuss the clinical effectiveness and safety of these two molecules with demonstration of their comparative effectiveness to a TNF alpha inhibitor, adalimumab. In addition, the effectiveness of switching between adalimumab and upadacitinib will be shown in patients who initially did not respond to the first agent. With the relatively recent discussion of the potential of venous thrombotic episodes with JAK inhibitors, a discussion of what was found with tofacitinib will be discussed and placed in clinical context. Despite this progress, there remains a great unmet need in the treatment of rheumatoid arthritis. A a majority of patients, no matter when medications are instituted and how aggressive the treatment is, do not reach true remission as defined by a SDAI $\leq$3.3 or a CDAI $\leq$2.8 and many still do not achieve low disease activity by these metrics as will be shown. There are a number of molecules in the early stage of development which may address this need in patients who do not reach target with our current medications. Preliminary results with molecules affecting GM-CSF, ICOSL + BAFF, CD-22, a nanoparticle blocking anti-CCP, BTK, IRAK4, and PIK3 will be discussed as well as their latest data from the 2020 ACR Convergence.

S10-4

Drug discovery through genomic analysis

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Conflict of interest: None

Development of novel therapeutic drug targets is an essential process of both basic and translational researches. Drug development costs and periods become larger every year, and integration of new resource layers into developmental pipelines is warranted. Recent development of genome sequencing technology changed the bottleneck of genomic studies from construction of large-scale genome sequence data into interpretation of the sequenced genomes. While the large-scale human genome studies (e.g., genome-wide association study; GWAS) have successfully identified thousands of genetic variants associated with human complex traits, the methodologies to utilize such big genome data towards elucidation of disease biology and identification of novel therapeutic targets are still under development. Utilization of disease genomics into drug development is now considered as an efficient strategy. Disease risk genes identified by large-scale GWAS is known to be enrich in overlap with the therapeutic targets of the drugs indicated for the diseases themselves. This fact accelerated utilization of the GWAS resources into drug development. There already exist a number of collaborations between pharmacological companies and existing genomics and biobanking resources. Novel analytical methodologies for genomics-driven drug discovery are massively developed. Of note, integration of omics resources and GWAS results can further provide useful information for drug discovery. Especially, transcriptome-wide association study (TWAS) integrating GWAS results and tissue-specific gene expression profiles can provide directional information of gene expression level changes, which can introduce directional gene dosage information in candidate targets screening. In this symposium, we would like to introduce latest methodologies and applications in genomics-driven drug discovery.

S10-5

Management of Rheumatoid Arthritis in the 21st Century: Lessons Learned and Problems Encountered

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is the most common autoimmune inflammatory arthritis in adults. RA has a significant negative impact on the ability to perform daily activities, including work and household tasks, and health-related quality of life, and it increases mortality. The development of evidence-based regimens has led to new treatment paradigms and the incorporation of the “Treat to Target” strategies has resulted in a significant improvement in clinical outcome for most patients with RA. This presentation will address 6 major topics: 1) use of traditional disease-modifying/conventional synthetic antirheumatic drugs (csDMARDs) biologic DMARDs (bDMARDS), and Janus Kinase inhibitors (JAKinhibs) including tapering and discontinuing medications, and a treat-to-target approach; 2) use of glucocorticoids; 3) use of biologics and DMARDs in high-risk populations (eg congestive heart failure, malignancy, and serious infections); 4) use of vaccines in patients starting/receiving csDMARDs or bDMARDs or JAKinhibs 5) screening for tuberculosis (TB) in the context of biologics or JAKinhibs and 6) laboratory monitoring of patients on all 3 classed of medications. The need for modifications of both disease activity measurements and management strategies in the setting of the COVID pandemic will also be presented.

S11-1

Rheumatoid arthritis and infection from the view of epidemiology

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Conflict of interest: Yes

Observational studies showed that patients with rheumatoid arthritis (RA) had a 2-fold increased risk of serious infection than general population even more than 50 years ago. In those days, a 2-fold increased risk of mortality was reported in patients with RA, and infection was the most frequent cause of death. In Japan, treatments for RA has been dramatically improved by approvals of biological disease modifying antirheumatic drugs (bDMARDs) in 2000s. bDMARDs enabled rheumatologists to treat patients with RA aiming at clinical, structural, and functional remission, which consequently led to better patients’ quality of life. There are, however, concerns about increased risk for serious adverse events (AEs) under the treatments with bDMARDs, and infection is the most frequent AE and one of clinically important complications because it hampers the appropri-

ate treatments for RA and sometimes it is fatal. Thus, many epidemiological studies over the world have focused on incidence rate and risk factors of serious infection in patients given bDMARDs since biologic era has started. Based on the published evidence, risk managements for patients given bDMARDs have been implemented in accordance with recommendations for RA treatments. After the introduction of bDMARDs, some epidemiological studies in Western countries showed that mortality risk in patients with RA was improved by better disease control. However, patients with RA still have a 1.5-fold higher risk of mortality than general population, and infection accounts about 20% of the causes of death. It is not always appropriate to apply the evidence in the Western countries to Japanese patients because prevalence of causes of death and patients' characteristics differ among ethnic groups. Thus it is needed to establish evidence in Japanese population. In this symposium, we will review the published epidemiological data investigating infection in patients with RA, and discuss topics in this essential research field.

S11-2

The impact of the new coronavirus for rheumatic diseases

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Conflict of interest: None

The new coronavirus, which was most recently discovered from the patients of severe acute respiratory distress syndrome at Wuhan, China in 2019, was named as SARS-CoV-2. This virus causes various symptoms (COVID-19), especially respiratory symptoms. Because the virus can be infected in even asymptomatic phase, the infection has been easily expanded to the world and reached pandemic. The elderly person, obesity, diabetes mellitus and heart diseases are considered as the causes of severe COVID-19. We studied that the rheumatic diseases and the treatment for rheumatic diseases could be associated risk factors of COVID-19 or not. 1. The rheumatic diseases increase susceptibility to SARS-CoV-2 or not. There were few reports that the susceptibility to SARS-CoV-2 increased among rheumatic diseases. The ratio of admission and death related with COVID-19 was reported as no significant difference between rheumatic diseases and normal population. 2. The rheumatic diseases are related to severe COVID-19 or not. There was no report of the relation with severe COVID-19 and rheumatic diseases. 3. The treatments for rheumatic diseases are related to severe COVID-19 or not. The treatment with more than 10 mg/day of prednisolone was reported to relate with severe COVID-19. Whereas, there was no report of severe COVID-19 related with synthetic DMARDs, biologic DMARDs, immunosuppressant, or JAK inhibitors. 4. The medicines for rheumatic diseases improve and/or prevent severe COVID-19 or not. The pathogenesis of severe COVID-19 was cytokine storm and hyper coagulation. Moderate dose of steroid (dexamethasone) are proved to suppress this state. Biologic DMARDs and JAK inhibitor were expected to have a beneficial effect on severe COVID-19 due to the principal mechanism of the drugs.

S11-3

Risk Management of Herpes Zoster in the Era of Molecular Targeted Therapy

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Conflict of interest: Yes

Herpes zoster is caused by reactivation of varicella-zoster virus (VZV) which belongs to the family Herpesviridae, and is characterized by unilateral grouped painful vesicles consistent with the dominant nerve region. The decrease in VZV-specific cellular immunity due to aging and various immunocompromised conditions is known to be a risk factor for the development of herpes zoster. In recent years, the use of biologics and molecular targeted drugs for the treatment of cancer and inflammatory diseases has improved disease outcomes, but also increased the risk of infectious diseases by these immonomodulatory effects. In this talk, I will discuss the risk of developing herpes zoster caused by biologics and JAK inhibitors used in rheumatoid arthritis, updates about early diagnosis and treatment, and vaccines for the prevention of herpes zoster.

S11-4

Progress in Clinical Management of Mycobacterium Infection in Rheumatic Patients

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Conflict of interest: None

It is well known that rheumatic patients will be susceptible to various infectious diseases, especially respiratory infectious diseases including acute pneumonia and chronic mycobacterial infections. Recent epidemiological trends demonstrated abrupt increase of pulmonary non-tuberculosis mycobacterial infections in patients, although exact reasons are not yet elucidated. Particularly in the era of biological treatment, it is critically important how to make diagnosis and treat pulmonary NTM in rheumatic patients. NTM is ubiquitous in nature, so people are equally exposed to inhalation of this organism as aerosol. If such people have structural and/or organic abnormality in lungs, especially bronchiectasis, NTM will easily colonize and start to infect in pulmonary environment. Cellular immunity is known to play a crucial role in host defense system against pulmonary NTM, but it is poorly understood how immunological abnormality in rheumatic patients is associated with pulmonary NTM infections. In this presentation, focusing on pulmonary NTM in rheumatic patients, recent trends and progress in diagnosis and treatment will be presented for following discussion with audience.

S11-5

The present situation and countermeasure of surgical site infection associated with orthopaedic surgery in patients with rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) patients are associated with increased risk of infection compared to non-RA patients. Previous reports demonstrated that oral glucocorticoid may increase the risk of surgical site infection (SSI) in a dose-dependent manner, while methotrexate may have little influence. Biologics may increase the risk of SSI especially in prosthetic replacement arthroplasty, and adequate duration of drug withdrawal is recommended. We still lack reliable evidences about the risk of SSI concerning JAK inhibitors. I would like to review the latest evidences and guidelines concerning SSI associated with orthopaedic surgery in patients with RA.

S12-1

Transition of Knee Surgeries for Rheumatoid Arthritis

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Conflict of interest: Yes

In recent years, the number of knee joint surgery for rheumatoid arthritis (RA) has been decreasing with the improvement of drug treatment such as biologics. Synovectomy has often been performed for highly active synovitis of the knee joint, which is difficult to control even with joint injection or oral medication. In particular, the number of cases had tended to increase with the spread of knee arthroscopic surgery. However, recently, with the development of drug treatment, its role has become limited, and the number of operations has decreased considerably. The number of cases of total knee arthroplasty (TKA), including those for osteoarthritis (OA), is increasing year by year, and the current number of cases in Japan exceeds 100,000 per year. However, the number of cases of TKA for RA is decreasing with the progress of drug treatment. Comparing clinical results of TKA for knee OA and RA, the infection rate of TKA for RA is slightly higher, but revision due to loosening, postoperative score, satisfaction, etc.

are not different. In implant selection for RA, if the posterior cruciate ligament (PCL) remains at the time of surgery, it is unlikely that postoperative posterior instability will appear, and it seems that PCL-preserving type can also be used. Cement was mainly used, but recently there are some results of cementless. In addition, although opinions are divided on the replacement of the patella, in the case of RA, the risk of causing problems after surgery seems to be low with resurfaced patella. Unicompartmental knee arthroplasty and high tibial osteotomy have improved postoperative results due to the development of surgical procedures and implants. Until now, both surgical procedures have not been basically indicated for RA. Although it may be possible to obtain good results if RA is relieved, it is currently considered that the procedure should be carefully selected.

S12-2

Current status of Total Hip Arthroplasty (THA) for Rheumatoid Arthritis

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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has been greatly improved by the use of methotrexate (MTX) and new anti-rheumatic drugs. The articular cartilage and bone destruction are suppressed by these drug therapies, therefore, the number of RA-related orthopaedic surgeries has been decreasing, especially in THA and TKA. We report the current status of THA for RA. (The rate of RA-THA in whole primary THA) The percentage of RA-THA in primary THA at was 7.3% in the period 1998-2005, and decreased to 2.3% in the period 2010-2017. (The degeneration of RA-hip) The number of THA cases for severe joint destruction such as acetabular protrusion was decreasing. Because of the aging of RA patients and improvement of drug therapy, RA hip joints with osteoarthritis changes is increasing. (Implants) Highly cross-linked polyethylene improved the wear resistance of articulating surfaces. As a result, the use of larger head size has become possible. 32 mm haed are currently popular. As for a femoral stem, the taper wedge stem replaced a fit and fill stem. (THA related complication) It has been reported that RA is one of the risk factors for dislocation, periprosthetic fracture (PPF) and infection. The rate of dislocation reduced with the larger head size and improved technique of implant placement. The aging of RA patients and osteoporosis are associated with PPF, however, short and thin taper wedge reduced the rate of PPF compared to the fit and fill stem.

S12-3

Rheumatoid hand and wrist surgery

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Conflict of interest: None

Early use of methotrexate and/or biologics have made it possible to better control the disease activity of rheumatoid arthritis (RA), and large joint surgery is on the decline. However, there are some reports that small joints surgery such as fingers and wrists is the same or increasing. In the past, many patients complained of pain and deformity due to joint destruction of the fingers at the same time, but in recent years, there are some patients who have no pain and only have complaints about the appearance of the deformed fingers. It is said that this situation is due to better control of disease activity, which has led patients with rheumatoid arthritis to desire better hand function and higher therapeutic goals. We use synovectomy, arthrodesis, or total joint replacement for rheumatoid arthritis related finger joint (including thumb joint) disorders, and for radial-carpal joint disorders, synovectomy, partial arthrodesis or total arthrodesis have been selected according to the patient's situation. In order to achieve higher treatment goals, arthroplasty or total joint replacement that preserves joint movement is the first choice, rather than total arthrodesis because of joint destruction, should be considered. This applies not only to the joints of the fingers including the thumb, but also to the radial-carpal joints. Since 2017, we can performe total wrist arthroplasty in Japan, and even in cases where only total wrist arthrodesis could be selected in the past, total wrist arthroplasty will be used to deal with it and preserve joint movement. In this presentation, we will introduce typical RA fingers (including thumbs) and wrist joint surgical treatments to achieve higher treatment goals.

S12-4

Foot and Ankle Surgery in Rheumatoid Arthritis Patients

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Conflict of interest: None

To obtain health expectancy in RA patients, the function of lower extremity should be maintained and/or developed with tight control and surgical treatment. Dysfunction by destruction or deformity could not restored by medical treatment any more. Surgical treatment for lower extremity should always be advanced to obtain more improved gait function, subsequently not only physical function, but also cognitive function should be maintained.

S12-5

Shoulder and elbow arthroplasties for rheumatoid arthritis

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Conflict of interest: None

The shoulder and elbow arthroplasties for rheumatoid arthritis (RA) are highly recommended because of their effectiveness in excellent pain relief. However, the number of cases of them is lower than that of knee and hip arthroplasty, making it difficult to obtain a learning curve for the surgeon. Caution should be paid for the specific complications, and if complications such as dislocation or loosening occur, revision surgery is not easy to perform. In the shoulder joint, where rotator cuff function is preserved, anatomical total shoulder arthroplasty (aTSA) by third-generation humeral head with offset is indicated. The 10-year survival rate with revision as an endpoint is over than 90%, although there are a few cases in which the patient does not achieve a satisfactory range of motion (ROM) postoperatively, which depends on the preoperative condition of the joint. Reverse shoulder arthroplasty (RSA) can be used in cases of rotator cuff tears, and excellent ROM can be expected postoperatively. RSA should be used with caution in RA patients with insufficient bone volume, weak bone structure, and susceptibility to infection. Artificial elbow replacements began in the 1940s with poor results, and hinged elbow replacements by Dee, Stanmore, Geshwend and others in the 1970s all had poor results. A number of good postoperative results of unlinked total elbow arthroplasty (TEA) have been reported in Japan, and unlinked TEA has been used in cases of primary TEA with preserved bone stock, whereas unlinked TEA has been used in cases of severe joint destruction such as mutilans-type RA, unstable joints with ligamentous dysfunction, or revision surgery. Over 10-years long-term survival rates have recently been reported to be exceeding 90%. Shoulder and elbow arthroplasty for RA, with good bone quality and soft tissue preservation, is expected to provide better long-term results in the future when disease activity is controlled by recent pharmacological treatment.

S12-6

The advance of the surgeries for cervical spine involvement in rheumatoid arthritis

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Conflict of interest: None

Cervical spine involvement is a common complication of rheumatoid arthritis, and resultant deformities may cause neurologic deficits, such as cervical myelopathy, paresis, and even death. After the use of methotrexate for RA was approved in 1999, the first biologic agent was introduced in 2003 in Japan. Among these drugs, BAs have shown strong effects in controlling disease activity and suppressing joint destruction, especially at the peripheral joints. With the advent of these agents, treatment paradigms for RA recently have undergone a major shift. The standard of care now entails initiating immediate treatment using aggressive therapy with DMARDs or a combination of DMARDs plus BAs. Rheumatic spondylosis significantly decreased from 1.6% in 2004 to 0.2% in 2015. Innovative biological agents have improved control of rheumatoid arthritis activity and reduced deterioration of cervical lesions. This has resulted in a marked decrease in surgical treatment for cases with severe instability or bone destruction. However, all patients do not always receive the best care immediately after RA onset. Occipitocervical fusion surgery effectively treats severe neck pain and myelopathy from craniocervical instability and spinal cord compression. This technique has shown fusion rates, ranging from 80% to 96%. Screw rod constructs may provide superior biomechanical rigidity and provide immediate postoperative stability, potentially eliminating the need for prolonged external immobilization. Advances in technology and anatomic knowledge have led to development of various rigid fixation constructs. Several reports have been published describing excellent results obtained when treating craniovertebral junction (CVJ) and upper cervical instability with OC fixation using a rod and screw system

S13-1

Recent progress and topics in Systemic Sclerosis including pathogenesis and treatment

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Conflict of interest: Yes

Systemic sclerosis (SSc) is characterized by excessive fibrosis of the skin and internal organs, microvascular injury, and autoimmunity represented by autoantibody production. However, there have been no concepts or findings which can explain these 3 characteristics simultaneously. From the point of view of the process of wound healing, SSc is the disease captured at the phase of fibrosis/remodeling but not at the inflammatory phase. Thus, the treatment approach is different from other connective tissue diseases such as rheumatoid arthritis, which can treat with immunosuppressive agents such as biologics. When these irreversible changes occur in vital organs, those are critical for the patients with SSc, which results in a poor prognosis that is comparable to malignancies. However, since there is no treatment approach which can achieve “reverse remodeling”, most of the treatment for organ involvements in SSc is categorized as a “symptom-relief” approach. Of these, interstitial lung disease (ILD) can be captured at the inflammatory phase and immunosuppressive treatment is expected to have a substantial effect on the succeeding fibrotic process. On the other hand, recent progress in the development of a novel treatment in idiopathic pulmonary fibrosis enables us to use an anti-fibrotic agent for SSc patients with ILD, which was recently approved in Japan. Furthermore, the establishment of the composite measure for the evaluation of disease activity of SSc has been an important issue. We have been used the modified Rodnan total skin thickness score as an outcome measure, but the limitation is recently recognized. The emergence of the new measure, The American College of Rheumatology Combined Response Index in Diffuse Cutaneous Systemic Sclerosis (ACR CRISS) score, is one of the topics and expected as a novel outcome measure for clinical trials. I would like to overview these topics and discuss future perspectives and issues in this session.

S13-2

Update on the Pathogenesis of Myositis: Role of Jo-1 in the Immunopathogenesis of the Anti-synthetase Syndrome and Nonimmune Mechanisms of Myositis

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Conflict of interest: None

The inflammatory myopathies-collectively, myositis-are a heterogeneous group of chronic muscle disorders [Nat Rev Rheumatol. 2011;7:297]. Immune pathomechanisms of myositis have been considered to involve immune cells-T cells, B cells, dendritic cells and macrophages-and their products, such as cytokines and antibodies. To address the role of histidyl-tRNA synthetase (HRS = Jo-1) in the pathogenesis of the anti-synthetase syndrome, Katsumata *et al*. immunized different congenic strains of NOD and C57BL/6 mice with emulsions of complete Freund’s adjuvant and recombinant murine HRS and demonstrated a direct relationship between B and T cell recognition of murine HRS and combined clinical features of low-grade myositis as well as striking perivascular/peribronchiolar lung inflammation [J Autoimmun. 2007;29:174, Curr Rheumatol Rep. 2015;17:56]. Notwithstanding such provocative findings linking the patterned adaptive immune response to HRS with clinical features of the anti-synthetase syndrome in humans (myositis and interstitial lung disease), this model has not fully elucidated factors governing T cell phenotype or the unique tissue tropism characterizing this disease. Subsequently, based on intramuscular immunization with recombinant HRS in the absence of additional exogenous adjuvant, Soejima *et al*. developed an alternative, antigen-induced model of myositis that features HRS-mediated activation of innate immune responses. Furthermore, Fernandez *et al*. defined the central role of MyD88-dependent signaling pathways in this model and highlights the unique capacity of HRS to interact with various endogenous/exogenous ligands of MyD88-dependent toll-like receptors. Besides, it is also suggested that nonimmune mechanisms, such as endoplasmic reticulum stress, hypoxia and autophagy, might affect the performance of muscle fibers and weaken muscle in the absence of inflammatory cell infiltrates. In this symposium, the update on the pathogenesis of myositis is to be discussed.

S13-3

Clinical significance of identifying systemic sclerosis- and myositis-specific autoantibodies

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Conflict of interest: None

Several disease-specific autoantibodies (autoAbs) have been identified in systemic sclerosis (SSc), polymyositis (PM), and dermatomyositis (DM). The identification of autoAbs in individual patients is clinically beneficial, since the particular type of autoAbs is often indicative of clinical features, severity, and prognosis. For example, anti-topoisomerase I and anti-RNA polymerase Abs are associated with diffuse skin thickening. However, the frequency of interstitial lung disease (ILD) and peripheral vasculopathy is higher in patients with anti-topoisomerase I Abs, whereas both complications are less frequent in those with anti-RNA polymerase Abs. In contrast, Anti-centromere Abs are associated with limited form and better prognosis. Anti-U3 RNP and anti-Th/To Abs have a frequency of less than 5%, although both have a characteristic clinical phenotype. Representative complications in patients with PM/DM include ILD and malignancy. Anti-ARS and anti-MDA5 Abs are major myositis-specific autoAbs (MSAs) associated with ILD, whereas anti-MDA5 Abs are more frequently associated with rapidly progressive ILD and less associated with muscle involvement. Anti-TIF1 and anti-NXP-2 Abs are associated with malignancy in adults, but are also representative MSAs in juvenile DM. Patients with anti-Mi-2 Abs have typical skin rashes and severe myositis, but ILD and malignancy are less frequent. The first step for identifying SSc-associated autoAbs and MSAs is to confirm the presence of anti-nuclear Abs by indirect immunofluorescent (IIF) staining of HEp-2 cells. Enzyme-linked immunosorbent assay (ELISA) is widely used for identification in routinely clinical practice because of its simplicity. How-

ever, ELISA systems are only available for limited autoAbs and there is a possibility of false positives. Physicians should pay attention to the consistency between ELISA results and clinical phenotype as well as the results of IIF staining.

S13-4

Update on the treatment of Systemic Sclerosis related Interstitial lung disease

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Conflict of interest: None

Interstitial lung disease (ILD) in Systemic sclerosis (SSc) is a vital organ involvment frequently (50-70%) detected by HRCT and its increasing proportion in the causes of death in SSc over the years. Even though cyclophosphamide and mycophenolate mofetil have been reported as effective treatments for SSc-ILD, these treatments have not been shown to improve the long-term prognosis. Thus, additional treatment options have been expected. Conventionally, we usually treated patients with immunosuppressants. However, recent RCT has been shown the efficacy of anti-fibrotic agent for SSc-ILD. In 2019, the SENSCIS study was performed to evaluate the safety and efficacy of nintedanib in patients with SSc-ILD, which was already approved for the treatment of idiopathic pulmonary fibrosis. Patients were eligible to enroll when they have >10% fibrosis on the HRCT and the onset of the first symptom of non-Raynaud within the past seven years. This study showed that the patients treated with nintedanib exhibited significantly less decline in mean adjusted annual change in Forced vital capacity (FVC). Another topic is that tocilizumab (TCZ) was recently approved for SSc-ILD by FDA. The focuSSced study was performed to evaluate the safety and efficacy of tocilizumab (TCZ), an anti-interleukin-6 receptor antibody, in patients with SSc. Patients with diffuse cutaneous SSc for 60 months or less and mRSS of 10–35 at screening were included. Treatment with TCZ showed preventive effect on ILD progression. As mentioned above, there are new findings regarding the treatment of SSc-ILD, but it should be noted that the background of the patient in each study is different. I would like to overview SSc-ILD treatment, consider the patient background and ILD pattern, and discuss future perspectives and issues in this session.

S13-5

Cutting edge treatment for myositis

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Conflict of interest: Yes

Poymyositis and dermatomyositis are the leading inflammatory myopathies in which rheumatologists are involved to manage disease activity as well as disease damage. Myositis-specific autoantibody (MSA) is detected in approximately 70-80 percent of patients with these types of myositis. Myositis is considered to be one of the autoimmune diseases, suggesting that immunosuppressive therapy is effective for myositis. In terms of treatment with muscular lesions, corticosteroid is the cornerstone drug, usually initiated with intermediate-dose to high dose of prednisolone (PSL). Several immunosuppressive agents, such as methotrexate and azathioprine, are introduced initially concomitant with PSL to avoid short-term and long-term organ damages caused by increased cumulative dose of corticosteroid, and disease flares. However, in daily practice, it is difficult to discontinue maintain treatment with PSL in most patients with myositis. Recently, there have been emerging agents for myositis in clinical trial which have been already approved for treatment with other various autoimmune diseases such as rheumatoid arthritis and lupus. Those novel agents may have a potential ability to reduce cumulative dose of PSL, and to replace maintenance therapy with low-dose corticosteroid as a novel treatment option. With regard to ILD associated with myositis, a novel therapeutic algorithm has been proposed jointly by the Japanese Respiratory Society and the Japanese College of Rheumatology in 2020. This algorithm is drawn up based on the patient stratification by established prognostic factors including MSA. In this session, we would like to introduce the current issues and future perspectives regarding myositis treatment.

S14-1

The mystery of gender difference in autoimmune diseases: From the perspective of functional genomics

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Conflict of interest: Yes

Most of the autoimmune diseases show strong sex bias and predominated by female patients. This is the distinctive feature of autoimmune diseases, and to understand the reason of gender difference might lead to understanding the pathogenesis of these disorders. So far, some hypotheses have been proposed to explain gender difference in autoimmune diseases. Regulation of immune-associated genes by sex hormone is one of those examples. Clinical findings that systemic lupus erythematosus predominantly affects women of childbearing age and frequently flares during pregnancy can be considered to support the relevance of sex hormone in its pathogenesis, although causal relationship is still unclear. The other possible explanation is the association of X chromosome inactivation (XCI) escape genes to autoimmune pathogenesis. The fact that individuals with Klinefelter syndrome, who carry extra X chromosome, show 14 times more prevalence of SLE supports the relevance of XCI escape genes in disease pathogenesis. In addition, many other hypotheses have been proposed, although not conclusive. To verify these hypotheses, using multi-omics dataset can be a useful approach. Our group has constructed functional genomics database, “ImmuNexUT”, which consist of 28 kinds of immune cells from 10 kinds of immune-disease patients. Using our database, we identified cell type specific XCI escape genes, some of which showed differential expression in autoimmune diseases. Moreover, applying functional genomics approaches including expression quantitative trait loci (eQTL) analysis and allele specific expression (ASE) analysis, we identified some examples of female-specific mechanisms of gene regulation, which can be relevant to disease pathogenesis. In this session, we want to review the reports about the gender difference in autoimmune diseases and discuss about the utility of multi-omics dataset for the elucidation of this mystery.

S14-2

A short overview of female reproductive endocrinology

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Conflict of interest: None

The management of the female patients with autoimmune disorders is discussed from the various viewpoints including perinatology, assisted reproductive technologies (ART), recurrent pregnancy loss, oncofertility, and menopausal medicine in this symposium. A short overview of female reproductive endocrinology is provided for a better understanding of its close relationship with autoimmune disorders. (1) Folliculogenesis: irreversible decrease of “ovarian reserve” with age. (2) Reproductive hormone dynamics in the menstrual cycle: follicle growth, ovulation, and implantation of blasocyst with the help of luteum.

S14-3

Autoimmunity from the point view of infertility and pregnancy loss

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Conflict of interest: None

Since autoimmunity is often observed in women, obstetricians sometimes see patients with autoimmunity. However, it is not clear whether autoimmunity may affect pregnancy or infertility treatment. Since there are some medications that may not be used during pregnancy, it is necessary to control both pregnancy and autoimmunity. In terms of infertility (pregnancy) treatment, important autoimmune antibodies are anti-centromere and anti-sperm antibodies. As to pregnancy loss, important auto-

immune antibodies are anti-phospholipid antibodies. Interestingly, when the same types of antibodies are detected, the phenotypes are different between patients in internal medicine and obstetrics. I will present autoimmunity from the point view of infertility and pregnancy loss based on data in Reproduction Clinic Osaka and Tokyo. Reproduction clinics can see both patients with infertility and pregnancy loss at the same institute and same time. This is only one clinic in Japan except for University hospitals. Besides that, our clinics dealt with the second most ART cycles (including IVF and ICSI) in Japan. Therefore, we have most patients who suffered from both infertility and pregnancy loss. Our data suppose to be the largest number of such patients in Japan. Anti-centromere antibodies are parts of anti-nuclear antibodies, which is known to often show abnormal fertilization (multi-pronucleus; 3PN or more) at the time of fertilization. When anti-centromere antibodies bind to centromere, spindle cannot bind to it, resulting in non-disjunction of homologous chromosomes during meiosis. We don't have any consensus for positive anti-centromere antibodies, but administration of prednisolone and/or intravenous immunoglobulin (IVIG) or confirmation of spindle by polscope can sometimes avoid abnormal fertilization. Anti-phospholipid syndrome (APS) in patients with pregnancy loss seldom shows thrombosis. According to the 2010 report of the Ministry of Health, anti-phospholipid antibodies were detected only 10.2% for the total incidence of lupus-anticoagulant, anti-cardiolipin, and anti-β2GPI antibodies (included in the APS criteria), but 34.3% for anti-phosphatidylethanolamine antibodies (not included in the APS criteria). As a member of Japan anti-phospholipid antibody standardization committee, I will present recent data of APS in obstetrics.

S14-4

Issues which should be solved in pregnancy of rheumatic diseases

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Conflict of interest: Yes

The advent of new drugs, as well as the evolution of how to use therapeutic drugs has improved the prognosis of rheumatic diseases dramatically. It is the natural goal for patients, who wish to raise children, that they are able to have children. However, it cannot be denied that the theme of pregnancy in these diseases is, so to speak, an orphan, left behind by the progress of treatment. Thus, workshops on the theme of "pregnancy" reappeared at the annual meeting of the JCR in 2016 after a long interval. Rheumatoid arthritis (RA) is the most common disease among rheumatic diseases in pregnant patients. The problems of pregnancy with RA are limited in how anti-rheumatic drugs are used during pregnancy and lactation. Systemic lupus erythematosus (SLE) is a heterogeneous disease, so it is difficult to provide evidence of pregnancy from experience at only one institution. To improve this problem, A prospective cohort study on the short and long-term prognosis, including pregnancy outcomes, of young patients with Systemic Lupus Erythematosus in Japan (PLEASURE-J study which is the first cohort study managed by the JCR started in 2017. This study is constructed not only using clinical data entered by doctors and QOL data entered by patients about the relationship between initial treatment of SLE and the prognosis including pregnancy issues, but also studies using biological samples such as genome analysis. With the cooperation of many facilities, teachers and patients, I am confident that it will be a cohort study that we can be proud of overseas in the near future. Pregnancy remains an important theme for rheumatic diseases other than RA and SLE. In addition, I would like to present the direction of future research and clinical practice guidelines, including themes that are swayed by changes in antibody measurement methods, such as anti-SS-A antibody and antiphospholipid antibody syndrome.

S14-5

Health care for middle-aged and elderly women considering female hormones

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Conflict of interest: None

In Japan, a climacteric period is defined as "a period of 10 years before and after the last menstrual period." Additionally, menopause syndrome is defined as "the clinical state that occurs during a climacteric period, the other illnesses do not cause that, and that affects the woman's daily life." Menopausal symptoms are caused not only by reduced estrogen levels but also by sociopsychological factors. Menopausal symptoms are varied; however, one of the most specific symptoms is the so-called hot flashes. Alternatively, some studies report that Japanese women tend to show general fatigue, stiff shoulder, and forgetfulness. Most women simultaneously experience a variety of symptoms. When diagnosing menopause, it is imperative to first confirm whether the patient is in a climacteric period. Next, it is important to exclude the possibility of other illnesses. Women undergoing menopausal often complain of symptoms similar to rheumatoid and collagen diseases; therefore, the cause of symptoms often needs to be differentiated. We typically treat menopausal women using Kampo medicine and hormone replacement therapy (HRT). We also use antidepressants, especially for women suffering from severe depressive mood or anxiety symptoms. Two health care problem for women after menopause are hyperlipidemia and osteoporosis. Serum total cholesterol and LDL cholesterol start to rapidly increase among women aged approximately 50 years. The amount of bone mass is also known to be significantly associated with estrogen levels, and bone mass continuously decreases after menopause. Cardiovascular diseases caused by atherosclerosis and bone fractures caused by osteoporosis may result in a woman becoming bedridden. Therefore, early prevention and detection of such diseases are of particular importance. In conclusion, to ensure the maintenance of women's quality of life, endocrinal changes and diseases more common in women must be considered when administering the necessary treatment.

S14-6

Rheumatoid arthritis, estrogen deficiency and hormone replacement therapy

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Conflict of interest: None

RA is classified into gender differential diseases, because the peak of onset of RA in women appears at age of 45-55, the age group corresponding to menopausal onset which indicates the involvement of estrogen reduction and deficiency. Furthermore, RA onset frequency observed in early menopause women is twice as higher as that of normal menopause. Premature ovarian insufficiency patients are at higher risk of late-onset autoimmune diseases such as Hashimoto's disease. It is recommended to treat those patients with HRT up to the average menopausal age. HRT guidelines indicate that (1) Menopause increases the onset of joint pain due to estrogen deficiency. (2) HRT suppresses the onset of joint pain. (3) HRT reduces joint pain. (4) It has been shown that joint pain is deteriorated by discontinuation of HRT. Estrogen receptors in joint tissues and the estrogen directly protect biochemical structures and its function maintaining the healthy joint. Estrogen receptors ERα and ERβ have been identified in chondrocytes and animal studies have proven the cartilage protective effects of estrogen. However, the effects of HRT on RA have not been concluded. WHI study reported that RA was less developed in the HRT group, although it was not significant. The Swedish report found that the risk of ACPA positive RA was significantly reduced in HRT users compared with non-user. It was suggested that HRT may reduce the risk of developing ACPA-positive RA in postmenopausal women. It is hypothesized that estrogen decline in menopause may affect the mechanism of developing ACPA positive RA after menopause, since estrogen decline in menopause causes immune system abnormalities associated with RA. In this symposium, I would like to introduce about the interactions of estrogen, RA, and joint symptoms, along with research reviews, and the effects of HRT on joint symptoms in RA patients based on my experience at my clinical practice.

S15-1

Adult onset Still's disease

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Conflict of interest: Yes

Adult-onset Still's disease is a rare, systemic inflammatory disorder of unknown aetiology that is characterised by high spiking fever, evanescent rash, and polyarthritis. The pathogenic mechanisms of adult-onset Still's disease are not fully understood, but the pivotal role of innate immunity involving macrophage activation and Th1 cytokines, such as interleukin-1β and interleukin-6, has been demonstrated. Overall treatment, however, remains challenging because high dose glucocorticoids sometimes fail to cause remission, with occasionally fatal consequences, and dependence on glucocorticoids is frequently observed with a relapse of symptoms along with glucocorticoids dose tapering or discontinuation, which leads to organ damage accrual and long-term side-effects of glucocorticoids. Immunosuppressive agents, such as methotrexate and cyclosporine, have been used as a steroid-sparing drug, but their effectiveness is limited. Progress in the understanding of the critical role of those inflammatory cytokines in the pathogenesis of adult-onset Still's disease has led to pilot use of anti-cytokine agents, and direct inhibition of those inflammatory cytokines has shown promising outcomes. In this session, I am going to talk about recent findings of cytokines and cytokine inhibition in adult-onset Still's disease.

S15-2

Behçet's disease

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Conflict of interest: Yes

Behçet's disease is an intractable disease characterized by recurrent inflammation of the mucocutaneous membrane and the eyes, and also causes inflammation of the intestinal tract, the central nervous system, and the blood vessels, but the pathogenesis of the disease remains unknown. Both environmental factors and genetic factors are considered to be important in the pathogenesis of the disease. The involvement of microorganisms, such as *Streptococcus sanguinis* and *Herpes simplex* have been reported as environmental factors triggering inflammatory attacks. Genome-wide association analysis has found associations with several loci involved in innate immunity, including *MEFV, KLRC4*, and *IL1B*, in addition to HLA and other genes involved in acquired immunities. Based on these data, it is likely that innate immune responses to microorganisms, especially cells such as monocytes, neutrophils, and NK cells, and their genetic predisposition to hyper functionality contribute to the pathogenesis of Behçet's disease. In fact, therapeutic targets of colchicine, which is the first-line drug for Behçet's disease, are neutrophil migration and inhibition of inflammasome activation, and apremilast, which was recently approved for the treatment of oral ulcers in Behçet's disease, affects monocyte and macrophage cytokine production. In addition, our basic research has shown that M2 macrophage dysfunction is important (Nakano et al, Arthritis Res Ther, 2018). In this talk, I will present the latest findings on the pathogenesis of the innate immune system in Behçet's disease.

S15-3

Pathophysiology, diagnosis and management of polymyalgia rheumatica

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Conflict of interest: None

Polymyalgia rheumatica (PMR) is a frequent rheumatic condition in patients over 50 years of age. However, its pathophysiology is poorly understood. PMR is clinically diagnosed based on the symptoms but differential diagnosis is sometimes difficult. Genetic data revealed the association between the HLA-DRB1 and PMR. In addition, several gene polymorphisms such as ICAM-1, RANTES, TNF, IL-1 and IL-6 have been studied and reported to be associated with PMR. Since higher serum levels of IL-6 and soluble IL-6 receptor were found in early or refractory PMR, these findings support the use of IL-6 receptor blockade. PMR is clinically diagnosed based on the symptoms, although accurate diagnosis is difficult because the symptoms can occur in many other rheumatologic and inflammatory conditions. Recently, imaging such as ultrasonography, magnetic resonance imaging (MRI) and positron emission tomography have been reported to be useful for improving diagnostic accuracy and prognosis prediction in patients with PMR. We evaluated gadolinium-enhanced MRI findings for the diagnosis and predicting recurrence in patients with PMR and MRI could contribute to accurate diagnosis and prediction of recurrence. PMR is characterized by a prompt response to glucocorticoid (GC) in low doses IL-6 receptor blockade, in addition to high dose GC and/or MTX, has been reported to be useful in patients with refractory PMR and/or GCA. In this symposium, the current knowledge about pathophysiology, diagnosis and management of PMR will be reviewed.

S15-4

Systemic juvenile idiopathic arthritis

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Conflict of interest: Yes

Systemic juvenile idiopathic arthritis (s-JIA) is a unique subtype of JIA, characterized by arthritis and other systemic features including spiking fever, salmon colored skin rash, generalized lymphadenopathy, hepatosplenomegaly, and serositis. s-JIA is an auto-inflammatory condition and the hallmark of s-JIA is excessive activation and proliferation of T lymphocytes and macrophages. Inflammatory cytokines, including interleukin (IL)-1, IL-6, and IL-18, play pathogenic roles in the disease progression of s-JIA. Biological therapies that block IL-1β or IL-6 have dramatic effects in patients with s-JIA. However, recent studies revealed these biologics cannot suppress the progression to macrophage activation syndrome and also chronic arthritis in some patients were resistant to these biologic therapies. In the pathogenesis of MAS, overproduction of IL-18 plays a key role and recent reports showed the therapeutic effect of IL-18 binding protein for MAS. Furthermore, some studies showed IL-17 plays an important role in the pathogenesis of chronic arthritis in s-JIA. In this talk, I would like to review the pathogenesis of s-JIA and MAS, and will discuss the future perspectives.

S15-5

Inflammasome-associated autoinflammatory syndrome

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Conflict of interest: Yes

Autoinflammatory syndrome is a new disease concept proposed by Dr. Kasnter of the NIH in 1999. Since the human genome project as well as the rapid progress in gene analysis technology due to the next-generation sequencers brought identification of new causative gene for autoinflammatory syndrome, we have now more than 30 disease-causing genes for it. These gene discoveries have not only led to the diagnosis of unknown fever cases, but also to the elucidation of pathogenesis from the analysis of causative genes, and further to the identification of target molecules, leading to the development of therapeutic drugs. Cryopyrin-associated periodic syndrome is an autoinflammatory syndrome caused by *NLRP3* mutation, which is a good example on how the identification of a disease-causing gene (*NLRP3*) leads to the disease-mechanism (inflammasome) as well as the target molecule (IL-1β) ending to the therapy (canakinumab). This symposium will focus on "Inflammatory diseases associated with innate immunity" and will discuss the current status of pathogenesis, diagnosis, and treatment of the known inflammasome-associated autoinflammatory syndromes. We hope that the research on these hereditary diseases will lead to improvement in the treatment of autoinflammatory syndrome and more common non-hereditary inflammatory diseases.

S15-6

Autoinflammatory diseases and vasculitis

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and Child Health, Kurume University School of Medicine

Conflict of interest: None

Autoinflammatory disease is a disease concept proposed by Kastner et al. in 1999. It is caused by innate immunity-related genetic mutations without autoantibodies or autoreactive T cells. The main symptoms are periodic fever, rash, and arthritis. In recent years, with the advancement of genetic analysis technology, new responsible genes have been identified, and among them, an autoinflammatory disease with vasculitis as the main pathology and an autoinflammatory disease that can be complicated by vasculitis have been reported. The former includes ADA2 deficiency and STING-associated vasculopathy with onset in infancy (SAVI), and the latter includes a variety of autoinflammatory diseases. ADA2 deficiency is an autosomal recessive form of inherited disease caused by loss-of-function mutations in the *ADA2* gene; in 2014, the responsible gene was identified by whole exome sequencing in patients with polyarteritis nodosa and early-onset stroke. Anti-TNF agents have been reported to be effective in the treatment of vasculitis, and hematopoietic cell transplantation has been reported to be effective in the treatment of bone marrow failure. In Japan, there are at least 8 confirmed cases. SAVI is an autoinflammatory disease of neonatal and infantile onset with dermatitis and interstitial pneumonia, caused by a gain-of-function mutation in the *TMEM173* gene that results in overproduction of type I interferon. JAK inhibitors are partially effective as treatment. In this talk, we will review autoinflammatory diseases and vasculitis, and also report the clinical characteristics and omics analysis of ADA2 deficiency in Japan.

S16-1

The role of lung ultrasound in connective tissue diseases

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Conflict of interest: None

Interstitial lung disease (ILD) is frequently complicated in patients with connected tissue diseases (CTD) and associated with poor prognosis. Therefore, evaluation of ILD should be appropriately performed to identify patients with progressive ILD who need therapeutic intervention. Currently, chest high-resolution computed tomography (HRCT) is the gold standard for the diagnosis of ILD. However, repeated examination with chest HRCT should be avoided due to its high radiation exposure and high cost. Whereas, conventional methods such as auscultation, plain chest radiographs, and pulmonary function tests cannot evaluate ILD in detail. Recently, non-invasive lung ultrasound (LUS) has been emerged as a new imaging modality with easy access to evaluate CTD-associated ILD (CTD-ILD). The LUS findings associated with ILD include B-lines and pleural line alterations. Reportedly, B-lines and pleural line alterations have high sensitivity / specificity for identifying systemic sclerosis-associated ILD (SSc-ILD) with 59-100% / 59-99% and 74-85% / 99-100%, respectively. The total number of B-lines obtained from LUS (B-lines score) correlates positively with the severity of ILD by HRCT findings and serum KL-6 levels, and negatively with forced vital capacity and lung diffusion capacity in patients with SSc and idiopathic inflammatory myopathy. Furthermore, the B-lines score at baseline was associated with the progression of SSc-ILD at 12 months. Hence, LUS is useful in assessing the severity and predicting progression of ILD, and can be a non-invasive tool as a semi-quantitative indicator of morphological assessment of ILD. Some issues remain to be established for applying LUS in clinical practice in patients with CTD, including standardization of the technique, definition and quantification of the LUS findings, and the optimal timing for ILD follow-up with LUS. In this session, we will discuss the significance of LUS in patients with CTD introducing our experience of LUS in CTD-ILD.

S16-2

Vascular ultrasonography in patients with collagen diseases

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Conflict of interest: None

Musculoskeletal ultrasonography (US) in rheumatological practice is performed for all joints, especially for the fingers and wrist. Vascular US also scans blood vessels throughout the body, but in general, it is performed in blood vessels outside organs; hence, blood vessels in the brain, lung, and abdominal organs are excluded. Although there are various vascular lesions caused by collagen diseases, the pathological US findings of relatively large/medium blood vessels and not small blood vessels of organs are described in “The standard US evaluation method for vascular pathology” published by the Japan Society of Ultrasonics in Medicine. The probes used for vascular US are based on a high-frequency linear type, varying from convex to hockey stick type, and various frequencies from 3.5 to 24 MHz are used, depending on the size of the target blood vessels. In joint US, evaluation by B mode and power /color Doppler is common; however, in vascular US, fast Fourier transform analysis by pulse Doppler is also used. Takayasu arteritis: US can evaluate stenosis of the common carotid artery, subclavian artery, descending abdominal aorta, and renal artery. In particular, the US finding of end-stage inflammation is characterized by diffuse wall thickening of the common carotid artery, called the “macaroni sign”. Giant cell arteritis (temporal arteritis): Characterized by a “hypoechoic halo” around the superficial temporal artery and in the systemic large blood vessels as observed in Takayasu arteritis. Circumferential thickening of the carotid artery can also occur. Antiphospholipid antibody syndrome and vascular involvement in Behcet’s disease: Deep vein thrombosis (DVT) is a common pathology and also a common complication in patients without collagen diseases. US screening of DVT is performed with a vein compression method using a probe. The US screening and pathological findings of DVT are further discussed.

S16-3

Sonographic Diagnosis of Gastrointestinal Complications of Connective Tissue Diseases

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Conflict of interest: None

It is widely known that there are many gastrointestinal complications of connective tissue diseases (CTD). Most of the gastrointestinal lesions, however, are diagnosed with endoscopy and/or barium contrast study, both of which are invasive and require special preparation to cleanse the bowel tract. Although recently, transabdominal ultrasound (US) has become recognized as one of the options to evaluate the gastrointestinal tract, there have been only a few reports on the sonographic diagnosis of gastrointestinal complications of CTD. In this session, the clinical significance of ultrasound for the management of gastrointestinal complications is discussed. For the thorough screening of the gastrointestinal tract, systematic scanning is recommended. To scan systematically, we need to identify the fixed segments such as duodenum and ascending colon, which almost always are in the same positions in the abdomen. First, US can be the first modality to detect a gastrointestinal lesion that leads to the diagnosis of the causative disease. For example, detecting small bowel edema with US may lead to the diagnosis of systematic lupus erythematosus of the patient. Second, US is useful for the screening of gastrointestinal lesions in patients with known CTD, such as the screening of gastrointestinal amyloidosis in patients with rheumatoid arthritis. Third, US can be an alternative modality to endoscopy in the assessment of the therapeutic effect of already-known lesions. In conclusion, US is useful for the diagnosis and the management of gastrointestinal complications in patients with CTD in many aspects. However, we have to be aware of the fact that US is not suitable for the diagnosis of minute lesions or the lesions without wall thickening, which indicates the limitation of US.

S16-4

Current status of salivary gland ultrasonography in the diagnosis of Sjögren’s syndrome

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Conflict of interest: None

In 2012, the American College of Rheumatology (ACR) classification criteria for Sjögren's syndrome (SS) was published. Since then, imaging modality has been removed from the diagnostic and classification criteria for SS. However, the importance of imaging modality in SS diagnosis is gradually being reconsidered, and salivary gland ultrasonography (SGUS) in particular has garnered significant interest. Our department recognized the importance of SGUS early since the time when sialography was the mainstream method for the imaging diagnosis of SS, and this SGUS has been used for the diagnosis of SS. In SS, the destruction of salivary gland tissue progresses due to inflammation caused by the autoimmune reaction. However, the changes occurring in the gland parenchyma can be observed noninvasively with SGUS at low cost and easily. Sialography has several disadvantages such as the need for contrast agents, the complexity of the cannulation technique, and radiation exposure, but there are hardly any disadvantages associated with SGUS. A major difference between the two modalities is that sialography mainly shows changes in the duct system, while SGUS visualizes changes in the gland parenchyma. Over the past few years, invasive sialography have gradually gone out of use and instead non-invasive imaging modalities such as SGUS and magnetic resonance imaging have been adopted worldwide. However, since the testing technique of SGUS depends on the operator, and the SGUS diagnostic criteria for SS have not been unified yet, problems such as poor objectivity have been observed. Therefore, resolution of these problems will be a major influencing factor of whether SGUS can be incorporated into the diagnostic and classification criteria for SS in the future. To address these problems, we have actively studied the effectiveness of SGUS in SS diagnosis and disseminated the results to the world. I would like to introduce some of the previous studies on SGUS in this symposium.

S16-5

Skin ultrasound imaging of connective tissue diseases

Tsuneo Watanabe
Gifu University of Medical Science

Conflict of interest: None

Ultrasound (US) imaging is used for the assessment of connective tissue diseases, such as echocardiography for pulmonary arterial hypertension, sonography of salivary gland for Sjögren's syndrome, gastrointestinal US for Behçet's disease, and sonography of the temporal artery for giant cell arteritis. Then, how often US imaging is actually used in the dermatological field? It is well known that connective tissue diseases are a heterogeneous group of acquired immunologically mediated inflammatory disorders characterized by abnormal function or structure of one or more of the elements of the connective tissue, including skin symptoms. Over the last few years, there have been many improvements in high-resolution diagnostic US. Linear transducer with 33 MHz high frequency was developed and now is used in the daily medical practice. In addition, Superb microvascular imaging (SMI) is a novel US technique that can quickly and noninvasively monitor the microvascular distribution, which is a useful tool for the diagnosis of superficial lesions. Extensive subcutaneous calcium deposition is often found in patients with dermatomyositis, and US examination can clearly show the nature and extent of the deposition. Discoid lupus erythematosus lesions in SLE are histologically characterized by a hyperkeratosis with some atrophy of the epidermis and degeneration of the basal layer. US examinations can assess these lesions with less discomfort. Furthermore, neurologic manifestations are commonly observed in the patients with connective tissue diseases. Since the sural nerve targeted for the nerve biopsy exists under the skin, the nerve can be clearly observed using skin US. In this session, we focus mainly on the US findings of the skin lesions in the patients with connective tissue diseases and discuss the usefulness of this examination.

S17-1

Refinement of statistical method in observational study

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Conflict of interest: None

New therapeutic agents for connective tissue diseases have appeared in clinical practice through randomized controlled trials (RCTs). The results of RCTs have been obtained in limited situations in a limited population, and it is not known whether similar results can be obtained in real clinical practice. Against that background, observational studies are becoming increasingly important to validate the results of RCTs and to address many clinical questions that cannot be resolved by RCTs. The greatest advantage of RCTs is that theoretically, even unmeasured confounding can be adjusted for, and in this respect they are superior to the comparative quality of observational studies. To improve the quality of the comparative quality, various methods have been developed in observational studies. Observational studies, especially in a retrospective data set, often have missing values. These missing values can be divided into three categories: missing completely at random, missing at random, and missing not at random. If missing is completely at random, it is sufficient to exclude the sample (listwise deletion), but reduced sample can affect the statistical power. If missing is not completely at random, the multiple imputation method is often used. When comparing the exposure and the comparison in observational studies, confounding is the biggest factor that can skew the results. In addition to traditional multivariate analysis, propensity score analysis methods are used to adjust the difference of patient background. There are several comparison methods for propensity score analysis, including matching, stratification, and inverse probability weighting, Advantages and disadvantages of each method should be understood and used. Sensitivity analysis is used as a method to ensure the robustness of results in observational studies. We evaluate how the results vary by changing definitions, models, and analysis methods.

S17-2

Applied machine learning in rheumatic diseases

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Conflict of interest: None

With huge amount of data generated during clinical practice and medical research and advances in information technology, machine learning as a field of artificial intelligence is increasingly applied in medicine to assist patients and physicians. Rheumatic diseases are known for their complexity and heterogeneity in many aspects from pathogenesis to clinical manifestation and outcomes. Various factors contribute to the development of the diseases, multi-system involvement is common, and responses to treatment vary. machine learning, capable of analyzing massive data with high dimensionality or multiple variables, manifests itself as a promising tool to deal with the complex data and help improve early diagnosis, precision treatment, and prognosis prediction. Although there is a significant overlap in methods between statistics and machine learning, the application goals and scalability of solutions are generally different. Conventional statistics has a strong focus on accurate summaries of data samples, understanding statistical relationships between variables and correctly estimating population parameters. By contrast, the main goal of most machine learning methods is predictive performance on unseen data. In this session, the basics of machine learning and its subfields of supervised learning, unsupervised learning, and reinforcement learning will be offered. In addition, an overview of current machine learning applications in rheumatology will be provided.

S17-3

The use and limitations of medical information databases

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Conflict of interest: None

In healthcare settings, an increasing volume of administrative and clinical registry data is now routinely collected as part of daily work. The

RECORD statement published in 2015 defined routinely collected health data, referred to as real world data (RWD), as data collected from database-accumulated administrative claims, electronic medical records, epidemiological surveillance such as cancer registries and public health reporting data, and other broad resources unrelated to research utilization purposes. Commercial RWD databases are already widely used in clinical research. Well-known public medical information databases have been developed, such as the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) and MID-NET under the jurisdiction of the PMDA. Laws have been developed to promote the secondary use of medical information, such as the revised GPSP ordinance and the Next Generation Medical Infrastructure Act. Large prospective research-oriented registries such as IORRA, ANSWER, and LUNA provide detailed information on disease activity, duration, damage, quality of life, disease course, and comorbidity, but they are generally not without their challenges, including the effort of on-site data entry and the cost of quality control. RWD is attractive for its exactness, completeness, and cost-effectiveness. It is characterized by having no need for data entry or cohort management and for providing the ability to conduct analyses with large sample sizes due to independent collection for research purposes. However, if a researcher is responsible for processing raw data by himself, data processing, including structural transformation and data concatenation, requires time, effort, and expertise. In addition, we must consider other limitations in obtaining data from each database, such as complicated procedures for data extraction, inability to obtain the required items, and low reliability of case extraction. As access to various medical information databases is becoming easier, we must be aware of the limitations of each database and obtain real world data that are compatible with our research objectives from the user's perspective. Understanding the limitations of studies using RWD and prospective cohort studies, we need to further promote clinical research for the effective utilization of valuable medical information in the field of rheumatology, which includes many rare diseases.

S17-4

PMDA's medical review of drug applications in rheumatology

Mari Kihara
Office of New Drug 4, Pharmaceuticals and Medical Devices Agency (PMDA)

Conflict of interest: None

Pharmaceuticals and Medical Devices Agency (PMDA) is a governmental regulatory body which contributes to public health through 3 key roles. These are; 1) relief services for patients suffering adverse drug reactions, 2) review services, and 3) post-marketing safety measures. I work in the Office of New Drug 4 within PMDA, which plays a full part in encouraging the drug development process through clinical trial consultations and marketing application reviews, in order to promptly provide the public with more effective and safer pharmaceuticals, in the fields of rheumatology and infectious diseases. I will present how we work to review applications, to both assess clinical trials design, and evaluate benefits and risks from clinical trials data.

S18-1

Immunophenotyping in autoimmune diseases

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Conflict of interest: Yes

The pathogenesis of autoimmune diseases is characterized by abnormal immune responses consisting of activation of dendritic cells, T cells and B cells. As glucocorticoids and immunosuppressive drugs are non-specific therapeutic agents that cause many adverse reactions, the development of molecular target therapy with balanced effectiveness and safety is anticipated in the treatment of autoimmune diseases. Although multiple molecular-targeted therapies are available for the treatment of autoimmune diseases, the response to each treatment strategy often differs markedly among patients, and it is unclear how they are differentially selected for each patient. The establishment of precision medicine is especially important in heterogenous autoimmune diseases. Although some predictors of the treatment response are reported, precision medicine has not been sufficiently well evaluated in real clinical practice, especially for autoimmune diseases. We have used an immunophenotyping approach to categorize patients with immune-mediated diseases into distinct subgroups by comprehensive multicolor flow cytometric analysis. We have reported that active systemic lupus erythematosus patients can be divided into three subgroups based on T cell heterogeneity, which are associated with treatment resistance. In addition, psoriatic arthritis patients were classified into 4 phenotypes: Th1-dominant, Th17-dominant, Th1/Th17 hybrid, and normal phenotypes. We administered anti-IL-17 antibodies to patients with the Th17-dominant phenotype, anti-p40 antibodies to patients with the Th1-dominant phenotype, and TNF-targeted drugs to patients with the normal or Th1/Th17 hybrid phenotype. This approach was associated with significantly higher therapeutic response rates. Taken together, immunophenotyping of peripheral blood may help us not only understand the pathogenesis of autoimmune diseases but select the most appropriate molecular-targeted drugs for the individual patient.

S18-2

The role of autoantibody in the pathogenesis of dermatomyositis

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Conflict of interest: Yes

It was generally considered that autoantibodies were rarely involved in dermatomyositis. The reason is that many patients with dermatomyositis were negative for antinuclear antibody, and the only disease-specific antibody that can be measured by conventional tests is anti-Jo-1 antibody. In addition, the clinical phenotype is heterogeneous, and there are cases with malignant tumors and interstitial lung disease, and cases with rapidly progressive interstitial lung disease with a poor prognosis. Recently, however, more than 75% of autoantibodies such as anti-Mi-2 antibody, anti-ARS antibody, anti-MDA5 antibody, and anti-TIF1γ antibody were detected in patients with dermatomyositis. Furthermore, the autoantibodies are closely correlated with clinical symptoms. Anti-Mi-2 antibody is associated with typical dermatomyositis. Anti-ARS antibody is associated with chronic interstitial lung disease. Anti-MDA5 antibody is associated with rapidly progressive interstitial pneumonia and has a poor prognosis. Anti-TIF1γ antibody is associated with malignant tumors in adult patients. In addition, titer of anti-MDA5 antibody and anti-TIF1γ antibody reflects disease activity. Taken together, these autoantibodies may directly associate with the pathogenesis of dermatomyositis.

S18-3

Multi-omics research for precision medicine for rheumatic disease

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Conflict of interest: Yes

Rheumatic disease is systemic diseases that cause a variety of symptoms, and molecular-targeted therapies aimed at correcting abnormalities at the cellular and molecular levels involved in immunity and inflammation are gradually being applied to clinical practice. However, its efficacy and safety vary from patient to patient, and a method of medical management optimized for each individual has not been sufficiently established. In recent years, advances in omics technology for comprehensively acquiring information at the molecular and cellular levels in the body have made it possible to perform multi-omics analysis that integrates multiple of these. Multi-omics analysis research for the disease has also rapidly become widespread. In our group, omics analysis using untreated and post-treated clinical specimens of healthy subjects and patients with disease has been used to elucidate abnormalities at molecules and cells common to diseases, biomarker search, treatment responsiveness, and It has been useful for patient stratification based on prognosis. For rheumatoid arthritis, we compared the multi-omics data (transcriptome, proteome, and immune phenotype) of the patient's peripheral blood with healthy subjects, and developed an objective diagnostic model based on molecular information that distinguishes between the two. Furthermore, in multi-omics analysis of patients with Sjogren's syndrome, identification of gene

groups characteristic of the disease, association between cytotoxic CD8 + T cells, activated T cells, regulatory B cell and immune indicators, severity of salivary gland tissue damage, and drug discovery target molecules were clarified. A new multi-omics molecular profiling method that evaluates the state of the body that cannot be grasped by conventional indicators is expected as a prototype of a method for elucidating human molecular pathology and as a powerful approach for precision medical treatment based on the molecular pathology of diseases.

S18-4

Disease-specific iPS cells for clinical immunology research

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Conflict of interest: None

The pathogenesis of autoimmune diseases is generally influenced by genetic backgrounds. We are promoting the application of iPS cells (iPSCs) to research of autoimmune diseases. Especially, patient-derived iPSCs are thought to share genetic background with the autoimmune disease patients, and can be an ideal research tool for analyzing the biological mechanism affected by genetic risks on human cells. In addition, genome editing can insert or delete the causative variants in iPSCs, which make us possible to analyze the biological effects of variants on cell function in vitro. Now, we plan to perform not only the functional analysis, but also drug discovery screening in this system. Our team established the iPSC lines from familial SLE patients (SLE-iPSCs). Notably, dendritic cells (iPS-DCs) differentiated from SLE-iPSCs had enhanced dsRNA-stimulated type I IFN production, compared to healthy donor-derived iPSC lines. We tried a screening of rare variants related to the IFN pathway from whole exome analysis, and identified new rare variants involved in the enhancement of IFN production in SLE patients. Genome editing in SLE-iPSCs showed that converting this rare variant to wild type suppressed IFN production, which suggested this rare variant could contribute to the pathogenesis of familial SLE patients. We believe that the combination of genetic research and disease-specific iPSCs is one promising way to solve the questions of clinical immunology. Through this session, I hope to discuss with participants on clinical immunology and drug discovery research strategies using disease-specific iPSCs.

S19-1

T cell tolerance induction by thymic fibroblasts

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Conflict of interest: None

In thymus, autoreactive T cells are thought to be negatively selected by reference to the self-antigens expressed in medullary thymic epithelial cells, resulting in the central immune tolerance. The thymic medulla also contains non-epithelial stromal cells such as fibroblasts, but the contribution of these cells in T cell tolerance has been poorly examined. In this study, we identified a $PDGFR^{+}$ $gp38^{+}$ $DPP4^{-}$ thymic medullary fibroblast subset that is required for T cell tolerance induction. Transcriptome analysis revealed that medullary fibroblasts had a gene expression signature distinct from other thymic stromal cells. Notably, lymphotoxin-β receptor (LTβR) expressed in fibroblasts is required for the expression of medullary fibroblast-specific genes. The deletion of the LTβR in thymic fibroblasts caused an autoimmune phenotype with decreased expression of tissue-restricted and fibroblast-specific antigens and escape of certain T cell clones from negative selection. Thus, thymic medullary fibroblasts play an essential role in the establishment of central tolerance by the production of a diverse array of self-antigens.

S19-2

Tet2 and Tet3 in B cells are required to prevent autoimmunity

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Conflict of interest: None

Despite the importance of B cells in the pathogenesis of autoimmunity, the immune mechanisms that underlie initial breaks in B cell tolerance have been poorly defined. Here, we report that deficiency of ten-eleven translocation (Tet) DNA demethylase family members Tet2 and Tet3 in B cells led to hyper activation of B and T cells, autoantibody production and lupus-like disease in mice. Mechanistically, in the absence of Tet2 and Tet3, downregulation of CD86, which normally occurs following chronic exposure of self-reactive B cells to self-antigen, did not take place. The importance of dysregulated CD86 expression in Tet2- and Tet3-deficient B cells was further demonstrated by the reduced T cell activation and autoantibody production following anti-CD86 blockade. Tet2- and Tet3-deficient B cells had decreased accumulation of histone deacetylase 1 (HDAC1) and HDAC2 at the Cd86 locus. Thus, our findings suggest that Tet2- and Tet3-mediated chromatin modification participates in repression of CD86 on chronically stimulated self-reactive B cells, which contributes, at least in part, to preventing autoimmunity.

S19-3

Discovery of Treg inducing compound

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Conflict of interest: None

Regulatory T cells (Tregs) are essential to maintain immunological tolerance. And the conversion of disease mediating T cells into Tregs by Treg inducing drugs would be promising way to control hazardous immune responses such as autoimmunity, allergy and transplant rejection. But currently there are still various issues to be solved in realizing the therapeutic approach. Especially, we needed to overcome the difficulty in inducing Tregs from activated T cells in inflammatory conditions. We conducted screening of our chemical library and found a hit compound, AS2863619, which can convert activated T cells into Tregs even in the presence of inflammatory cytokines. We showed that AS2863619 induced Tregs by inhibiting CDK8/19. Furthermore, the treatment with AS2863619 can induce Tregs and suppressed inflammatory responses in mice inflammatory disease model. Our findings will accelerate the development of the therapeutic approach dependent on Treg induction from disease mediating T cells.

S19-4

Identification of novel autoantigens in Takayasu arteritis using SARF

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Conflict of interest: Yes

Anti-endothelial cell antibodies (AECA) are autoantibodies, which bind to the cell surface of endothelial cells. It is well known that AECA activities were detected in the sera of patients of collagen diseases such as systemic lupus erythematosus (SLE) and vasculitic syndrome and its pathogenic significance has been focused. Previously, we developed the method to identify endothelial cell surface autoantigens against AECA, named SARF (Serological identification system for Autoantigens using a Retroviral vector and Flow cytometry), as a novel expression cloning system. Using SARF, we identified several autoantigens in the patients of SLE, rheumatoid arthritis, necrotizing encephalopathy. Takayasu arteritis, a type of large vessel vasculitis, affects the aorta and its major branches. Cellular immunity, such as T cell, NK cell and macrophage, is involved in the pathogenesis of Takayasu arteritis, leading to the formation of arteritic aneurysm and stenotic lesions. 54.5% of Takayasu artetitis patient sera had AECA activity. Using SARF, we identified endothelial protein C receptor (EPCR) and scavenger receptor class B type 1 (SR-BI) as novel autoantigens against AECA in Takayasu arteritis. Anti-ERCP antibody and anti-SR-BI antibody were detected in 34.6% and 36.5% of Takayasu arteritis

patients. In addition, 68.6% of the patients of ulcerative colitis (UC) had anti-ERCP antibody. The binding of activated protein C (APC) to EPCR and the binding of high density lipoprotein (HDL) to SR-BI, as their ligands respectively, inhibit the activation of endothelial cells. EPCR is also expressed on T cell and the biding of APC to EPCR inhibit the differentiation toward Th17 cell. We demonstrated that anti EPCR antibody and anti SR-BI antibody in Takayasu arteritis patients blocked the inhibitory effect of these receptors on endothelial cell activation. And anti EPCR antibody in Takayasu arteritis also blocked the inhibitory effect of APC on the T cell differentiation toward Th17. Our results indicated that these autoantibodies may be the pathogenic antibodies in large vessel vasculitis and inflammatory bowel disease and enable further sub-classification of the diseases. The pathogenic mechanism which we propose in this study could be the novel pathogenic significance of autoantibody, "blocking of immune inhibitory system".

S19-5

Potential role of Tfh17 cells in regulation of autoantibody production and hyposialylation via OX40 in arthritis

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Conflict of interest: Yes

In patients with rheumatoid arthritis (RA), anti-citrullinated protein antibody (ACPA) have a pivotal role on diagnosis and prognosis. Recently, several reports indicate that ACPA have been changed the status not only in "quantity" but also in "quality" within RA. Follicular helper T (Tfh) cells are important to drive autoantibody production, and reported to be increased in RA. But it remains uncertain how Tfh cells, including IL-17 producing Tfh (Tfh17) cells, are associated to arthritis and whether its function includes promotion of antibody production and hyposialylation. In GIA model, an increase in Tfh, particularly Tfh17 cells that overexpressed OX40 was noted at the onset of arthritis. Then, we also checked the fluctuated numbers of plasmablasts, it was also increased at day 7 with downregulation of st6gal1, an enzyme responsible for sialylation. Blockade of OX40 *in vitro* and i*n vivo* prevented the development of arthritis with reduction in Tfh17 cells and plasmablasts, and recovery of st6gal1 expression with autoantibody sialylation. Affinity purified anti GPI antibodies from K/BxN mice and GIA at the onset phase demonstrated as hyposialylated by mass spectrometric analysis than those at the resolution phase. Inflammatory properties, especially TNFα production by GPI-immunocomplex via dendritic cells related to their difference in sialylation. Analysis of RA patients showed abundance of OX40-overexpressing Tfh17 cells and that their proportion correlated negatively with the expression of St6gal1. Thus, Tfh cells, especially Tfh17 cells, play a crucial role in the development of arthritis via regulation of autoantibody production, hyposialylation through OX40.

S20-1

Clinical epidemiology of hospitalized patients with COVID-19 in Japan

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Conflict of interest: None

We studied the epidemiological characteristics of 2638 patients participating in the COVID-19 Registry Japan, a registry of novel coronavirus infections in Japan. The median age of hospitalized patients was 56 years (interquartile range [IQR]: 40-71 years). More than half of the cases were male (58.9%, 1542/2619). Nearly 60% of cases were in close contact with confirmed or suspected COVID-19 cases. The median duration of symptoms to hospital admission was 7 days (IQR: 4-10 days). The most common comorbidities were hypertension (15%, 396/2638) and uncomplicated diabetes mellitus (14.2%, 374/2638). Non-severe cases (68.2%, n=1798) were twice as common as severe cases (31.8%, n=840) on admission. Respiratory support on admission consisted of those who did not receive oxygen support (61.6%, 1623/2636), followed by those who received supplemental oxygen (29.9%, 788/2636) and those who received IMV/ECMO (mechanical ventilation or extracorporeal membrane oxygenation) (8.5%, 225/2636). Overall, 66.9% (1762/2634) of patients were discharged home, but 7.5% (197/2634) died. When compared to existing studies of hospitalized patients in other countries, the results showed a trend toward fewer comorbidities and lower mortality. A first/second wave comparison was also performed. The total number of subjects was 5194 (3833 in the first wave and 1361 in the second wave). The proportion of critically ill patients at admission was lower in the second wave than in the first wave (12.0% vs. 33.1%), and the time from onset to hospitalization was shorter in the second wave than in the first wave (median, 4 days vs. 7 days). Second-wave patients tended to be younger (median age, 37 vs. 56 years), had fewer transfers from other hospitals (3.8% vs. 15.0%), and had fewer comorbidities such as cardiovascular disease (1.9% vs. 5.9%) and cerebrovascular disease (1.8% vs. 6.1%). Mortality (1.2% vs. 7.3%) was also lower in the second wave. The data from the second wave indicate that demographically younger patients, fewer comorbidities, lower proportion of critically ill patients on admission, and lower mortality rates. However, even when stratified by age and severity of illness at admission, mortality was lower in the second wave. This may be attributed to the shorter time from onset to hospitalization, differences in patient background and comorbidities, and advances in treatment.

S20-2

Immune response to COVID-19

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Conflict of interest: Yes

An epidemic of acute respiratory syndrome caused by a novel coronavirus (SARS-CoV-2) became widespread, and was named coronavirus disease 2019 (COVID-19). Spike protein of SARS-CoV-2, RNA virus, binds to cell surface angiotenisn-converting enzyme 2 (ACE2) and neuropilin-1 (NRP1), and the virus invades into the cells. In the infected cells, the viral proteins are synthesized and then the proliferated virus is released. Immune response to the virus includes innate immunity and acquired immunity. As innate immunity, NK cells responds to the viral infected cells. As acquired immunity, antibodies against the viral proteins are produced. The antibody-bound virus is phagocytized. Killer T cells also responds to the infected cells. Cytokines, such as TNF, IL-1, IL-6 and IL-8, are produces by the SARS-CoV-2 infection. Excessive cytokines develop cytokine storm, which may develop acute respiratory distress syndrome (ARDS). SARS-CoV-2 also infects to endothelial cells. Damage of vascular endothelium may develop thrombosis. For treatment of COVID-19, in addition to the antiviral agent, cytokine inhibitor and anti-thrombosis agent are developing. Approved vaccine is to develop antibody against spike protein.

S20-3

JCR COVID-19 registry

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Conflict of interest: None

At the end of 2019, a group of pneumonia patients confirmed in Wuhan, China was found to have been caused by the new Corona virus (COVID-19 infection), which soon led to a world-wide pandemic due to its high potential of infection during the latent phase. In Japan, the extraction and isolation of the "close contacted persons" has been the priority of the public health policy on this infection, and with the declaration of emergencies in April or with the health insurance coverages of the dexamethasone or remdesivir, the epidemic once remedied in phases, but re-outbreaked in November. The mechanism of infection in this new-emerging virus remains unknown and obviously, it is of particular concern of people with rheumatic diseases who are receiving immunosuppressant reagents. Those drugs may induce higher incident rates or poor outcome, but at the same time, some of them, such as steroids, anti-IL-6 inhibitors or anti-malarial drugs have been studied for prevention/treatment of the disease including its severe complication such as cytokine-storm. To address the huge knowledge gap, Japan College of Rheumatology has developed physician-reporting case registry using the Electric Data Capture

(EDC) system. It was aimed to gather demographic and clinical characters of the rheumatic patients in Japan affected with COVID-19 that include the symptoms, treatments, laboratory data or prognosis. As of November 2020, 76 facilities across the country are registered. In this session, the details of the registry data are introduced as well as the comparative review with the similar foreign-registry data.

S20-4

Treatment for COVID-19 on rheumatic disease patients

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Conflict of interest: None

Since the end of 2019, the SARS-CoV-2 virus infection (COVID-19), which originated in China, has spread worldwide rapidly. Medical treatment can be considered at various stages from the establishment of infection to the aggravation of the infection. Some treatments are expected to have antiviral effects, and others are expected to control the inflammation of cytokine release syndrome (CRS), which is thought to be involved in the pathology of the severe state of COVID-19. Hydroxychloroquine, an antimalarial drug indicated for SLE, has been administered in the early stages of this pandemic because it is expected to have an antiviral effect. Negative reports have been made on both the prevention and the mortality, and it is not recommended as a therapeutic drug at this time. Currently, in Japan, remdesivir, an RNA-dependent RNA polymerase inhibitor, and dexamethasone, a corticosteroid, are approved for SARS-CoV-2 infections. At present, a large number of clinical trials are underway all over the world, which means that there is no established treatment. Clinical trials are needed in various settings, such as prevention of COVID-19, prevention of aggravation of mild cases, and therapeutic effect on severe cases such as ARDS. Also, vaccinations of SARS-CoV-2 are being vigorously carried out, and it is expected that measures against COVID-19 will be further advanced from the viewpoint of prevention. But there are some uncertainties as to whether the vaccine could be terminated this pandemic in a short period of time because there are concerns such as the persistence of the effect and virus mutation. It is thought that clinical trial results will be accumulated gradually, and we with the treatment for COVID-19 will be established. In this talk, I would like to consider the current treatment of COVID-19, focusing on patients with rheumatic disease under this pandemic.

S20-5

What is "New Normal" in rheumatic diseases

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Conflict of interest: Yes

I am writing this abstract in the midst of the "third wave" of coronavirus infection. While the number of infected people and the number of seriously ill patients are reaching the highest level every day, the pros and cons of continuing the Go To campaign are being discussed every day. Around this time of the previous year, the completion ceremony of the new national stadium was held, and it seems to be a phantom that it was about to get excited for the Olympics. It is unpredictable what the world will be like when this conference is held. In recent years, large-scale disasters have continued, so preparations for disasters, preparation of materials for patient support in the event of a disaster, and establishment of an information provision system have been promoted. However, the situation such as the epidemic of coronavirus infection was unexpected. From the beginning, the news that "people with underlying diseases and those who are undergoing immunosuppressive treatment should be careful" has been repeated loudly, while fragmentary information that "therapeutic drug for rheumatic disease is effective for coronavirus infection" was also spread. Therefore, it is speculated that patients with rheumatoid arthritis may feel more anxious than necessary or may have been swayed by uncertain information. The medical staff has many experiences for the first time, and they continue to practice while searching in the dark every day. I can't find a clear answer to the title "What is New Normal in rheumatic diseases?", but I would like to think about problems and future issues, focusing on what I felt through my experience and adding a review of the literature.

S20-6

Current status and problems of vaccine development for SARS-CoV2

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Conflict of interest: None

The pneumonia caused by SARS-CoV2 was identified in early 2020 at a seafood market in Wuhan City. It was named COVID-19. This infectious disease has spread throughout the world and has been recognized as a pandemic. At present, the pandemic continues into early 2021. This pandemic has been a considerable burden for both medical care and socioeconomic activity. For these reasons, vaccine development is an urgent necessity. The mRNA vaccine and adenovector vaccine have been developed in the UK, US, and Russia. Furthermore, the development of other vaccines, such as DNA vaccines, continue. Both pro and con opinions about safety and efficacy have been expressed. This lecture will explain the current understanding of SARS-CoV2 vaccine's mechanism of action and development.

S21-1

An overview of pathogenesis and treatment of spondyloarthritis

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Conflict of interest: None

Spondyloarthritis (SpA) is a group of diseases characterized by axial arthritis, such as spondylitis and sacroiliac arthritis, as well as peripheral arthritis, enthesitis, and dactylitis, which are strongly associated with the HLA-B27 gene. However, positive for HLA-B27 in Japanese is lower than in Westerners, and the prevalence of SpA is also very low compared to Westerners. Therefore, clinical experience in patients with SpA has been limited in Japan. In addition, some cases do not receive proper diagnosis and treatment due to lack of clinical experience. Ankylosing spondylitis and psoriatic arthritis are representative disease of SpA, but cases that are difficult to classify into these diseases share common features such as inflammatory back pain, enthesitis, HLA-B27 positivity, uveitis, and inflammatory bowel disease. The Assessment of spondyloarthritis international society (ASAS) published the criteria for the classification of axial and peripheral SpA. The pathogenesis of SpA strongly involves a cytokine network centered on the Interleukin (IL)-23/Th17 pathway. IL-23 produced from dendritic cells and macrophages activates Th17 cells and increases the production of IL-17 and IL-22. In addition to genetic factors such as HLA-B27, environmental factors such as mechanical stress at the enthesis are thought to be interrelated, causing innate lymphoid cells to overproduce tumor necrosis factor (TNF)-alpha and IL-17 at the enthesis resulting in chronic inflammation. Since these cytokine networks are common to the pathology of psoriasis, SpA is frequently associated with psoriasis. Anti-cytokine therapy with biologics targeting TNF-alpha, IL-17, and IL-23 has been clinically applied and shown to be highly effective for the treatment of SpA. With increasing rates of SpA diagnosis and advances in biologics and other therapeutics, there is also increasing information about the disease. This talk will review the pathogenesis, diagnosis and treatment of SpA.

S21-2

Treatment of PsA (TNF inhibitor)

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Conflict of interest: Yes

Psoriatic arthritis (PsA), one of the spondyloarthritis, mainly presents

with cutaneous and joint symptoms, and in addition, various extra-articular symptoms are also present. Among them, joint symptoms cause irreversible joint destruction due to peripheral arthritis, etc., which directly causes ADL disorders and employment disorders, and significantly lowers the QOL of patients. As mentioned above, PsA is a disease that causes irreversible joint destruction, but it has been conventionally recognized that the rate of progression of joint destruction is relatively slower than that of RA. However, in recent years, it has been shown that PsA also causes joint destruction from the early stage of illness, and in cases with high disease activity and rapid progression of joint destruction, strict monitoring (tight control) of disease activity is performed. Choosing the right treatment is important for maintaining a patient's quality of life over the long term. Under these circumstances, in recent years, the types of drugs that can be used for PsA are increasing, such as MTX, TNFi, IL-17i, IL-12 / 23, IL-23i, and apremilast. With the diversification of formulations with different mechanisms of action, patients' desire for effects on skin conditions, in addition to suppressing joint destruction and relieving pain, is becoming higher than ever. While there are various options for the mechanism of action, today, based on our experience, we will consider the role of TNF inhibitors in the treatment of PsA and their position based on our own cases.

S21-3

Treatment of PsA (IL-17 inhibitors)

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Conflict of interest: Yes

Psoriatic arthritis (PsA) is a multiple musculoskeletal disorder that is usually preceded by psoriasis and accounts for about 15% of psoriasis. The clinical manifestations of PsA are diverse and include peripheral arthritis, axial arthritis, enthesitis and dactylitis. Enthesits, the central lesion of inflammation, could trigger secondary synovitis or tenosynovitis and develop bone destruction and new bone formation. The major pathophysiology of PsA is considered to be the activation of IL-23-IL-17 pathway. IL-17, that derives not only from Th17 cells but also from CD8+T cells, γδT cells, innate lymphoid cells, NK cells, etc, induces recruitment of neutrophils and activation of osteoclasts, and subsequently, bone destruction by coupled with TNF. Moreover, IL-17 promote mesenchymal proliferation at entheseal site and develop new bone formation by mineralization of fibrocartilage through hedgehog signaling, osteoblast differentiation through bone morphogenic proteins (BMPs) or Wnt proteins. These data suggest that the inhibition of IL-17 is the most effective treatment. Actually, most clinical randomized controlled trials showed higher efficacy of IL-17 inhibitors (secukinumab and ixekizumab as a monoclonal antibody to IL-17A, and brodalumab as a monoclonal antibody to IL-17 receptor A). In several recommendations for the management of PsA, IL-17 inhibitors are indicated for peripheral arthritis and/or dactylitis with inadequate response to NSAIDs and csDMARDs, axial arthritis and/or enthesitis with inadequate response to NSAIDs. However, unmet needs remain including the effect for axial lesion or inhibition of bone formation. In this symposium, I will review both the efficacy and the safety of IL-17 inhibitors in clinical trials for PsA and present the positioning of IL-17 inhibitors in PsA treatment.

S21-4

Evidence of TNF inhibitor for axial spondyloarthritis

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Conflict of interest: None

In this session, we review about the evidence of TNF inhibitors (TNFi) for axial spondyloarthritis (axSpA) including ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA). In Japan, Infliximab and adalimumab was approved as therapeutic agent for AS in 2010, and then TNFi provided new treatment options for AS patients in addition to conventional NSAIDs and DMARDs. Many clinical trials and cohort studies have demonstrated that TNFi relieved pain and stiffness of axial and peripheral joints with reduction of BASDAI and ASDAS scores and could improve inflammatory findings on MRI in AS patients. It has also reported that the efficacy of TNF is affected by age, disease duration and CRP level. Furthermore, the long-use outcome of TNFi over 4 years showed that long-term TNFi could significantly prevent new syndesmophytes' formation and progression. Due to accumulation of TNFi evidence in AS, TNFi is positioned as significant therapeutic option in clinical guideline. In Japan, the guideline of TNFi use for AS published by JCR recommended TNFi use when conventional therapy such as NSAIDs and physical therapy failed (BASDAI>4). Additionally, ACR/SAA/SPARTAN recommendation for the management of AS recommend TNFi as second line therapy when conventional therapy failed, and TNFi is strongly recommended to use initially in biologics Currently, TNFi is not approved as therapeutic agents of nr-axSpA in Japan but is commonly used in western countries. According to ASAS/EULAR recommendation, TNFi is recommended when conventional therapy (BASDAI>4, ASDAS>2.1 and additional parameters of activity (increased CRP levels and/or MRI showing inflammation of SI joints)) failed in nr-axSpA patients, similar to AS patients. Finally, we review about the efficacy and effect of TNFi for extraarticular manifestations and comorbidity of axSpA, and discuss about the positioning and possibility of TNFi on future therapeutic strategy of axSpA.

S21-5

Treatment of axial spondyloarthiritis: IL-17 inhibitor

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Conflict of interest: Yes

Spondyloarthritis (SpA) is classified into two groups, axial spondyloarthritis and peripheral spondyloarthritis according to the site of inflammation, and axial SpA includes ankylosing spondylitis (AS) and non-radiographic axial SpA (nr-axSpA) that does not meet sacroiliac joint X-ray findings defined by modified New York criteria. Nr-axSpA is a group of diseases newly proposed by the ASAS classification criteria of axSpA announced in 2009, and was initially positioned as a pre-stage of AS. Recently, it has also become clear that not all patients with nr-axSpA progress to AS. However, the characteristics of nr-axSpA was similar to that of AS, and there were some patients who were difficult to control with the administration of non-steroidal anti-rheumatic drugs (NSAIDs). TNF inhibitors have already approved for AS in 2010, and its efficacy and safety has been demonstrated, and IL-17 inhibitors were approved as a therapeutic agent for AS in 2018. In addition, IL-17 inhibitors were newly approved for nr-asSpA in 2020. Data from clinical trials show that it improves not only clinical symptoms but also inflammation on laboratory test and MRI findings, and is comparable in safety to TNF inhibitors. On the other hand, it is necessary to continue collecting information on the deterioration of inflammatory bowel disease. IL-17 inhibitors Unlike TNF inhibitors have not been shown to be effective against the extra articular symptom of SpA, uveitis. Therefore, TNF inhibitors should be selected over IL-17 inhibitors for patients with recurrent uveitis problems. The ASAS/EULAR and SPARTAN recommendations state that TNF inhibitors that have been approved first and have a lot of evidence such as efficacy and safety should be selected first, by accumulating information on the efficacy and safety of IL-17 inhibitors, we believe that IL017 inhibitors can become a new "First line Bio" in the future.

S22-1

How single cell studies and AMP are changing understanding of adaptive immunity in RA

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Conflict of interest: None

We will describe previous concepts for T cells in RA and how data from high dimensional CyTOF and single cell RNA sequencing is leading

to new concepts for adaptive immunity in RA. This will include discovery of a new CD4 T cell population, T peripheral helper cells (Tph cells) that are expanded in RA synovium and drive B cell responses, and how they are distinct T follicular helper (Tfh) cells. New insights into CD8 T cell populations and innate T cells and how they account for most of the IFN gamma will be shown. Other unexpected populations of T and B cells found in RA will be summarized.

S22-2

Pathways of B cell Activation in Human SLE

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Conflict of interest: None

Chronic autoimmune diseases, and in particular Systemic Lupus Erythematosus (SLE), are endowed with a long-standing autoreactive B-cell compartment that is presumed to reactivate periodically leading to the generation of new bursts of pathogenic antibody-secreting cells (ASC). Moreover, pathogenic autoantibodies are typically characterized by a high load of somatic hypermutation and in some cases are highly stable even in the context of prolonged B-cell depletion. Long-lived, highly mutated antibodies are typically generated through T-cell-dependent germinal center (GC) reactions. Accordingly, an important role for GC reactions in the generation of pathogenic autoreactivity has been postulated in SLE. Nevertheless, pathogenic autoantibodies and autoimmune disease can be generated through B-cell extrafollicular (EF) reactions in multiple mouse models and human SLE flares are characterized by the expansion of naive-derived activated effector B cells of extrafollicular phenotype. We will discuss the properties of the EF B-cell pathway, its relationship to other effector B-cell populations, its role in autoimmune diseases and other human immune responses, and its contribution to human SLE. In addition, we will discuss the molecular networks driving the pathogenic expansion of these B cells and the epigenetic regulation responsible for the engagement of these programs. Finally, we will present recent data regarding events that take place during early B cell development in the SLE bone marrow.

S22-3

The MHC and SLE: have we finally solved it?

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Conflict of interest: None

The Major Histocompatibility Complex (MHC) constitutes the strongest genetic association signals in SLE and Sjögren's syndrome. Consistently associated alleles at the MHC are: HLA-DRB1*03:01 and HLA-DRB1*15:01 (in Europeans) and HLA-DRB1*15:02 (in East Asians). The DRB1*03:01 allele resides on an extended MHC haplotype which extends through the entire classical MHC region from HLA class I, through class III to HLA class II. The extensive linkage disequilibrium and structural variation in the MHC have made identifying the causal genes very challenging. Using NG sequencing data, we undertook a detailed haplotype analysis accommodating class III structural variation involving the candidate genes coding complement C4A and C4B. To further improve the resolution of the association, we have employed a transancestral mapping approach in SLE: examining cohorts of European ancestry and African American ancestry in SLE. The linkage disequilibrium is much less extensive in the African genome at the MHC compared with other common ancestries and this greatly facilitated resolution of the genetic associations. Comparing European and African data, we have shown that the association signals in SLE are best explained by signals arising from: 1) copy number variation of the complement component 4 (*C4*) genes in the MHC locus and 2) by a shared region in the class II region on the HLA-DRB1*15:01 (in Europeans) and HLA-DRB1*15:03 (in Africans) that operate to elevate HLA class II gene expression. The *C4* locus generates a 7-fold variation in risk for lupus (95% CI: 5.88-8.61; $p<10^{-117}$ in total) and 16-fold variation in risk for Sjögren's syndrome (95% CI: 8.59-30.89; $p<10^{-23}$ in total), with *C4A* protecting more strongly than *C4B* in both illnesses. The *C4* alleles acted more strongly in men than in women. These results support the non-antigen specific genetic risk in these diseases, with risk from the innate immune system and non-selective conveyed by HLA class II.

S22-4

Functional genome analysis of autoimmune diseases

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Conflict of interest: Yes

As genome research matures, functional genome analysis which evaluate relationships between genetic polymorphism and transcriptome has become a prominent approach for the understanding of autoimmune diseases. Numerous attempts to stratify diseases using functional genome analysis are being carried out all over the world. In this context, we constructed a gene expression and eQTL database, ImmuNexUT, which consist of nearly 10000 RNA-seq samples derived from 28 immune cell subsets of >400 donors with 10 immune-mediated diseases (IMDs) and healthy controls. Our data integratively revealed characteristic gene expression signatures across immune cells and IMDs. Examination of context-dependent eQTL revealed transcriptionally regulated hidden modules associated with IFN signal, aging, and cell proliferation. Of the 29 suggested associated loci in recently reported Japanese SLE GWAS, 20 showed colocalization with at least one immune cell eQTL with stringent criteria. Notably, some showed subset-specific or directionally opposite eQTL effects among immune cells, and some regulated genes which have not been reported to be associated with SLE. We also performed epigenomic analysis of synovial fibroblasts from rheumatoid arthritis (RA) patients and unveiled the dynamic change of super-enhancers under cytokine stimulation. Super enhancers under multiple cytokine-stimulation condition showed significant overlap with RA associated GWAS risk loci and explained the functions of these loci. Our results show critical role of functional genome analysis in the identification of disease-related pathways and genes in IMD.

Educational Lecture

EL1

What is new in rheumatoid foot

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Conflict of interest: None

The treatment of rheumatoid arthritis (RA) has improved dramatically over the last few decades. The development of new medicines, including molecular-targeted drugs, and improvement in treatment strategies using recommendations, guidelines, and T2T has contributed to this paradigm shift. Rheumatoid foot has also received attention recently. This is because the needs of RA patients have gradually transferred to improvements in function and appearance of small joints as more than half the patients can gain clinical remission owing to the development of treatment for RA. Physicians tend to skip examining the rheumatoid foot because it is time-consuming in daily practice, and feet are not included in the 28-joint assessment for evaluating disease activity. However, it has been reported that some patients who were judged to be in clinical remission on evaluation of Disease Activity Score 28 still had synovitis in their feet. At our institute, we researched whether we could assess synovitis with socks and stockings on, to find a way to reduce the examination time of the feet. I will be showing our results in this presentation. In terms of surgeries for rheumatoid foot, Japan is the most advanced country worldwide. Surgeries for rheumatoid forefoot deformities have improved dramatically from joint-sacrificing surgeries to joint-preserving surgeries, and many researchers have reported good surgical outcomes. Although arthrodesis used to be the only surgical option for rheumatoid ankles, excellent outcomes with total ankle arthroplasty have been described recently. In this presentation, I will describe the etiology and diagnosis of and conservative and surgical treatments for rheumatoid foot. I hope that this presentation will be useful for all physicians.

EL2

Roles of Hand Surgeons in the Treatment of RA Patients -Development of Novel Surgical Treatments for RA Wrist-

Norimasa Iwasaki
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Conflict of interest: None

The development of biologics has dramatically changed the surgical indication and strategy against rheumatoid arthritis (RA). One of the changes is to expand the indication for surgical treatment of small joints, such as wrist or finger joint. This leads to an increase in the number of operations for these joints. Human hands play a functionally important role in activities of daily living, occupation, and sports. In addition, emotional expressions include hand movement. Therefore, well controlled RA patients by biologics demand nearly normal hand function. On the other hand, most of hand surgeries that are widely performed for RA patients do not meet the above demands. Hand surgeons, consequently, must develop novel surgical procedures to overcome the limitations of current procedures. The author will present the current status of hand surgeries for RA hand and the development of a novel surgical procedure for RA wrist joint.

EL3

Relationship Between Rheumatic Diseases and Herpes Zoster

Daisuke Watanabe
Department of Dermatology, Aichi Medical University Nagakute, Aichi, Japan

Conflict of interest: Yes

Herpes zoster is caused by reactivation of varicella-zoster virus (VZV), which belongs to the family Herpesviridae. VZV causes varicella in primary infection. After that, the virus then becomes latently infected in carnival nerve and dorsal root gangliaa. Subsequently, when the virus reactivates, it migrates to the periphery of the sensory nerve and forms a unilateral banded painful vesicular skin lesion consistent with one dominant nerve region. Aging (over 50 years of age), various immunodeficiency diseases and immunosuppressive conditions, and physical and mental stress are risk factors for the development of herpes zoster, and a decrease in VZV-specific cellular immunity has been shown to be the pathogenic mechanism. There is also an increased risk of severe disease and complications in immunocompromised patients with herpes zoster. Complications of herpes zoster include those of the central nervous system, vascular system, peripheral nervous system, ophthalmologic, and otolaryngologic, with particular attention to head and neck shingles. In this talk, we will discuss the clinical manifestations and complications of herpes zoster in immunocompromised cases, with a focus on rheumatic diseases such as rheumatoid arthritis and systemic autoimmune diseases.

EL4

Introduction to designing clinical research and how to write an original article

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Department of Clinical Epidemiology and Health Economics, Graduate School of Medicine, The University of Tokyo

Conflict of interest: None

In this lecture, I will explain methods for designing clinical research and how to prepare a manuscript of an original article. Themes of clinical research lurk in the field of daily clinical practice. The first step in clinical research is to structure a clinical question (CQ) developed from experience and insight into a testable research question (RQ) and select an appropriate research design. The PE (I) CO framework is used to structure the RQ. That is, we should identify Patients in the study, define Exposure or Intervention, set Control, and define Outcomes. We should then consider FINER for structured RQ. That is, it should be considered whether the study is feasible, interesting, novel, ethical, or relevant. Also, I will explain the basic knowledge of epidemiology that is essential for clinical research, including differences between interventional studies (randomized comparative studies, etc.) and observational studies; types of observational studies (cross-sectional studies, cohort studies, case-controlled studies, etc.); classification of errors (random error and systematic error), types of systematic error (selection bias, information bias, and confounding), and statistical methods for controlling confoundings. Furthermore, I will explain procedures for writing a paper following the design of clinical research. Before data collection, it is recommended to complete the literature review, finalize the research plan, and write Introduction and Methods at that point. As a result, it is possible to write Results and Discussion immediately after data analysis.

EL5

Epidemiology and treatment of elderly-onset rheumatoid arthritis

Takahiko Sugihara
Tokyo Medical and Dental University, Tokyo, Japan

Conflict of interest: Yes

The age of onset of rheumatoid arthritis (RA) shifted to elderly side in line with the increasing life expectancy. Recently, management of elderly-onset RA is common in clinical practice for rheumatologists. Acute-onset and high elevation of CRP were characteristic of elderly-onset RA, and baseline disease activity of elderly-onset RA was higher than younger-onset RA, and prognosis of joint destruction was similar or worse in elderly compared to younger patients. The aims of treatment for RA are abrogation of disease activity, no progression of joint damage, normal physical function and improvement of long-term outcomes as presented in principles of treat-to target strategy. Our previous prospective study showed that achieving low disease activity (LDA) and structural and functional remission were realistic goals for patients with elderly-onset RA. In this study, the treatment was scheduled in advance to achieve LDA, and 32% of the patients were receiving biological DMARDs at week 52. A high dose of MTX was intolerable, and GCs use was associated with serious infection. Clinically relevant radiographic progression (CRRP) was observed at 40% of the patients, and anti-CCP antibody positive, high disease activity, presence of bone erosion were all associated with CRRP. Interestingly, no response by EULAR response criteria and non-achievement of LDA at week 24 were both strongly associated with CRRP. Rapid improvement of dis-

ease activity and achievement of LDA followed by improvement of physical function are clearly major targets of the treatment strategy of elderly-onset RA. Essential roles of biological DMARDs are emphasized in the study. In this seminar, I will present new data about three-year outcomes of T2T strategy for elderly-onset RA. I will also introduce recommendation for treatment of elderly-onset RA in the recent JCR guideline.

EL6

Ethical Principle for Medical Research

Ryuji Koike
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Conflict of interest: None

Clinical research, studies involving humans is essential for evolution and development of medicine. Reliable evidence of novel medical technology especially depends on clinical trials participated by actual patients. However, there is a dilemma between the basic principle of medicine and unestablished efficacy and safety in clinical trial because physicians principally have to provide with best-proven medical care to any patients. In the era without even patient-physician relationship, it was possible that physicians could plan unethical clinical trials ignoring this dilemma. With this history in mind, medical ethics and transparency of research have been pursued and universal ethical principle for clinical research has been established. But ethical principle for medicine may be viable because human society is continuously changing. We have had to discuss medical ethics aware of this variability. As the most basic principle of ethics in clinical research, the Declaration of Helsinki (DoH) would be reviewed and checked with its historical background in this lecture. And we would discuss novel viewpoints and interpretation of medical ethics considering recent society and medicine.

EL7

Imaging findings of chest X-ray and CT associated with collagen-vascular disease

Hiroaki Sugiura
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Conflict of interest: None

The basic reading of chest X-rays and chest CT findings associated with various collagen-vascular diseases are shown in this lecture. In reading the chest X-ray, the overall view should be checked first. Check for lung volume reduction and differences between the left and right sides of the lungs. Next, check the thorax, soft tissues, airway system, mediastinum, and mediastinum-lung borders. Finally, check the lung fields. It is important to compare the difference between the left and right lung fields and to confirm that each pulmonary vessel is properly delineated from the hilar to the periphery. In the lung field, the areas overlapping the pulmonary apex, hilar, mediastinum, and diaphragm are particularly often overlooked, so it is important to read them with awareness. Various pulmonary lesions can be seen in collagen-vascular diseases. Diffuse lung diseases associated with Representative collagen-vascular diseases including rheumatoid arthritis, scleroderma, polymyositis and dermatomyositis are shown. Pneumocystis pneumonia, cryptococcosis, and drug-induced pneumonia will also be addressed as complications of treatment.

EL8

Basic Principles for Understanding Renal Histology

Keiju Hiromura
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Conflict of interest: Yes

In rheumatic diseases, the kidney often becomes the primary target organ. Especially in systemic lupus erythematosus and ANCA-related vasculitis, the degree of renal lesions affects the treatment strategy and prognosis. Therefore, renal biopsy is important to evaluate renal lesions. There is a risk for bleeding in renal biopsy. It should be performed after considering its indications carefully and explaining the necessity and risk to the patient. “Renal Biopsy Guidebook 2020” has been produced by the Japanese Society of Nephrology, and it shows the indications and risks of renal biopsy. The renal biopsy specimen was examined by light microscopy (LM), immunofluorescence microscopy (IF), and electron microscopy (EM). Rheumatologists are expected to read the pathology report, not only to obtain the pathological diagnosis but also to obtain the correct information of the pathological findings. In LM, glomerulus, tubule and, tubulointerstitium, and blood vessels are respectively evaluated. Pathological terms should be understood correctly, such as diffuse/focal, global/segmental, mesangial proliferation, endocapillary hyperplasia, tuft necrosis, extracapillary proliferation, karyorrhexis, sclerosis, collapse, adhesin, double contour, tubular atrophy, interstitial fibrosis, tubulitis, arteriolar hyalinosis, and fibrinoid necrosis. IF is used to know the depositions of immunoglobulins and complements. EM is used to know the fine structures of glomeruli and the distribution of electron-dense deposits. In the lecture, evaluating renal lesions will be explained using renal biopsy specimens of lupus nephritis and ANCA-related nephritis.

EL9-1

Thrombotic APS and obstetric APS; Are the antiphospholipid autoantibodies different?

Kenji Oku
Hokkaido University Hospital

Conflict of interest: None

Antiphospholipid antibody syndrome (APS) is an autoimmune disorder with arterial/venous thrombosis and/or pregnancy morbidity. As the phenotypic difference of these two major manifestations is apparent and the coexistence relatively low, they are often referred as thrombotic APS and obstetric APS. Clarifications of the pathological mechanisms of these APS manifestations has always been in line with the clarification of the pathogenesis of the antiphospholipid antibodies (APL). APL are autoantibodies that target anionic-phospholipid-bound plasma proteins such as beta 2GPI or prothrombin bound to cardiolipin or phosphatidylserine. The protein-phospholipid complex forms an immune complex with APL on the surface of hemocytes or endothelial cells and by activating these cells, induce tissue factor (blood-borne tissue factor). This procoagulant feature of the antibody, explain well the thrombotic APS but not the obstetric APS. Recently, the complement activation was raised as a main candidate for the pathogenesis of recurrent miscarriages in APS. The APS patient has a high rate of complement activation and the autoantibody against C1q (aC1q) is considered as an initiator of the activation. Interestingly, C1q is another phospholipid bound plasma protein that mimics APL targeting protein; the autoantibody targets the collagen-like lesion which will be uncovered by the conformational change following the phospholipid binding. In fact, aC1q was highly found in the sera of recurrent miscarriage women including APS, and the aC1q-administered murine model shows high frequency of miscarriage. Various autoantibodies against anionic phospholipid bound proteins are found in the sera of APS. The classical APL is linked more to the thrombotic APS and aC1q may possibly related more to the manifestation of the pregnancy morbidities such as miscarriages.

EL9-2

The new insights of pathogenesis and implications of treatment emerged from recent studies with obstetric antiphospholipid syndrome

Kayoko Kaneko
National Center for Child Health and Development

Conflict of interest: None

The cases of non-thrombotic organ complications such as cardio valvular lesions, chorea, and epilepsy complicated with patients with the anti-phospholipid syndrome had been reported since some time ago. Recently, some studies have shown new insights that these organ damages are caused by the direct action of antiphospholipid antibodies on β2GP1 expressed cells within the placental trophoblast cell layer. The production of inflammatory cytokines and activation of complement is seemed to be the main factors of anti-phospholipid related obstetric adverse outcomes. Also, even if APS is diagnosed due to obstetric complications, all of the

patients would cause thrombotic events. there are a few cases that could survive without developing cerebral infarction or pulmonary embolism for a while. Based on these observations, the patients with APS could be divided into two types: Obstetric APS and Thrombotic APS. The obstetric APS indicated the patient complicated with only obstetric complications while Thrombotic APS means those diagnosed with thrombotic events. Spanish researchers have conducted the European Registry on Obstetric Antiphospholipid Syndrome (EUROAPS) since 2010 and they have reported the preliminary report about the prognosis of obstetric APS from 1000 cases of registered data. In this talk, I will explain and discuss the pathogenesis, diagnosis, and treatment of obstetric APS.

EL10

pyrin-associated autoinflammatory disorder

Kiyoshi Migita
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Conflict of interest: Yes

MEFV gene, which encodes the protein named pyrin, was identified as a responsible gene for a genetic autoinflammatory disease, Familial Mediterenean fever (FMF). FMF had been considered to be an autosomal recessive disease caused by mutations of *MEFV* gene. The recessive nature of FMF had led to the postulation that the underlying molecular mechanism was a loss-of-function of the mutated pyrin. However, Japanese patients with heterozygous *MEFV* mutations or polymorphisms presented with the clinical expression of FMF. Recent studies uncovered novel functions of pyrin and new pathogenic mechanisms of FMF. The existence of pyrin inflammasome has been proposed, in which bacterial toxins trigger an inactivation of Rho GTPases resulting in formation of pyrin inflammasome. These findings also support a gain of function model, where the mutated pyrin induces an inflammasome activation and IL-1b induction and pyrin is an important element of the innate immunity and contribute to the inflammatory processes of autoinflammatory disorders. These pathogenic effects of pyrin may contribute to the various phenotypic autoinflammatory disorders, pyrin-associated autoinflammatory disorder (PAAD). More recently, an autosomal dominant syndrome caused by distinct *MEFV* mutations, termed as pyrin-associated autoinflammation with neutrophilic dermatitis (PAAND) has been identified. This new concept of PAAD may develop to link different subtypes of disorders of the same genetic origin.

EL11

Current status and perspective on musculoskeletal ultrasound in rheumatic diseases

Kei Ikeda
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Conflict of interest: Yes

Musculoskeletal ultrasound has provided a paradigm shift in the diagnosis and evaluation of rheumatic diseases with its sensitive detection of soft-tissue inflammation and morphological change in bone. Since ultrasound helps students, health professionals, and patients to intuitively understand rheumatic pathologies, it also plays substantial roles in education and physician-patient communication; therefore, the use of ultrasound has been widely spread. On the other hand, as its use increased worldwide, the issues with ultrasound have been raised in its reproducibility, specificity, and impact on clinical outcome. These issues give us opportunities to review the fundamentals of musculoskeletal ultrasound and reconsider the pathophysiologies of rheumatic conditions. In this lecture, the current status and perspective on musculoskeletal ultrasound in rheumatic diseases will be discussed based on recent evidence.

EL12

The basics to evaluate cutaneous manifestations in connective tissue disease

Akiko Tanikawa
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Conflict of interest: None

Disease of connective tissue include a large number of different disorders that can affected many different organs and presented various skin manifestations. The cutaneous lesions of connective tissue disease can divide into two groups, specific and non-specific lesions. The former related with definitive diagnosis, and non-specific lesions are useful for evaluating the disease in initial stage. In systemic lupus erythematosus (SLE), 25% of the patients the disease onset with skin symptoms; about 80% patients presented various cutaneous lesions during the entire course of the disease. SLICC presented various specific lesions of lupus. Non-specific lesion in SLE including pernio-like eruptions, Raynaud's phenomenon, livedo, etc. In dermatomyositis (DM), Heliotrope rash and Gottron's sign are well known as specific lesions of DM. Reverse Gottron-sign is a skin manifestation directly related with the prognosis of the patients who are positive with anti-MDA5 autoantibodies, less or lack of muscle symptoms and in high risk to develop rapidly progressive interstitial pneumonia. Annular erythema with Sjögren syndrome (SS) is a characteristic cutaneous manifestation of SS and the lesions are well tolerated with hydroxychloroquine. But hypergammaglobulinemic purpura and insect bite-like erythema are still intractable. In SSc, edema of the hand and Raynaud's phenomenon are initially sign of the disease. Life guidance is essential for keeping the patient's quality of life (QOL). Although RA, adult onset still disease, antiphospholipid syndrome, Bechet's disease, IgG4 related disease, vasculitis is also having many different types of skin manifestations. All those of cutaneous lesions are visible thus not only have high value for early diagnosis, also useful for evaluating the therapeutic effect and predict prognosis of the disease. Face and hands are the most notable area and the properties of rash such as erythema, purpura, nodule and ulceration are also helpful. In this session, I will present some cases with the clinical pictures, discuss and summarized the basics to evaluate cutaneous manifestations in connective tissue disease.

EL13

Rheumatoid arthritis and psychiatric disorders

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Conflict of interest: None

Depression is the psychiatric condition that is most commonly associated with rheumatoid arthritis (RA). A meta-analysis revealed the prevalence of major depressive disorder according to the Diagnostic and Statistical Manual criteria to be 16.8% and that of depressive symptoms that do not meet the full diagnostic criteria to be 14% to 48% (Matcham et al., 2013). Depression is associated with poor outcomes in patients with RA, including pain, inflammation, and disability. Decreased adherence to medical treatment caused by depression reduces the treatment response rate in patients with RA. Depression in patients with RA is associated with increased mortality due to both suicide and non-suicidal causes. Recently, the biological mechanisms underlying the association between RA and depression have drawn attention, including the relationships among cytokines, central sensitization, and psychological stress. Meanwhile, the associations between RA and other psychiatric conditions have recently been in the spotlight. A population-based cohort study of more than 10,000 cases of RA in Canada between 1989 and 2012 demonstrated that the incidence of depression was higher in the RA cohort [incidence rate ratio (IRR) 1.5], as were the incidences of anxiety disorder (IRR 1.2) and bipolar disorder (IRR 1.2). The incidence of schizophrenia did not differ between the RA group and matched-individual group (Marrie et al., 2018). A meta-analysis showed that the incidence of bipolar disorder in patients with RA was 2 times higher than that in individuals without RA (Charoenngam et al., 2019). Conversely, the incidence of schizophrenia in patients with RA was lower than that in individuals without RA (odds ratio 0.48) (Euesden et al., 2015). The incidence of Alzheimer's disease in patients with RA was also lower than that in individuals without RA (odds ratio 0.6), but the evidence to suggest causation is insufficient (Policicchio et al., 2017).

EL14

Infection Control Strategies against COVID-19 by Maximizing our Experience and Intelligence

Kazuhiro Tateda[1,2]
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Japan, [2]President of Japanese Association for Infectious Diseases

Conflict of interest: None

In Japan, we are facing to 3rd wave of pandemic of COVID-19. So far, approximately 130,000 people infected, and more than 2,000 death were reported (December 6). Mortality rate is getting decrease, but still it is around 2%, especially high in elderly people. Cluster buster teams worked hard and found three key situations as risk factors, Close, Clouded and Closely. Also, we knew that micro-droplet produced in vocalization may be a critical transmission mechanism in COVID-19 and wearing mask quite effectively blocked spreading and transmission of virus. We experienced setback of diagnostic strategy against COVID-19 in molecular testing, but now spread of several diagnostic methods, such as molecular testing and antigen detection methods, improved situation. We do not have specific treatment strategy, but combination management of anti-virus, anti-cytokine and anti-coagulation therapy improved mortality rates of elderly individuals from 25% to 8% during the second waves of pandemic. It is very important to share information, new evidence and idea how to fight against COVID-19 in the middle of pandemic. Especially for infection control measures against COVID-19, universal precaution and universal masking strategies may be a key for effective and sustainable strategies of this pandemic infectious diseases, which was characterized in transmission by asymptomatic but virus carrying state of individuals.

EL15

SLE classification criteria and its guideline by JCR/MHLW

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a prototype of systemic autoimmune disease. Multiple organs and tissues are affected in patients with SLE in a different way, and such heterogeneity of clinical aspect is making difficult to diagnose the affected patients. Unlike plasma glucose levels for the diagnosis of diabetes, there has no gold standard for SLE diagnosis. On the other hand, one needs any criteria of SLE for clinical trials as well as daily clinical practice. The “classification criteria” of SLE was coined for this purpose. Considering the clinical heterogeneity, it is extremely difficult to standardise the management of lupus patients in clinical practice. In the history, corticosteroids (CS) dramatically improved the mortality of lupus patients; on the other hand, major or minor adverse events of CS would significantly affect to their morbidity. Recently, the potent immunosuppressants are efficiently used for the remission induction in patients with SLE. Amongst the lupus organ involvements, lupus nephritis (LN) is one of the most common and important manifestation, and the better use of immunosuppressnats are described in two major guidelines for lupus nephritis. Hydroxychroloquine was described as the basic drug for all LN patients, Mycophenolate mofetil (MMF) has been recommended for the initial and maintenance treatment. Cyclophosphamide (CY) and tacrolimus (TAC) are commonly used immunosuppressants. TAC has been approved for LN in a maintenance phase of the treatment in Japan. In clinical practice, however, TAC is often considered as a partner for MMF or CY in the induction phase for cases with insufficient response for MMF or CY. JCR and MHLW have collaborated to established SLE guideline according to the GRADE method. In this guideline, recommendation statement was classified into 3 categories; recommended, suggested and proposed. Referring another SLE guideline, we discuss the significance of the Japanese SLE guideline for our daily clinical practice.

EL16

Recent Topics and Medication for Osteoporosis

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Conflict of interest: None

Rheumatoid arthritis (RA) is a major autoimmune disease that causes progressive synovitis and joint damage. The advent of the anchor drug, methotrexate (MTX), and biologics has led to dramatic advances in drug therapy, and the number of RA remission cases based on the treat-to-target (T2T) concept is increasing. In recent years, the introduction of Janus kinase (JAK) inhibitors has led to further advances in RA treatment. However, excessive bone resorption in RA mainly by osteoclasts is a pathological condition known to cause secondary osteoporosis at a high rate. At present, approximately 12.8 million patients suffer from osteoporosis in Japan. The number of fragility fractures ensued from osteoporosis, especially those of the proximal femur, is increasing yearly and drastically reduces healthy life expectancy. Better prevention of osteoporosis and proximal femoral fractures is therefore urgently needed. The adequate intake of bone-related minerals and vitamins, including the three important nutrients for bones (calcium, vitamin D, and vitamin K), in addition to appropriate exercises and activities that stimulate bones are very important for preventing osteoporosis. I would like to discuss these bone-related minerals and vitamins as well as introduce our newly developed program, “Exercise to increase bone mineral density”. Recently, such new osteoporosis drugs as denosumab, romosozumab, teriparatide, ibandronate, and minodronate have been approved in Japan. These advances have expanded the drug choices for osteoporosis and increased our knowledge on the relationships with lifestyle-related diseases and secondary osteoporosis. Our group has already reported on numerous cases of drug treatment in post-menopausal osteoporosis, pediatric osteopenia with multiple fractures, post-pregnancy osteoporosis, osteoporosis associated with dialysis and diabetes, and osteoporosis in super-elderly patients. In this lecture, I would like to cover the following points: 1. Recent topics in osteoporosis 2. Importance of nutrition and exercise for the skeleton and skeletal muscles 3. Various efforts to extend healthy life expectancy in Nagano Prefecture (measures against osteoporosis and locomotive syndrome, etc.) 4. Topics on the bones and teeth 5. Pharmacological treatments of osteoporosis based on the latest data from Shinshu University and its related hospitals (including RA complication cases) It is my desire for us to carefully consider the importance and future directions of osteoporosis prevention together.

EL17

Evaluation of disease activity in systemic sclerosis

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Conflict of interest: None

Systemic sclerosis (SSc) is an intractable disease, and a lot of tools of its disease activity index have been established. Since the therapeutic agent specific for SSc has not been developed as far, the treatment for SSc is allowed to perform the conventional therapy against impairment of organs. That is the reason why we have to estimate the disease activities of a variety of organs. Especially, we usually use the disease activities for lung, heart, kidney, peripheral circulation, skin, muscle, and joint. Distinct from disease activity index against each organ, the evaluation method of global clinical trials for new therapies has been developed recently, which is CRISS (combined response index systemic sclerosis) estimation. In addition, we always used PRO (patient reported outcome) for disease activity of SSc as well as the other collagen diseases. In this lecture, I am going to explain those disease activity index and discuss its problem points.

EL18

Evaluation of imaging of joints in rheumatic diseases: pros and cons

Atsushi Kawakami
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Conflict of interest: None

Joint imaging findings of rheumatoid diseases are not very specific to each disease, but it is well known that those are indispensable techniques for diagnosis, prognosis prediction, and monitoring. This is mainly developed for rheumatoid arthritis (RA), its gold standard being X-ray, other modalities such as ultrasound (US), MRI, PET-CT and also being used, but due to insurance medical treatment, X-ray, ultrasound, MRI are commonly utilized. RA X-ray scoring is typified by mTSS for bone erosion

and joint space narrowing, but these are considered cumulative changes and the scores are (very) unlikely to improve. US and MRI detect arthritis more frequently than physical examination, with US for articular synovitis, periarticular inflammation (such as tenosynovitis and enthesitis), bone erosion, and MRI for articular synovitis, periarticular inflammation, bone erosion, bone marrow edema. EULAR RA imaging recommendations (2013) make up a significant portion of US and MRI, and articular synovitis, tenosynovitis on US/MRI and bone marrow edema on MRI have been described as useful for early diagnosis as well as prediction of subsequent progression of joint damage in RA patients. US synovitis is often semi-quantitatively evaluated by gray-scale (GS) and power-Doppler (PD), but a combined score of GS and PD has also been proposed. Synovitis and bone marrow edema are improved by DMARDs treatment, but bone erosion is still (very) rarely improved by US and MRI. Recently, imaging of spondyloarthritis (SpA) has also attracted attention. SpA is classified into an axial SpA and a peripheral SpA. Unlike RA, mainly contributed articular synovitis, enthesitis is initially occured and articular synovitis secondary developed in SpA. In addition, new disease concepts such as non-radiographic axial SpA and unclassified peripheral SpA are spreading. In this lecture, we will explain the advantages and pitfalls in joint imaging, including the understanding of pathophysiology.

EL19

What is a role of rheumatologists in improving prognosis of pulmonary hypertension associated with connective tissue disease?

Masataka Kuwana
Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

Prognosis in patients with connective tissue disease complicated with pulmonary hypertension (PH) used to be very poor, with a survival of <20% at 3 years after diagnosis. Recent introduction of molecular-targeting pulmonary vasodilators and their use in combination have improved functional capacity and hemodynamics as well as survivals in patients with pulmonary arterial hypertension (PAH), including connective tissue disease (CTD)-associated PAH. In Japan, medical administration for intractable diseases, which is borne by public funds for medical expenses, enables expensive medical treatment such as upfront combination of pulmonary vasodilators and rapid increase in the dose of epoprostenol. As a result, normalization of hemodynamics is achieved in some patients. A recent national registry involving specialized PH centers in Japan has revealed that the 3-year survival rate of incident cases exceeds 90%. On the other hand, new challenges for PH medical care have emerged and include: (i) careless introduction of aggressive therapy of pulmonary vasodilators and resultant adverse outcomes in patients with systemic sclerosis in case of concomitant pulmonary venoocclusive disease, left heart disease and interstitial lung disease; (ii) unnecessary and inappropriate use of pulmonary vasodilators in patients suspected to have PAH; and (iii) missing the timing of immunosuppressive treatment in patients with PAH associated with systemic lupus erythematosus, mixed connective tissue disease, or Sjogren's syndrome, especially in early disease phase. Increase in treatment options and accumulation of evidence have leaded to requirement of high expertise and specialty of PH. It is now time to discuss roles of rheumatologists in PH management in patients with CTD.

EL20

Dysbiosis in rheumatic diseases

Atsushi Kumanogoh, Yuichi Maeda
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Conflict of interest: None

Rheumatoid arthritis (RA) is a systemic autoimmune disease, caused by both genetic and environmental factors. Recently, researchers have focused on the gut microbiota, which is thought to be an environmental factor affecting the development of RA. In this symposium, we review the evidence from animal and human studies that supports the role of the gut microbiota in rheumatic diseases. We and others have demonstrated that the abundance of *Prevotella copri* is increased in some of early RA patients. We have also used gnotobiotic experiments to show that dysbiosis in RA patients contributed to the development of Th17 cell-dependent arthritis in intestinal microbiota-humanized SKG mice (Arthritis Rheumatol. 2016; 68:2646-2661). Metagenomic shotgun sequence revealed that other *Prevotella* species such as *Prevotella denticola* are also increased in early RA patients (Ann Rheum Dis. 2020; 79:103-111). In summary, *Prevotella* species are involved in the pathogenesis of arthritis.

EL21

IgG4-related disease -2019 ACR/EULAR classification criteria for IgG4-related disease and our experience in Japan using them -

Mitsuhiro Kawano
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Conflict of interest: None

IgG4-related disease (IgG4-RD) is a systemic inflammatory disorder that affects almost all organs in the body. Old men are most susceptible to it, and patients often have allergic diseases. The diagnosis is based on the typical organ involvement of for example lacrimal and salivary glands, pancreas, kidneys, or retroperitoneum, elevated serum IgG4 levels and marked IgG4-positive plasma cell infiltration in the affected organs. Since the proposal of comprehensive diagnostic criteria for IgG4-RD in 2011 from Japan was published, these criteria have been used to make the diagnosis of this disease worldwide. In 2019, ACR/EULAR classification criteria for IgG4-RD were devised. These criteria comprise three steps. First, only patients who meet the entry criteria, i.e. who have one of 11 typically affected organs are classified. In the next step, several mimickers such as ANCA-associated vasculitis and multicentric Castleman's disease need to be excluded according to the exclusion criteria. Then, the points of each of the 8 domains (1. serum IgG4 levels; 2. histological findings; 3. IgG4-immunostaining; 4. lacrimal, parotid, sublingual, or submandibular gland lesion; 5. thoracic lesion; 6. pancreas and bile duct lesion; 7. kidney lesion; 8. retroperitoneum lesion) are totalled and if their sum exceeds 20 points, the patients are classified as having IgG4-RD with a sensitivity of 82.0% and specificity of 97.8%. We conducted a validation study of these criteria in 162 patients and 130 mimickers in our hospital and obtained a sensitivity of 72.8% and specificity 100%. The reason why sensitivity was about 10% lower than in the original research was due to the high proportion of IgG4-RD patients who met the exclusion criteria. Although 18 patients fulfilled the exclusion criterion of positive disease-specific autoantibodies, only 2 of them had specific clinical symptoms related to such autoantibodies, and were diagnosed with a specific autoimmune disease complicated by IgG4-RD.

EL22

Molecular basis of autoinflammation in patients with inborn errors of immunity

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Conflict of interest: Yes

Primary Immunodeficiency Diseases (PID) are rare genetic diseases that are caused by a defect in a molecule involved in the immune system; and most of the diseases are monogenic. Classical symptoms of PID include susceptibility to a variety of microorganisms. Lately, immune disorders which are characterized by autoimmunity, predisposition to malignancy, or autoinflammation (autoinflammatory diseases: AID) have been identified; and thus the term, inborn errors of immunity (IEI), is used for the genetic immune disorders in International Union of Immunological Society (IUIS) working party. More than 400 responsible genes have been identified for IEI so far; and the number has been constantly increasing after introduction of massive parallel sequencing technology. Classical IEI was mainly caused by loss of function mutation; and newly identified IEI are mostly those caused by gain of function, dominant negative function, or haploinsufficiency type of mutation. Adult onset IEI is not uncommon. From our IEI registry adult IEI consists about 50% of all the IEI. IEI includes more than 50 different autoinflammatory diseases (AID) that are classified into type I interferonopathy, defects affecting the inflammasome, or non-inflammasome-related conditions. Phenotype of AID includes SLE,

Behcet disease, or polyarteritis nodosa. Diseases of immune regulations include those caused by CTLA4 haploinsufficiency and STAT3 GOF mutation, which exhibit autoimmunity, colitis, and other conditions. Genetic cause of IEI with colitis include IL-10 deficiency and XIAP deficiency. We often encounter immunodeficiency patients with vasculitis, arthritis, and other collagen disease manifestation. Molecular causes of the disorders are yet to be determined in many cases. These "outliers" would give us a clue to understand molecular basis of more common rheumatic diseases, inflammatory bowel disease, and other organ-specific autoimmunity. We also started to see IEI that shows vulnerability to specific pathogen. Although not yet listed in IUIS classification for IEI, a recent study identified gene defect in molecule (s) in type I interferon pathway in patients with severe COVID-19. In this lecture, I will share latest findings on IEI that exhibits rheumatic manifestations or autoimmunity and will discuss susceptibility or resistant genes for the rheumatic disorders from a point of view of molecular study on IEI.

EL23

Risk communication for patient safety

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Conflict of interest: None

The purpose of this lecture is to consider how to utilize the concept of risk communication, which is an activity for society, for patient safety. Risk communication is defined as "activities in which each layer of society shares diverse information and perspectives through dialogue, co-consideration, and collaboration for more appropriate management of risk." Each stakeholder has a role to play for "more appropriate management of risk", and it is desirable that dialogue, co-consideration, and collaboration be actively carried out among stakeholder. Each stakeholder will mutually understand and approach the differences in perceptions and views on risk information, and clarify the division of roles such as what authority each has and what responsibility they have to deal with risk. This is necessary for proper risk management. Risk communication has been required for safety measures regarding problems that involve certain risks such as disasters, environmental problems, and fostering public understanding of nuclear facilities, and that require sharing of awareness among related parties. This is a scene where it is necessary to share awareness and cooperative relationships. It can be said that this is an activity in the same direction as an activity that enables medical practice, which has long been tackled by patient safety, to carry out medical practices that inevitably have inherent risks, satisfying both safety and security. However, compared to the above areas, medical care is considered to be the area with the largest information asymmetry between the provider medical staff and the patient in the receiving position, and information sharing has been delayed. In recent years, with the spread of the Internet, the information gap has narrowed, and on the other hand, as the number of reports of medical accidents that cause medical distrust has increased, it is necessary to share information and awareness in medical care as well.

EL24

How to differentially use biological DMARDs and JAK inhibitors in patients with rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis is a systemic autoimmune inflammatory disease characterized by synovitis and joint destruction. Because joint damage progresses rapidly after onset, resulting in irreversible physical dysfunction and deformation of the affected joints, proper diagnosis and treatment are required in the early stages of the disease. In the standard initial treatment after the diagnosis of rheumatoid arthritis, methotrexate, a conventional synthetic DMARD, should be used if it is not contraindicated. However, when no improvement is observed within 3 months or when no remission is achieved within 6 months, despite an increase to the full dose of methotrexate, the addition of biological DMARDs, targeting TNF, IL-6 or T cells, or Janus kinase (JAK) inhibitors is recommended. Orally available small products targeting JAK family, essential for the signaling pathways of various cytokines, are available as targeted synthetic DMARDs. Furthermore, if the therapeutic goal is still not achieved, biological DMARDs or JAK inhibitors should be altered approximately 3-6 months later. Results from recent controlled trials indicate that patients with insufficient response to a biological DMARD may respond to a Janus kinase inhibitor and vice versa. Although JAK inhibitors are all orally administered drugs, they have multi-target effects based on the inhibition of intracellular signaling and exert clinical effects just as promptly and strongly as biological DMARDs. However, JAK inhibitors should not be used without careful consideration as they are orally administered drugs with multi-target effects. Screening before their use and monitoring during treatment should be strictly performed. It is necessary to establish evidence on its long-term safety regarding the development of infections such as herpes zoster and malignancy.

EL25

Ocular manifestations and treatment of Behçet's disease

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Conflict of interest: None

Behçet's disease (BD) is a systemic inflammatory disorder that manifests with oral ulcers, uveitis, skin inflammation, genital ulcers, and inflammation in other organs. Multiple genetic and environmental factors are believed to contribute to BD susceptibility. *HLA-B*51* is known as the strongest genetic factor related to the potential onset of BD. In 2010, we conducted the first genome-wide association study (GWAS) for BD in a Japanese population, identifying the genes *IL23R-IL12RB2* and *IL10* with genome-wide significance. In addition, our genetic studies have identified several genes related to innate immunity. Thus, our genetic findings have revealed that multiple immune pathways intricately contribute to the pathogenesis of BD. Uveitis of BD is called "ocular inflammation attack", and it is characterized by sudden occurrence. BD uveitis is mostly bilateral but the ocular attack is usually unilateral. It is usually a non-granulomatous inflammation, including anterior uveitis (iridocyclitis), sometimes accompanied by hypopyon in the anterior chamber. It may also include posterior uveitis (retinochoroiditis), which sometimes results in severe visual loss. Repeated attacks of eye inflammation may cause irreversible impairment of visual function. In recent years, TNF inhibitors have been used with the effect that the prognosis of visual acuity in patients has improved markedly. Nonetheless, there are cases in which visual function is impaired due to uncontrolled inflammation. It is difficult for the clinician to obtain enough data and knowledge for the treatment of this rare disease with lesions in multiple organs. Therefore, we recently published a comprehensive clinical practice guideline for BD with the aim of achieving standardization of BD treatment. We established recommendations for a total of 150 clinical questions (CQs), which are required in clinical practice. Algorithms for treating an incidence of BD are provided based on the results of these CQs.

EL26

Specific autoantibodies detected in patients with idiopathic inflammatory myopathies

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Conflict of interest: None

Idiopathic inflammatory myopathies (IIMs) are a disease group characterized by proximal muscle weakness and myalgia due to muscle inflammation. IIMs include polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM). If one has typical cutaneous lesion such as Gottron's sign or papules or Heliotrope rash, the patients is diagnosed as DM. However, it has been well known that some patients only show typical skin manifestations without or mild muscle inflammation with no obvious muscle symptoms and these patients are defined as amyopathic DM (ADM) or clinically ADM (CADM) as they have no muscle weakness or myalgia clinically. Previous studies revealed that autoantibodies directed

against nuclear or cellular components are found in patients with IIMs. Most of these autoantibodies are found exclusively in patients with this condition and are called myositis-specific antibodies (MSAs). Antibodies against aminoacyl tRNA synthetases (ARS) such as anti-Jo-1 antibody, signal recognition particle (SRP) or Mi-2 have been found in early times and are well-established PM/DM specific antibodies. In the 2000s, additional autoantibodies specific for IIMs have been discovered and reported by several investigators. Although clinical manifestations of IIMs are extremely diverse as well as response to treatment and prognosis of muscle disturbance itself and complicating other organ involvement, these novel MSAs have proven useful for precise diagnosis, treatment selection, prognosis prediction, and classification of IIM patients into clinical entity.

Meet the Expert

MTE1

Pulmonary arterial hypertension associated with connective tissue diseases

Yasushi Kawaguchi
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Conflict of interest: Yes

Pulmonary arterial hypertension (PAH) is complicated more frequently with systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and mixed connective tissue disease (MCTD) than in other connective tissue diseases. Since 20 years ago, vasodilators with high specificity for pulmonary arteries have been developed and the treatment of PAH have been remarkably improved. At the same time, basic research on idiopathic PAH has been activated, and the difference in pathological findings from connective tissue diseases (CTD)-associated PAH has been demonstrated from the pathological aspect as well as from the aspect of drug effect. Furthermore, it has become clear that even with CTD-associated PAH, PAH associated with SSc have different pathological conditions form PAH associated with other CTDs. It is important to carry out treatment according to the pathological condition. In PAH associated with SLE and MCTD, a combination of corticosteroids and immunosuppressive drugs is used according to the treatment of vasculitis. Treatment for this pulmonary artery is highly effective, and the prognosis for PAH associated with SLE and MCTD is currently improving. At the same time, not only the immunosuppressive drug but also one of the endothelin receptor antagonist (ERA) and the phosphodiesterase 5 inhibitor (PDE5i), which are PAH therapeutic agents is combined. On the other hand, the treatment of SSc-PAH is performed by combining three types of vasodilators, ERA, cGMP enhancer and cAMP enhancer, which are PAH therapeutic agents. Considering the pathological condition, combined use of anti-fibrotic therapy is desired, but at present, there is no effective treatment method. If treatment is started after the subjective symptoms have worsened according to the conventional diagnostic criteria, the prognosis for SSc-PAH is poor. Therefore, it is necessary in the current treatment strategy to make a diagnosis at the earliest possible stage and start treatment.

MTE2

Key points for adult rheumatologists to successfully treat patients with pediatric rheumatic diseases

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Conflict of interest: Yes

Pediatric rheumatic diseases are extremely rare when compared to adult rheumatic diseases. The number of patients with rheumatoid arthritis is about 600,000 to 700,000, while the number of pediatric patients with juvenile idiopathic arthritis (JIA) is around 5000. Similarly, the total number of patients with systemic lupus erythematosus (SLE) is about 60,000 to 100,000, but the number of patients under 15 years old is about 1,500. Fewer than 100 pediatric specialists have a board of rheumatology, and there are still many areas absent pediatric rheumatologists. In many areas, pediatric rheumatology patients are treated with the help of adult rheumatologists. Fortunately, with the exception of some diseases, the disease structure is similar in children and adults. In fact, in children as well as in adults, JIA (rheumatoid arthritis), SLE, and dermatomyositis/polymyositis are the most common, in that order. Thus, experienced adult rheumatologists can treat patients with pediatric rheumatic diseases with the help of a pediatrician, bearing in mind several points. In order for adult rheumatologists to better treat pediatric patients, they should know: 1) the differences between adult and pediatric patients, 2) the goals of treatment in children, 3) the use, tolerability, and side effects of drugs in children, 4) transitional care and the medical support system, and 5) the meaning and pleasure of caring for pediatric patients. In pediatric patients, growth retardation due to steroids should be noted. In pediatric patients, growth retardation caused by steroids should be noted. I would like to emphasize the need for the aggressive introduction of immunosuppressive drugs and biologics for the reduction of steroids. In addition, it is important to reduce chronic damage as much as possible, as lifelong treatment is often re-

quired. This seminar will focus on JIA and SLE and discuss what adult rheumatologists should be aware of when treating pediatric rheumatic patients.

MTE3

Intravital multiphoton imaging dissecting bone cell dynamics *in vivo*

Masaru Ishii
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Conflict of interest: Yes

During the last decade, intravital optical microscopy has launched a new trend in the field of biology. By using this advanced imaging technique we have established a new system for visualizing in situ behavior of a diversity of living cells within intact tissues and organs. Among them, we 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 presentation I will present the recent update on intravital imaging studies on bone and immune systems for clarifying in vivo behaviors of cell dynamics.

MTE4

Corticosteroids and psychiatric symptoms

Tatsuya Tokura
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Conflict of interest: Yes

Corticosteroids are widely used as a therapeutic drug in various diseases including autoimmune diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). On the other hand, there are many side effects associated with corticosteroids. It has already been reported that corticosteroids can cause psychiatric symptoms for more than 50 years, which are side effects that cannot be overlooked clinically. These side effects, also called corticosteroid-induced neuropsychiatric disorders (CIPD), are symptoms that appear within 8 weeks after the introduction or increase of corticosteroids, and completely recover in the process of reducing corticosteroids. Its occurrence rate is affected by various factors such as the patient's underlying disease and corticosteroid usage, but it has been reported to be about 3 to 10%. The psychiatric symptoms that can be induced range from mood symptoms such as insomnia, depression, hypomania and mania, psychotic symptoms such as hallucination and delusion, delirium, panic attacks and cognitive impairment. There are reports that suicide-related behavior has a hazard ratio of about 7 with the first use of corticosteroids. Furthermore, since autoimmune diseases themselves can also cause psychiatric symptoms, it is often difficult to distinguish whether psychiatric symptoms appear due to autoimmune diseases or corticosteroids. For example, in SLE, neuropsychiatric symptoms called neuropsychiatric systemic lupus erythematosus (NPSLE) appear at a high rate, and the symptoms are as diverse as CIPD. The frequency of NPSLE in SLE patients is estimated to be over 50%. Based on the above findings, when treating autoimmune diseases, it is necessary to pay attention to the appearance and exacerbation of psychiatric symptoms, so it is desirable to understand psychiatric symptoms.

MTE5

Essential basic knowledge for clinical use of ultrasound examination

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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.

MTE6

Essential Medical Statistics for Clinical Research

Ayumi Shintani
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Conflict of interest: None

In this seminar, essential concepts of medical statistics will be introduced including 1. meaning of p-values and their pitfalls 2. P-value adjustment for multiple comparisons 3. how to select proper statistal tests 4. sample size computation 5. analyzing real-word data with adjustment for confounding.

MTE7

Remission in RA

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Conflict of interest: Yes

Remission is the desirable outcome for all new patients with RA. This end-point is increasingly achieved especially with T2T approach, and he talk will discuss how to optimize remission rates. Guidance for managing patients with RA who achieve clinical remission ≧6 months with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) is imprecise. Recommendations for these patients are to taper (with the aim of potentially stopping) csDMARDs, although without specific advice on how to proceed, as there is currently no validated biomarker permitting prediction of sustained remission. New data using biomarkers will be described enabling prediction of who can successfully taper. Tapering of patients in remission on bDMARDs has been widely documented and will be reviewed. The talk will provide practical guidelines of how to best manage this situation.

MTE8

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

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Conflict of interest: None

Treatment modalities for rheumatoid arthritis (RA) that contains edu-

cation 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.

MTE9

Anatomical factors involved in finger deformities in patients with rheumatoid arthritis

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Conflict of interest: None

In the era of biologic agents, the number of cases with severe joint destruction such as arthritis mutilans has dramatically decreased. However, it should be noted that “joint deformation” and “joint destruction” are not synonymous. Finger joints and wrist joints are the most commonly affected joints in rheumatoid arthritis, and joint swelling due to synovitis occurs early in the onset. It is possible to prevent joint destruction by administrating strong medications such as biologic agent from the early onset of disease. However, when the joint swells, the tendons and ligaments surrounding the joint have already been stretched by the swelling. Physicians involved in rheumatoid arthritis patients must recognize that these “soft tissue imbalances” are an important factor in “joint deformation”. In rheumatoid arthritis, the fingers exhibit various deformations. The finger deformation is mainly caused by an imbalance of the extensor mechanisms. It is desirable to intervene at an appropriate time, since leaving the deformation causes irreversible contractures. The purpose of this program is to understand the finger deformation of rheumatoid arthritis.

MTE10

Steroid Today

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Conflict of interest: None

Although steroids have been clinically used for 70 years, they are still important therapeutic agents in a wide variety of rheumatic diseases. Notably, steroids are indicated for COVID-19 and Duchenne muscular dystrophy. So far, the science of steroids has made remarkable progress by the advanced technology; identification of steroid receptor GR, elucidation of mechanism of action and side effects of steroid, etc. GR is a member of the nuclear receptor superfamily, and it was revealed that the essential mechanism of steroid action is GR-mediated regulation of gene expression. That is, the essence of steroid therapy is “artificial gene expression control targeting GR”. Since GR is present in all nucleated cells, the action and side effects of steroids are considered to be inseparable in principle. By the way, sex steroids and vitamin D have the same principle of action, but their receptors are significantly different from steroids in that they are expressed specifically in particular target tissues. Although there were developments of various synthetic steroids with weakened electrolyte-retaining action and introduction of pulse therapy, we can hardly realize that the steroid science has been clinically fed back. In the real world, physicians still carefully consider the optimal steroid therapy for each disease, patient, and condition, relying on the disease treatment guidelines that have been developed based on the vast amount of past experience. In addition, the emergence of new modalities such as biologics has changed the positioning of steroids. However, recently, there have been promising developments in the field of steroid research. The omics analysis and bioinformatics facilitate closing the gap between basic steroid research and clinical practice. Given such progress in steroid science, I would like to introduce recent topics and discuss with you about the problems of steroid therapy and their solutions.

MTE11

Current status of the clinical practice on autoinflammatory syndrome

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Conflict of interest: Yes

Autoinflammatory syndromes are hereditary diseases in which inflammation is the main pathology. Familial Mediterranean fever is a rare disease with a prevalence of approximately 1 in 100,000, while other autoinflammatory syndromes are extremely rare with a prevalence of about 0.1 in 100,000. However, it is important for rheumatologists to know the existence of autoinflammatory syndromes because early diagnosis can prevent complications of organ damage and improve patient QOL. In this Meet the expert session, we will focus on the diagnosis of autoinflammatory syndromes, especially genetic testing, which is not familiar to rheumatologists, and discuss various aspects of autoinflammatory syndromes, including treatments and information on newly identified autoinflammatory syndromes.

MTE12

Key Points in the Management of Infectious Diseases in Patients with Rheumatic Diseases

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Conflict of interest: None

Suppression of the immune response is essential for the treatment of rheumatic diseases. Patients with rheumatic diseases are therefore at increased risk of infection. The management of patients with rheumatic diseases is more difficult than infections in patients without rheumatic diseases. What are the causes of this “difficulty”? First, the immune response is suppressed because of the treatment of the underlying disease, and the inflammatory response cannot be relied upon to diagnose infection. For example, if the serum C-reactive protein level is not high, or if the patient does not have a fever, an infection can be difficult to rule out. And it is not possible to predict the presence of an infection based on the inflammatory response alone. Another reason for the “difficulty” is that it is difficult to determine whether the inflammation is due to an infection or a rheumatic disease. For example, if pneumonia is found, it is difficult to immediately distinguish whether it is infectious pneumonia or pulmonary lesions of rheumatoid arthritis. In addition, opportunistic infections caused by uncommon pathogens may occur, which contributes to the difficulty in management. In addition to common bacteria, physician must also consider the presence of mycobacteria, fungi, viruses, and sometimes even protozoa. What can be done to confront these difficulties? The key is to know how to treat infections in immunocompromised patients. It is important to know what type of immunodeficiency the patient has, and to recall the microor-

ganisms that are characteristic of each type. Knowing these principles will greatly simplify the management of infectious diseases in patients with rheumatic diseases.

MTE13

Basic, laboratory, and clinical aspects on antinuclear antibodies

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Conflict of interest: None

The indirect immunofluorescence assay on HEp-2 cells has long been used to detect antinuclear antibodies (ANA), and the results have been classified into five patterns; peripheral, homogeneous, speckled, nucleolar and centromere. This classification, however, needs to be revised according to the increase of our knowledge of novel antibodies including those reactive to the cytoplasmic antigens, and the relevance to clinical pathology. In this situation, International Consensus on ANA Patterns (ICAP) committee elaborated the first international consensus on standardized nomenclature of antinuclear antibody HEp-2 cell patterns in 2015 (Front Immunol, volume 6, article 412). The clinical relevance of this new classification has been discussed (Ann Rheum Dis 2019;78:879), and expected to become popular in clinical environment. In addition, since new classification criteria for systemic lupus erythematosus defined positive ANA (a titer of 1:80 or higher on HEp-2 cells or an equivalent positive test) as a required entry criterion (Arthritis Rheumatol 2019;71:1400), significance of the ANA test seems to be re-evaluated. Recently, automated solid phase immunoassays which use a plate, bead or membrane coated with a series of representative purified or recombinant nuclear antigens have been introduced into clinical laboratories, and discussion about the merits and demerits of these innovative methods and a classical HEp-2 assay have been reported one after another. On the other hand, progress in basic immunology have gradually revealed molecular mechanisms of innate immunity since the beginning of this century. Antinuclear antibodies exist in the peripheral blood as immune complexes formed with nuclear auto-antigens released from dead cells. When monocytes, macrophages, dendritic cells or vascular endothelial cells endocytose the antibodies, sensors such as Toll-like receptors, AIM2, or cGAS recognize the attached nucleic acids and lead to activation of the downward pathways. These mechanisms are speculated to be involved in the pathogenesis of various connective tissue diseases and further progress to reveal the overall picture is eagerly expected.

MTE14

Diagnosis and management of axial spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis (SpA) includes axial spondyloarthritis (axSpA), psoriatic arthritis, reactive arthritis, and inflammatory bowel disease-associated SpA, whose inflammation primarily occur in enthesis. axSpA is a disease concept proposed by the Assessment of SpondyloArthritis International Society (ASAS), includes non-radiographic axSpA (nr-axSpA), and commonly used as a name of the disease. Although the classification criteria for axSpA can make early diagnosis of axSpA, it is observed very often that nr-axSpA does not develop to radiographic axSpA (r-SpA). Furthermore, false positive in MRI is well known, and fat metaplasia on MRI has become important for the diagnosis. The disease burden of nr-SpA equal to r-SpA indicates requirement of appropriate treatment. However, axSpA should be carefully diagnosed with using ASAS criteria. The difficulty with diagnosis of axSpA may cause late diagnosis, and also overdiagnosis and overtreatment. Therefore, it is necessary to know the details on ASAS criteria and the differential diagnosis, and following after the diagnosis is also important. It is noted that other SpA can cause axial disease. The progression of axial disease is various among patients, and it is unclear how extent of spinal ankylosis can be inhibited with current medication. The risk factors, existence of syndesmophytes, HLA-B27, male, high inflammatory makers, smoking, have been reported. The decision of step-up treatment is mostly made by the clinical symptoms. In this lecture, I would like to review diagnosis and management of SpA, mainly axSpA.

MTE15

Behavioral economics in the medical field

Kei Hirai
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Conflict of interest: None

Many healthcare professionals have difficulty with patients who “cannot decided” no matter how many times they explain the purpose of treatment, its effects, side effects, or who choose treatment methods with high risk and uncertain effects at the end of life. Behind this “miscommunication” of communication between the patient and the healthcare professional, the decision-making that both the healthcare professional and the patient are rational and that the correct decision can be made if the correct information is available. It is considered that there is a system design that presupposes such rationality. Behavioral economics is a discipline that unravels the “framework of irrational thinking when a person makes a decision” (bounded rationality), and solves problems related to human decision-making on the premise of that. In medical communication, various biases of both medical staff and patients are the cause of miscommunication. Therefore, it is possible to identify and correct it from the viewpoint of behavioral economics. What is important in this correction is the concept of libertarian paternalism. This is attracting attention as a concept that leads to better decision-making while respecting individual freedom of action and choice by combining both libertarian-based self-determination and paternalism well. In libertarian paternalism, the designer of choices who is responsible for organizing and arranging the context in which people make decisions is called the Choice Architect. In the case of medical care, the medical staff is the choice architect. The mechanism for promoting decision-making and behavior change, including this choice architect, is called NUDGE. In this lecture, I will explain Nudge as a mechanism to promote decision-making and behavior change based on a specific bias in order to make communication in the current medical situation smoother and more productive, using actual cases, including ethical issues in the theory and implementation.

MTE16

Treatment strategy for women of child-bearing age (WoCBA) with autoimmune diseases

Mikako Goto
Japan Drug Information Institute in Pregnancy, National Center for Child Health and Development

Conflict of interest: None

Many physicians find it challenging to examine patients who wish to have a baby or are pregnant. As a Rheumatologist, it is unavoidable that he or she will treat women of childbearing age. Rheumatologists lack basic knowledge of pregnancy. It is even more challenging to know the effects of pregnancy on diseases and their effects on pregnancy. In patients with autoimmune diseases, the continuation of medication is often necessary. In the past, the choice may have been stopped taking medications during pregnancy to fear the risks of causing fetal abnormalities. It is now preferable to consider the mother and child’s risks of not receiving treatment and weigh the fetus’s risks from the medication against the fetus’s risks. Can the medication you are administering be used in pregnant women? What if a patient gets pregnant after taking a “contraindicated” drug in the Pregnant Woman section of the package insert? In this lecture, I will answer the above questions and explain the knowledge of obstetrics that we need to know to treat patients who wish to have an enthronement or who are pregnant without hesitation, the general theory of pregnancy and collagen disease, and even the use of medications used for collagen disease during pregnancy.

MTE17

Interstitial lung disease: Up to date

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Japan

Conflict of interest: Yes

In this lecture, I would like to review the Interstitial lung disease (ILD) which has recently been attracting attention from the viewpoints of diagnosis, treatment, and prognosis. ILD includes various diseases with known causes such as ILD associated with connective tissue disease (CTD), hypersensitivity pneumonitis, etc., and a group of unknown causes named idiopathic interstitial pneumonia (IIPs). In addition, provisional diagnosis using certainty has come to be used for a group of patients for which a definitive diagnosis cannot be obtained because of inadequate clinical data or major discordance between clinical, radiologic, and pathologic findings (unclassifiable ILD). In CTD, respiratory manifestation is extremely important as a prognostic factor and is still the leading cause of death in patients with RA, SSc, PM/DM and MCTD. ILD is the most common respiratory manifestation in CTD and has the greatest impact on survivals. Furthermore, if respiratory manifestations are observed during the courses of immunosuppressive therapy, including corticosteroids, immunosuppressive drugs, and molecularly targeted drugs, it is necessary to consider not only the lesions due to the disease itself, but also the manifestations due to other causes such as infections and drug-induced lung injury. In addition, although a disease-specific mechanism is important in the early phase of ILD disease, recent studies demonstrated a shared perpetuating fibrotic process regardless of initial cause or trigger, and for such latter progressive fibrosis phase, antifibrotic drugs are reported to be effective. Because anti-inflammatory therapy is often the basis for CTD-ILD, it will be crucial to use it properly with anti-fibrotic drugs. Therefore, CTD-ILD is an important issue for both pulmonologists and rheumatologists from the viewpoint of diagnosis, treatment/management, QoL, and prognosis, thereby leading to the publication of “The guide for the diagnosis and treatment of CTD-ILD 2020”.

MTE18

Total shoulder arthroplasty update (from anatomical to reverse shoulder arthroplasty)

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Conflict of interest: None

The characteristics of rheumatoid shoulder was rotator cuff insufficiency or tears owing to the The characteristics of rheumatoid shoulder was rotator cuff insufficiency or tears owing to the invasion of synovitis and osteoclasts into a bare area. Anatomical total shoulder arthroplasty (TSA) in the destructive rheumatoid shoulders with cuff insufficiency usually makes patients pain relief but never gets good satisfaction for range of motion. Therefore, the treatment for that bothers orthopaedic surgeons for ages. The history of TSA was started in 1893 and mono-block prosthesis was developed in 1050th, however, restoration of anatomical kinematics was limited. Subsequently, modular and eccentric humeral head were invented. Recent device can choose glenoid component according to its curvature. However, there are few patients with RA who are suitable for anatomical TSA since most of them have rotator cuff insufficiency. Reverse shoulder arthroplasty (RSA) was invented in 1986 by Paul Grammont and it enables patients with cuff tear arthropathy (CTA) to recover use of the deltoid muscle through the medialization of the center of rotation and lengthening of the deltoid muscle. The long-term outcomes of RSA in cuff tear arthropathy (CTA) showed satisfactory results and Several reports recently showed that the short and mid-term outcomes of RSA in patients with RA were comparable to that in CTA. Early design of the Grammont type RSA have minor complication such as scapular notching. The next generation device was invented to have lower neck-shaft angle to decrease scapular notching and can lateralize humerus to use internal and external muscle effectively and choose glenoid inferior offset to decrease scapular notching. Recent advances in the treatment of RA have increase treatment options for rheumatic shoulder and that will make improvement of ADL and QOL in these patients if that kind of options were gradually recognized among rheumatologist and orthopaedic surgeon.

MTE19

Differential diagnosis of arthritis in the elderly in daily practice

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Conflict of interest: Yes

For rheumatoid arthritis (RA), availability of various oral DMARDs including MTX and biological products has increased treatment options, improving both short-term and long-term outcomes and QOL. Appropriately-tailored treatment of individuals with RA in daily practice, however, depends on an accurate differential diagnosis which includes other autoimmune diseases, but is still often based on experientially-derived clinical judgement. A recent systematic literature review reported that the 2010 ACR/EULAR RA classification criteria have a moderate specificity of 61% (1), suggesting that clinical application of these criteria are only valid after careful consideration of alternative diagnoses. In this session, we aim to characterize the distinguishing clinical features of competing autoimmune and musculoskeletal diseases, especially focusing on the elderly population, helping us to avoid both under-diagnosis and misdiagnosis of RA, an otherwise treatable disease, and emphasizing the need for early diagnosis and its differential diagnosis. **References** 1. Radner H, *et al*. *Ann Rheum Dis* 2014; 73: 114-23

MTE20

Efficient strategy of data accumulation and analyses for medical doctors in rheumatology

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Laboratory for Statistical and Translational Genetics, RIKEN Center for Integrative Medical Sciences

Conflict of interest: None

Advancement of data processing by CPU and expansion of datastorage has been helping medical knowledge to expand in anunprecedented scale. A doubling time of medical knowledge was 3 and a half years in 2010 and was estimated to be 73 days in 2020. There is a huge demand to efficiently and accurately accumulateand analyze medical data especially under the view point of medical doctors working in hospitals and seeing the patients. To achieve this goal, this lecture aims to help participants -to recognize critical points to accumulate data (relevant to study design) -to understand basics and pitfalls in data analyses -not to get caught by p-values regardless of their significance -to recognize importance of confidence intervals -to understand why a direction of effect size is important -to understand what overfitting is -to understand differences and similarities among statistical models

MTE21

Difficult-to-treat RA

Eiichi Tanaka
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Conflict of interest: None

The sufficient methotrexate use and the introduction of bDMARDs and/or tsDMARDs (JAK inhibitors) has 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 61.7% in 2020. On the other hand, despite these advances in RA treatment, there is still a population of RA patients with moderate or high disease activity. Appropriate treatment of these patients is considered to be unmet needs. Different various concepts exist on difficult-to-treat RA, such as refractory RA, multidrug-resistant RA, persistent active RA, or failed treatment goals. Depending on the criteria used, the estimated prevalence of difficult-to-treat RA from 5% to 20%. Since uniform terminology and a clear definition for these patient groups 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 for D2T proposed in 2020 was as follows; (1) Treatment according to EULAR recommendation and fail-

ure of ≧2 bDMARDs/tsDMARDs (with different mechanisms of action) after failing csDMARD therapy; (2) presence of at least one of the following: at least moderate disease activity; signs and/or symptoms suggestive of active disease; inability to taper glucocorticoid treatment; rapid radiographic progression; RA symptoms that are causing a reduction in quality of life; and (3) the management of signs and/or symptoms is perceived as problematic by the rheumatologist and/or the patient. At this Meet the Expert, we will first share the process leading up to the definition of D2T RA and the content of this definition. In addition, I would like to explain various issues that can contribute to D2T RA such as refractory RA, multidrug-resistant RA, complications, and medication adherence, using data from registries include the IORRA cohort and clinical trials.

MTE22

Learn about advances in SLE treatment

Kazuhisa Nakano
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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) exhibits a diverse clinical course and organ damage due to its complex pathology. In 2014, a Treat-to-target (T2T) recommendation was proposed, which is a strategy for regularly adjusting treatment with the disease indicators. Remission and LDA have been proposed as targets for treatment in SLE. For patients who achieve remission or LDA, the target progresses to the maintenance of remission. In SLE, an adequate intensity of treatment should be provided to control disease activity as early as possible. In Japan, hydroxychloroquine (HCQ), mycophenolate mofetil (MMF), and belimumab, a fully human anti-BAFF monoclonal antibody, have been covered by insurance for several years. These drugs have enabled the practice of T2T in line with global standard treatment algorithm of SLE. In 2019, guidelines for SLE treatment were also formulated in Japan, and treatment policies classified by pathological condition were shown. However, at present, the 10-year survival rate of SLE is 90%, and considering that the age of onset is young, further improvement in prognosis is desired. In this talk, I will also mention the development status of molecular-targeted drugs, which are expected to be launched as new treatment options. In addition, I would like to think about better SLE treatment practices with participants while presenting actual cases.

Morning Seminar

MS1-1

Innate immunity up to date

Sachiko Miyake
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Conflict of interest: None

Immune system is composed of innate immunity and acquired immunity. In addition, innate lymphocytes and innate T cells attracted attention as bridging cells between these two components. Bechet's disease as well as psoriasis and spondylitis are characterized by the inflammation mediated by innate cells and T cells without the detection of specific autoantibodies. A variety of inflammatory cytokines including TNF-α are involved in the inflammation. This lecture overviews the basic idea of how innate immunity and innate T cells work in the inflammation.

MS1-2

Positioning of Apremilast in the Treatment of Behcet's Disease

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Conflict of interest: None

Behcet's disease is a disease that causes chronic recurrent inflammation such as oral aphthous ulcer, genital ulcer, and uveitis. It is thought that activation of innate immunity such as hyperneutrophil function is involved in the pathological condition, and in recent years, it has come to be regarded as an autoinflammatory disease. Furthermore, although a high association with HLA-B51 has been known for a long time, recently since HLA-B51 and ERAP-1 are epistatic, the concept of MHC-1-opathy has been proposed along with ankylosing spondylitis and psoriatic arthritis which have the same MHC-1 as the susceptibility gene. Behcet's disease, which can lead to blindness from uveitis, has long been designated as a specific intractable disease in Japan, but other than uveitis, the symptoms that plague Behcet's disease patients are painful and recurrent. It is an intraoral aphthous ulcer. Oral aphthous ulcer is almost inevitable in patients with Behcet's disease, and often consults a medical institution as the first symptom. Symptoms relieved spontaneously and exacerbated repeatedly, and the patient's QOL may be significantly impaired. In the past, topical corticosteroids were applied topically. In the case of refractory disease, colchicine and corticosteroids were also taken orally. In 2019, apremilast was newly approved for oral ulcers caused by Behcet's disease, which is ineffective with local therapy. Apremilast is a drug that selectively inhibits PDE4, which is an intracellular second messenger, and increases the concentration of intracellular cyclic AMP (cAMP) to suppress intracellular signal transduction. As a result, protein kinase A (PKA) is activated and AP-1 (activator protein 1), which is a transcription factor, is activated from the phosphorylation of CREB (cAMP responsive element binding protein), and IL-10, which is an anti-inflammatory cytokine, it raises the initial valve and exerts an anti-inflammatory effect. In addition, CREB dissociates CEB (CREB binding protein) required for the activity of NF-κB (nuclear factor κB) and suppresses the transcriptional activity of NF-κB, thereby reducing the production of inflammatory cytokines. Currently, apremilast is the only approved oral drug for Behcet's disease and is indicated for oral aphthous ulcer, but its mechanism of action is expected to be effective for symptoms other than oral aphthous ulcer. Future clinical data is awaited.

MS2

Guidepost for remission shown by the SELECT studies

Hideto Kameda
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Conflict of interest: Yes

While more than half of patients with rheumatoid arthritis (RA) achieve clinical remission, the remaining patients do not because of inher-

ent problems in the clinical evaluation, significant limitations in treatment options due to complications, relative insufficiency of the doses of therapeutic drugs for highly active diseases, and special conditions refractory to disease-modifying antirheumatic drugs (DMARDs) with various mechanisms of action. Clinical remission is an important target from the viewpoint of patient's quality of life and work productivity, and therefore, the elucidation/clarification of the reasons for non-achievement of clinical remission is the first step for the management of "difficult-to-treat" patients. Upadacitinib (UPA) is a Janus kinase (JAK) inhibitor, and 15 mg once daily is the optimal starting dose for Japanese RA patients from the risk-benefit standpoint. Based on the results of domestic and overseas studies of the SELECT series, UPA showed favorable efficacy in various RA patient groups who were eligible to be enrolled in clinical trials (SELECT-EARLY, -COMPARE, -NEXT, -SUNRISE, -BEYOND), and the efficacy of UPA monotherapy was similar to that of UPA combination therapy with conventional synthetic DMARDs (SELECT-EARLY, -MONOTHERAPY). Currently, the real-world outcomes in accordance with the package insert and the proper use guide for all-case post-marketing surveillance by the Japan College of Rheumatology have been accumulated in Japan. These will provide meaningful evidence on the clinical significance of the relatively high selectivity to JAK1, and the indication of the daily 7.5 mg dose, which is unique to Japan, as well as its comparison with the standard 15 mg dose in terms of safety and effectiveness. For the latter issue, the long-term result of the SELECT-SUNRISE is the only evidence available to date. Further discussion will be awaited on the positioning of biologics and JAK inhibitors in remission induction of RA.

MS3

Innovative strategies for the treatment of patients with rheumatoid arthritis

Arthur Kavanaugh
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Conflict of interest: Yes

The main goals of treatment for RA are to alleviate pain, prevent or limit joint damage, optimize quality of life, avoid complications of therapy, and improve or preserve function. Remission, once a purely hypothetical consideration, is now considered to be an appropriate and attainable goal, largely because of the introduction of new therapies, and new treatment paradigms. There are an impressive number of established therapies available currently for the treatment of RA, with additional treatments available each year. Biologic agents, particularly inhibitors of tumor necrosis factor (TNF), have changed the treatment paradigm for RA. 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. Biologic agents have different mechanisms, methods of delivery, and potential side effects. A patient who does not respond to or cannot tolerate one may still have a good outcome with another. Although they are commonly used in combination with methotrexate, biologic agents usually are not given in combination with each other, because this approach may increase risk without much increase in benefit. Because biologic agents modulate part of the immune response, there is concern about potential side effects related to impaired immune function, such as increased risk of minor and serious infections and secondary malignancies. The newest group of RA therapies are jakinibs. These agents inhibit kinase within the Jak 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, and further research and experience using them will optimize their use.

MS4

Pathogenesis and Treatment Strategies for SLE and Lupus Nephritis

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a systemic inflammatory disorder caused by immune abnormalities of T and B cells. There are many causes for the onset and disease activity, and genetic predisposition, environmental factors, and the hormonal environment are thought to influence the disease. The complex pathogenesis of SLE involves multiple cellular components of the innate and immune systems, the presence of autoantibodies and immune complexes, the involvement of the complement system, dysregulation of several cytokines including type I interferon, and impaired nucleic acid clearance after apoptosis. Lupus nephritis (LN) has been reported to occur in 40-50% of patients with SLE (Nat Rev Dis Primers. 2020 Jan 23;6 (1):7.). In clinical trials, only 30-50% of LN patients achieve remission, and 10-20% of patients develop the end-stage renal disease (ESRD) within 10 years of diagnosis. The ultimate goal of LN treatment is to preserve normal kidney function in the long term and to achieve this goal, and it is crucial to ensure the induction of remission and prevention of relapse. Until now, the therapeutic target of LNs has been immune cells, mainly T and B cells. Localized inflammatory cell infiltration through cytokines and chemokines produced by these immune cells, and mesangial cell proliferation via autoantibodies and complement, and altered podocyte function are essential as a pathogenic mechanism of LN. In the last 30 years, steroids and immunosuppressants have improved the life prognosis of SLE, and the 5-year survival rate in Japan is considered to be more than 95%. Furthermore, in recent years, biologics such as mycophenolate mofetil, belimumab, as well as hydroxychloroquine, have been approved in Japan for the treatment of SLE and LN, and are expected to improve the life expectancy of SLE patients. However, the life expectancy of patients with SLE still depends not only on disease-specific tissue damage but also on treatment-related complications, such as the increased risk of coronary artery disease and infection. Future treatment of SLE requires an optimal balance of therapeutic risks and benefits, from the selection and timing of drug administration to taper and withdrawal. In this talk, we can discuss the pathogenesis of SLE, especially LN, and treatment strategies aimed at low disease activity and remission.

MS5

Diagnosis and Management of Pulmonary Artery Hypertension in Systemic Sclerosis

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

Conflict of interest: None

In the treatment of patients with pulmonary artery hypertension (PAH), PAH-specific drugs have demonstrated survival benefit including hemodynamics, symptoms, quality of life, and functional capacity. However, prognosis and therapeutic response of PAH-specific drugs are worse in PAH associated with connective tissue diseases (CTD-PAH) than in other PAH categories. Because CTD-PAH has increased risk of death, CTD-PAH is one of the most serious complications of the disease. SSc patients may have category 1 (PAH), 2 (PH associated with left heart disease), or 3 (PH associated with lung disease/hypoxia) PH. Among CTD-PAH, PAH associated with systemic sclerosis (SSc-PAH) has most severe prognosis. Therefore, it is necessary to detect and treat SSc-PAH early in its course. An early diagnosis through systematic screening of asymptomatic SSc patients has the potential to identify SSc-PAH at an early stage. Current methods for detecting SSc-PAH are to perform multimodarity test, such as right heart catheterization, chest CT, pulmonary function test with diffusing capacity for carbon monoxide and lung perfusion scintigraphy. Monotherapy of PAH-specific drugs rarely resulted in substantial and sustained clinical improvement in SSc-PAH. Recently, several studies demonstrate that there are evidence of benefit for management of SSc-PAH including monotherapy of selexipag and up-front combination therapy of ambrisentan and tadalafil. In clinical practice, SSc-PAH contain scarcity of disease, complexity of pathogenesis and diversity of hemodynamics by individual cases. In the SSc-PAH treatment, we need an exact evaluation of pathogenesis and management paying attention to adverse events. It is the important factor that rheumatologists have a close referral relationship with a cardiologist or pulmonologist. In this session, we provide an up-to-date focused review of SSc-PAH, strategy of SSc-PAH treatment based on evidence and management of SSc-PAH for improvement of prognosis.

MS6

Efficacy of denosumab in rheumatoid arthritis with osteoporosis

Hiroaki Matsuno
Matsuno Clinic for Rheumatic Diseases

Conflict of interest: Yes

The therapeutic effect of denosumab (DMAb) was assessed in female osteoporosis patients using radial dual-energy X-ray absorptiometry (radial DXA): those with postmenopausal osteoporosis (PO group), PO with rheumatoid arthritis (RA group), and PO with RA receiving glucocorticoids (RA + GC group). In all, PO patients 60 years of age or older with a% young adult mean value of <70%, as determined by radial DXA were treated with DMAb. The DMAb treatment group comprised PO group, RA group, and RA+GC group. The control group comprised PO group and RA group who received oral bisphosphonate (BP). The bone mineral density (BMD) was determined by using radial DXA. The bone turnover marker, type I collagen cross-linked N-telopeptide, (NTx) were also measured. Radial DXA revealed a significant increase in the DMAb treatment, but not in the BP treatment. The onset of an increase in BMD with DMAb was slower in RA group than in those without. The effect of DMAb in preventing increased NTx levels was smaller in the RA and RA + GC groups than in the PO group. The adherence to DMAb treatment was statistically significantly greater than for BP treatment. RA is commonly associated with osteoporosis but there is no established treatment approach. DMAb may be first-line osteoporosis drug in rheumatoid arthritis patients.

MS7

Standard of Care in Lupus Nephritis from a Nephrologist's Perspective: Reviewing the past and thinking about the future

Hiroki Hayashi
Department of Nephrology, Fujita Health University School of Medicine, Japan

Conflict of interest: Yes

First, I will review the renal histology emphasized in the EULAR/ACR classification criteria for SLE, including the 2018 revision of the ISN/RPS classification for Lupus Nephritis. Next, I will introduce several landmark trials and major guidelines for lupus nephritis and review the "previous" standard of care. Finally, I will review the emerging evidence for belimumab therapy which was approved as a new treatment for lupus by FDA in 2011 for the first time in 56 years, including the BLISS-LN trial reported last year, and consider the "future" of lupus nephritis treatment.

MS8

Roles of Interleukin-6 as an inflammatory cytokine

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Conflict of interest: Yes

Biological drugs such as therapeutic antibodies target a wide range of diseases, including rheumatoid arthritis, vasculitis, asthma, and atopic dermatitis. In addition, biological drugs are used to treat cancer by targeting immune checkpoint molecules. Additional novel biological drugs are expected to be approved in the coming years. Therefore, regardless of their specialty, physicians must understand the immunological modes of action of these drugs and master their use. The application of therapeutics targeting tumor necrosis factor-α (TNF-a) and interleukin-6 (IL-6) in rheumatoid arthritis spearheaded the rise of biological drugs.

MS9

Characteristics and future issues of Filgotinib

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Conflict of interest: Yes

To achieve the goal of rheumatoid arthritis (RA) treatment, it is advantageous to have multiple DMARDs with different mechanisms of action as option. The EULAR Recommendation on RA was revised in 2019 and the JCR Guidelines for RA treatment were revised this year. After accumulating clinical evidences, there is a consensus that Janus kinase (JAK) inhibitors and biologic drugs (bDMARDs) are essentially equivalent in the drug treatment algorithm. Filgotinib, the fifth JAK inhibitor to be introduced in Japan, has been approved for RA (including the prevention of structural damage of the joints) with the efficacy and safety verified in the international Phase III FINCH study, and is now available for clinical use. Filgotinib has a unique profile, including selectivity for JAK1, and its active metabolites. Filgotinib met the primary endpoints in each of the FINCH trials in patients with moderately to severely active RA patients who were either inadequate or intolerant of MTX and bDMARDs. It showed excellent inhibition of joint destruction, as seen in the change of mTSS from baseline at the 52-week. In addition, patient-reported outcomes such as pain and fatigue also showed relatively rapid improvement. In an integrated safety analysis based on the Darwin and FINCH trials, Filgotinib was well tolerated with no new profile being observed. Future work will require the establishment of evidence for drug selection, the accumulation of drug continuation rate and safety data in Japanese patients, and perioperative management. In this seminar, we will review the selectivity of Filgotinib for JAK1, the efficacy and safety of Filgotinib in the overall population and in Japanese patients, with a focus on the FINCH1 study for MTX-IR patients and the FINCH2 study for bDMARD-IR patients, and discuss the clinical significance of Filgotinib as a treatment for RA and its future issues to be resolved.

MS10-1

The potential of JAK inhibitors for rheumatoid arthritis pain

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Conflict of interest: None

When some joint symptoms remain in some rheumatoid arthritis (RA) patients who should have achieved clinical remission, by making full use of imaging exam such as ultrasound (US) to confirm the presence or absence of slight residual synovitis or structural changes, it is possible to fill the gap with clinical judgment and learn by oneself and improve the quality of medical care. Even if US or MRI is performed, the cause of joint symptoms cannot be identified and it is often difficult to make a judgment. Arthralgia in RA is thought to be mainly nociceptive pain associated with synovitis, which can be improved by Treat to target, but it is sometimes necessary to anticipate the coexistence of pain sensitization, descending pain suppression system disorders and functional neuropathic pain. It has been reported that neuropathic pain coexists in about 10 to 30% of patients with RA, obesity and high TJC / SJC ratio are risk factors, and they are predictors of poor pain improvement. Familiarity with not only nociceptive pain but also pain sensitization and neuropathic pain, and pain control including lifestyle and exercise guidance can be expected to achieve better outcomes. JAK inhibitors have been reported to have excellent analgesic effects. In the head-to-head study (RA-BEAM study) of baricitinib and adalimumab, the rate of improvement in the number of swollen joints was similar, and the significant difference between baricitinib and adalimumab was obtained for the first time after 52 weeks. In patient pain VAS, the significant difference in baricitinib to adalimumab was obtained from 2 weeks after the start of treatment and persisted until 52 weeks. The discrepancy causes JAK inhibitors to expect not only analgesia through improvement of synovitis, but also the existence of different mechanisms of action and the effects on patients mentioned above. We discuss the potential of JAK inhibitors especially in their mechanisms in analgesia.

MS10-2

JAK inhibitor as an option in the treatment of rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) treatment has evolved significantly over the last two decades, significantly reducing the proportion of patients with uncontrolled disease activity. There is no doubt that the development of biologics and JAK inhibitors has contributed significantly, but the main reason should be that the concept of Treat-to-Target (T2T) has been well understood and implemented. Pain is the most common chief complaint of RA patients, and it is also the patient's greatest hope that the pain disappears. However, even if the pain disappears with the administration of anti-inflammatory analgesics and glucocorticoids, it is not recognized that the T2T strategy is being practiced. This is because the goal of RA treatment is functional remission and maintenance and improvement of quality of life. Structural remission should be achieved to reach to functional remission, and clinical remission is required to achieve structural remission. In other words, it is meaningless unless it is clinical remission in a state where structural remission can be expected. It is insufficient just to eliminate the pain. What we need to do for the final goal is to practice T2T with a sense of speed. It is important that remission is achieved as early as possible and maintained long. In implementing this strategy, we are fortunate to live in an era when so many therapeutic agents are available. EULAR recommendation 2019 puts bilologics and JAK inhibitors in the same position for treatment of patients with RA who have inadequate response to methotrexate. Clinical studies have also been conducted that directly compare the medicines of both strains, and the author believes that the effects of both are equivalent. In this talk, I would like to outline the need for speed in the T2T strategy, the results of direct comparisons of biologics and JAK inhibitors, and new options for RA treatment.

MS11-1

Natural history of intestinal Behcet's disease and differential diagnosis including related diseases

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Conflict of interest: Yes

Intestinal Behcet's disease is classified as a special type of Behcet's disease. Punched-out ulcer lesions in the ileocecal region are typical and often pose a risk of hemorrhage and perforation. Diagnosis is made based on systemic Behcet's disease symptoms and endoscopic morphological findings. Endoscopically related diseases include simple ulcers without other Behcet's symptoms and gastrointestinal ulcer lesions associated with trisomy 8 in myelodysplastic syndrome. In addition, esophageal lesions and lesions at other gastrointestinal sites have been reported; in such cases, it is necessary to distinguish from other diseases such as inflammatory bowel disease. Although the natural history of intestinal Behcet's disease is not entirely clear, operation rate, postoperative recurrence rate, and cumulative re-operation rate are high, thereby resulting in severe impairment of patients' quality of life. Although punched-out ulcers, referred to as volcano type, are said to be a risk factor for surgery, treatment strategies to avoid surgery or preventive measures for postoperative recurrence have not been completely established. Herein, we discuss mainly the natural history and diagnosis of intestinal Behcet's disease based on the Clinical Practice Guidelines for Intestinal Behcet's Disease 2020.

MS11-2

Treatment of Behcet's disease -ocular lesion-

Kenichi Namba
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Conflict of interest: None

Ocular manifestations in Behçet's disease are acute onset uveitis called ocular inflammatory attacks, which are characterized by frequent occurrences. Ocular inflammatory attacks mainly include anterior uveitis type that occurs in the iris and ciliary body, posterior uveitis type that occurs in the retina and choroid, and panuveitis type that occurs in both sites; however, when posterior uveitis type or the panuveitis type occurs frequently, atrophic changes develop in retina and choroid, leading to permanent loss of visual function. Although the number of patients with Behçet's disease has been declining in recent years, this disease is still one of the serious uveitis that can lead to blindness. The medical practice guideline for Behçet's disease has published last year at the Behçet's Disease Research Committee of the Ministry of Health, Labor and Welfare. In this lecture, I will introduce the contents of it. Treatment of Behçet's disease is divided into "Treatment for ocular attack" that is performed when ocular inflammatory attack occurs and "Treatment for preventing ocular inflammatory attack" that is performed for the purpose of preventing the subsequent ocular inflammatory attack and maintaining the remission. The treatment for ocular attacks is periocular injection or intravenous drip infusion of corticosteroids, which is performed to minimize the damage of the ocular tissue by promptly extinguishing the inflammation. In severe cases, it is performed every day for a week. These treatments have not changed much from the past. Oral colchicine is still the first-line drug for preventing ocular inflammatory attack (Step1), and if colchicine does not provide enough clinical remission, the next step2 will be required. In Step2, cyclosporine is used first in cases with a low risk of visual impairment, and then if clinical remission is not obtained with it, TNF inhibitors are used. In cases with a high risk of visual impairment, TNF inhibitors are recommended to be used directly without using cyclosporine. Unfortunately, other biologics have not been adopted for Behçet's disease in Japan. Infliximab and adalimumab are TNF inhibitors adopted for Behçet's disease. Infliximab has been adopted since 2007 and has been reported to be highly effective in preventing ocular attacks. Adalimumab has been adopted since 2016, has been reported in some reports on its effect. In this lecture, I will talk about current situations and problems of these treatments from an ophthalmological point of view, and I hope that they will be useful to the medical practice of audiences.

MS12

Past and Future of TNF Inhibitors-Verifying TNF Inhibition Therapy from Recent Research Results-

Katsuya Suzuki
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Conflict of interest: Yes

TNF inhibition therapy is used as a trump for treatment of various immune and inflammatory diseases such as inflammatory bowel disease, psoriatic arthritis, and ankylosing spondylitis, starting with rheumatoid arthritis (RA). Currently, in Japan, a total of five types of TNF-alpha-targeted antibody preparations and TNF-beta-targeting TNF receptor decoy preparation are covered by medical insurance as originators. In addition to having neutralization of soluble TNF as a common mechanism of action, antibody preparations are also expected to act directly on membrane-type TNFs on TNF-producing cells. The physiological activity of TNF in innate immunity and adaptive immune system and the pharmacological characteristics of these preparations will be summarized in relation to the pathophysiology of immune and inflammatory diseases. Next, I will summarize the important matters in actual clinical practice, such as the selection of TNF inhibitory therapy for RA and the determination of its effect. In the second half, I would like to touch on the results of recent molecular-level analysis of TNF inhibition therapy for RA and recent research topics. Based on the results of recent research, I will verify past and future of TNF inhibition therapy from both basic and clinical perspectives.

MS13-1

Significance of T cell targeted therapy in rheumatoid arthritis

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Conflict of interest: Yes

Abatacept, which selectively inhibits T cell activation through blocking costimulation signal, has been reported efficacious and safe in the treatment of rheumatoid arthritis (RA), thereby, has become one of the first-line biologic disease-modifying antirheumatic drugs (DMARDs). However, although approximately ten biological DMARDs including TNF inhibitors, IL-6 inhibitors, CTLA4-Ig and five JAK inhibitors are

available for the treatment of RA, the manner in which they are differentially selected for each patient remains unclear. Since the response to each targeted therapy often differs markedly among patients due to the heterogeneities in the pathogenesis of this disease, the establishment of precision medicine is considered particularly important. Abatacept strongly suppresses the activation of follicular helper T (Tfh) cells, which control the maturation and activation of B cells, and suppresses the production of autoantibodies from B cells. Previous studies reported a difference in the predictors of the response to treatment; patients who had higher titers of RF or anti-CCP antibody were shown to respond well to abatacept. Thus, patients with active Tfh cell-B cell-autoantibody axis are expected as good responder for abatacept. By contrast, abatacept has little effect on the innate immune system and seems to be safe as regards the risk of serious infections for elderly patients. Recently, new mechanisms of action such as direct action on bone metabolism have been reported. Abatacept suppresses the differentiation of osteoclast progenitor cells and dendritic cell-derived osteoclasts from monocytes in vitro. In this seminar, we would like to highlight recent advances the pertain to basic and clinical significance of T cell targeting in the treatment of RA based on the results of our clinical registry and immunophenotyping analysis.

MS13-2

Risk management of elderly patients with rheumatoid arthritis

Masato Okada
Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: Yes

Comorbidities are important factors in the decision of management of elderly patients with rheumatoid arthritis. In addition to the age, kidney function impairment, pulmonary lesions including interstitial lung disease and smoking related conditions, diabetes and cardiovascular diseases are all risk factors of serious infection and suboptimal treatment outcome in rheumatoid arthritis. As the autoimmune musculoskeltal problems are chronic immune disregulations which require long-term pharmacological therapy, future development of the aforementioned pathologies and also gradual deteriorations over years have to be considered even at the initial stage of management. Comparison of benefits and risks of csDMARD, bDMARD, tsDMARD needs to be individually evaluated for the success of achieving treatment goal. Each category of DMARDs are reviewed including the safety profile and data of efectiveness of abatacept.

MS14

Selectivity of JAK inhibition in RA treatment

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic inflammatory synovitis, progressive joint destruction, and multiple organ manifestations and is clinically associated with severe disability and mortality. The combined use of methotrexate, a synthetic DMARD, and biologic DMARDs has revolutionized treatment of the disease. Clinical remission is now realistic targets, achieved by a large proportion of the patients, and rapid and appropriate induction of remission by intensive treatment with biological DMARD and methotrexate is prerequisite to halt joint damage and functional disabilities. However, biological DMARDs are limited to intravenous or subcutaneous uses and orally available small but strong molecules have been expected. Various cytokines and cell surface molecules bind to receptors on the cell surface, resulting in the activation of signaling pathways including phosphorylation of kinase proteins. Among them, the Janus kinase (JAK) plays a pivotal role in the pathological processes of rheumatoid arthritis. JAK inhibitors differ in their selectivity for different JAK isoforms and pharmacokinetics profiles. Although they are all orally administered drugs, they have multi-target effects and exert clinical effects just as promptly as biological DMARDs. JAK inhibitors can be used alone or in combination with methotrexate. However, JAK inhibitors should not be used without careful consideration and screening before their use and monitoring during treatment should be strictly performed. It is necessary to establish evidence on its long-term safety regarding the development of infections such as herpes zoster and malignancies. Taken together, JAK inhibitors are novel therapies for rheumatoid arthritis, but further studies are needed to determine their risk-benefit ratio and selection of the most appropriate patients for such a therapy.

MS15

Staying at the cutting-edge: Latest update of Upadacitinib

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Conflict of interest: None

Rheumatoid arthritis is a systemic disease with predominant involvement of the joints. Over the past 40 years we have had the introduction of much improved treatment strategies and a multitude of new molecules and MOA which have dramatically improved the functional outcomes of patients. Despite these advances, there remains a large unmet need as many patients are still unable to achieve and sustain deep remission with stringent metrics. The pathophysiology of RA is complex. Over the past decade several effective oral small molecular inhibitors of the JAK pathway have been approved including upadacitinib recently. The pivotal phase 3 clinical program investigated upadacitinib as both monotherapy and in combination with MTX in patients with an incomplete response to MTX and in combination with csDMARDs after failure of a bDMARD. These clinical trials have shown that upadacitinib is clinically and functionally effective in these patient populations with sustained benefit. Importantly, two powered head to head trials of upadacitinib in combination with MTX compared to a bDMARDs with different MOA have been completed: SLECT-COMPARE, versus adalimumab, and, SELECT-CHOICE versus abatacept. In SELEC-COMPARE, upadacitinib 15 mg daily plus MTX was superior to adalimumab plus MTX in achieving an ACR50 response by week 12, improvement in patient function, and reduction in pain, sustained through 72 weeks. Radiographic inhibition compared to placebo plus MTX, comparable to adalimumab plus MTX was shown. This trial also demonstrated for the first time that a patient failing a JAKi may respond to a TNFi as well as patients improving on either initial medication, but not achieving LDA by CDAI, may benefit with a switch to the alternate medication. SELECT-CHOICE showed superiority of upadacitinib versus abatacept, both plus MTX, by a difference in the change in DAS28 (CRP) at week 12 with similar PRO improvements. These results, unique for upadacitinib, will be fully discussed.

MS16-1

Challenges left in treatment for RA

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Conflict of interest: Yes

Drug therapy for RA has made great strides in the last 20 years, establishing standardized therapies centered on MTX and b/tsDMARDs. This has made it possible to induce clinical remission in many patients, but on the other hand, the existence and characteristics of a group of patients "difficult-to-treat RA (DTRA)" that cannot induce remission with current drug therapy became clear. Patients with DTRA may be refractory to any of the current DMARDs, or may not be able to start or continue appropriate medication due to visceral complications associated with RA or other comorbidities. Those based on therapeutic agents or factors of inflammation control are first considered. In addition, although inflammation is well controlled by proper administration of DMARDs, there exist many patients who have residual unpleasant symptoms due to pain disorders or psychological factors, which hinders improvement of QOL. In addition, the advent of an aging society has had various impacts on medical care including RA in Japan. Compared to general age, elderly RA is characterized by more cases of acute onset, severe inflammation, major arthropathy type, and negative serologic reaction. In elderly patients, the risk of adverse events is higher due to the decrease in organ reserve, and the delay in the onset of therapeutic effect can easily lead to a decrease in ADL. Therefore, special attention in management for elderly RA should be paid.

In this talk, the issues remaining in treatment for RA will be summarized to outline the countermeasures.

MS16-2

How to use JAK inhibitors in the treatment of rheumatoid arthritis aiming at efficacy and safety

Masao Tanaka
Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Graduate School of Medicine

Conflict of interest: Yes

Molecular-targeted drugs, which target disease at the molecular level during drug discovery, first developed in the field of cancer treatment and then introduced into the field of rheumatic diseases to bring a revolution to the treatment of rheumatoid arthritis (RA). In Japan, antibody / receptor drugs targeting TNFα, IL-6, and CD80 / 86 have appeared as the first wave since 2002, and then inhibitors of JAK molecules, which are cytokine signaling molecules, has been introduced as the second wave since 2013. Currently, five JAK inhibitors as anti-rheumatoid drugs are available: tofacitinib, baricitinib, peficitinib, upadacitinib, and filgotinib. How to properly use these five JAK inhibitors for each case is a new issue in future RA treatment. Here, I would like to mention three candidate criteria for proper use: selectivity of JAK family molecules of each drug, metabolic pathway, and side effects. First, consider the selectivity of JAK family molecules (JAK selectivity). The basic efficacy of JAK inhibitors on RA is thought to be due to JAK1-mediated blocking of IL-6 signal and type I interferon, and all five drugs have JAK1 inhibitory effects. Upadacitinib inhibits only JAK1, but tofacitinib has an inhibitory effect on JAK2 and JAK3, baricitinib and filgotinib have an inhibitory effect on JAK2, and peficitinib has an inhibitory effect on JAK2, JAK3 and TYK2. Cytokines related to JAK other than JAK1 include GM-CSF and IL-12 / -23, but it remaines to be clarified whether their blocking has a significant additional effect on the pathophysiology of RA. In addition, there are reports that question whether these JAK selectivity is actually reproduced in vivo, and verification is required. Next, regarding the metabolic pathway, baricitinib is typically the renal metabolic type, peficitinib is the hepatic metabolic type, and the other three drugs are in the middle position to varying degrees. In elderly patients who often have impaired renal function, those that are not of the renal metabolic type are desirable. Lastly, as a side effect, there are many infectious diseases such as herpes zoster, nasopharyngitis, pneumonia / bronchitis in common, and there is not much difference among the five drugs. Only testicular toxicity has been reported for filgotinib and its careful use is required for male patients. As mentioned above, in this lecture, I will add the latest findings and consider how to use JAK inhibitors aiming at efficacy and safety.

MS17

Specificity of pulmonary hypertension examined by a physician specializing in collagen disease

Tomonori Ishii
Clinical Research, Innovation and Education Center, Tohoku University Hospital

Conflict of interest: Yes

Pulmonary hypertension associated with collagen disease has several features that are not found in other types of pulmonary hypertension. The most important point in diagnosing pulmonary hypertension is that patients with collagen disease are at an increased risk for developing pulmonary hypertension. This means that with careful screening, pulmonary hypertension can be detected in pre-severe situations, or even before symptoms appear. However, it is not clear whether such an early diagnosis actually improves the prognosis of patients. It is necessary to collect data in order to verify how to select patients who need early intervention, and for that reason, it is important to develop a screening method for easily finding patients with early pulmonary hypertension. In the diagnosis, the diversity of pathological conditions of pulmonary hypertension associated with collagen disease is also an issue. In collagen disease, not only problems in the pulmonary artery, but also problems in the cardiac function itself, the presence of lung lesions, abnormalities in the pulmonary venous system, and so on can occur. All of these are pathological conditions that can cause pulmonary hypertension, and in cases of collagen disease, it is not uncommon for them to be complicated in various ways. Careful diagnosis is required to distinguish them well as they affect the treatment. On the other hand, regarding treatment, there are cases in which immunosuppressive therapy is effective because it is an autoimmune disease that can cause inflammation of blood vessels. However, immunosuppressive therapy is not effective because it is an autoimmune disease, and there are some pathological conditions such as pulmonary hypertension associated with systemic scleroderma, where the effect of immunosuppressive therapy cannot be expected. Pulmonary hypertension associated with collagen disease is expected to have different vascular lesions due to idiopathic pulmonary arterial hypertension, and it is thought that a unique perspective is required to understand the course, therapeutic effect, and prognosis. In order to collect the information necessary to consider the optimal treatment strategy for collagen-related pulmonary hypertension, it is necessary to formulate a clinical study unique to collagen-related pulmonary hypertension.

MS18

Positioning of denosumab in treatment of rheumatoid arthritis. - Data on denosumab discontinuation in RA patients without osteoporosis -

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Conflict of interest: Yes

It has been reported that denosumab (dmab), an anti-RANKL antibody, exhibits excellent effect for bone mineral density (BMD) increase and fracture prevention in osteoporotic patients, but there are cases in which rapid bone turnover elevation and BMD decrease are occurred after discontinuation, resulting in multiple vertebral fractures (MVFs). Therefore, when dmab is discontinued, the use of antiresorptive agents should be considered. In Japan, dmab was additionally approved for “suppression of progression of bone erosion associated with rheumatoid arthritis (RA)” in 2017. RA patients treated with dmab include those who are younger without osteoporosis but are at high risk of bone destruction. In these patients, discontinuation of dmab may be required during pregnancy or for other reasons, but the impact of discontinuation in RA patients has not been determined. There is also no consensus on sequential treatments. We investigated the occurrence of fractures in RA patients without osteoporosis who discontinued dmab after participating in DESIRABLE study, a Japanese phase III study in RA patients. Fracture was observed in 2 of the 81 patients surveyed. One of these patients had a symptomatic vertebral fracture, which occurred 13 months after the last dose of dmab. The patient was 75 years old, had YAM 72% lumbar spine BMD 5 months prior to the fracture, and had been taking minodronic acid at the time of the fracture. And, there was the steep decrease from YAM 88% to YAM 75% on total hip BMD before and after the fracture. Though the number of fracture was not increased by dmab discontinuation in the study, the treatment of osteoporosis after dmab discontinuation should be cared, because MVFs have occurred in a case. We are currently investigating changes in a bone turnover marker and progression of bone erosion after dmab discontinuation. In this lecture, I would like to show the results of these studies as well as to show how to utilize dmab in the treatment of RA.

Luncheon Seminar

LS1

Pain management in rheumatic diseases

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Conflict of interest: Yes

Pain has long been one of the most complaining symptoms of patients and is known to occur in a variety of causative disorders. In recent years, therapeutic agents for some rheumatic diseases such as rheumatoid arthritis (RA) have made great advances and it has become easier to control the disease process, however, many patients still complain of pain. In addition, rheumatic diseases include not only diseases with a background of immune disorders such as RA, but also diseases with pain as the main symptom such as osteoarthritis. Thus, they often need pain control in clinical practice. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin were commonly used for collagen diseases such as RA and systemic lupus erythematosus before the advent of glucocorticoids. At that time, it was usually given in large doses as an anti-inflammatory drug rather than an analgesic. However, with the advent of glucocorticoids and effective anti-rheumatic drugs, even selective cyclooxygenase-2 inhibitors are rarely used with the expectation of more than analgesic effects. In addition, the pain caused by rheumatic diseases can be caused not only by nociceptive pain associated with inflammation but also by various causes. That is, pain management in rheumatic diseases needs to be widely prescribed without being limited to NSAIDs. Although the analgesic effect of opioids, a historical analgesic, is remarkable, the use of narcotic opioids in the treatment of non-cancerous chronic pain is generally not recommended due to various adverse reactions including addiction. On the other hand, many formulations of non-narcotic opioid, tramadol with different pharmacokinetics have been approved for the treatment of chronic pain in Japan. Other analgesics include acetaminophen, which is a weakly effective but historical drug with satisfactory safety. In addition, as pain management for some rheumatic diseases, vaccinia virus-infected rabbit inflamed skin extract, neuropathic pain relievers such as pregabalin, and antidepressants such as duloxetine and amitriptyline have also been approved. In this seminar, I would like to summarize the mechanisms of action of various analgesics mentioned above and their indications, and provide JCR members with recent information on pain management in rheumatic diseases.

LS2

Evolution of T cell biology and role of CTLA4-Ig in rheumatoid arthritis

Motomu Hashimoto
Osaka City University Graduate School of Medicine, Japan

Conflict of interest: Yes

Historically, there were two major theories for the pathogenesis of RA; “T cell centric theory” and “Cytokine theory”. Early “T cell centric theory” highlighted the role of autoantibodies such as RF. It was followed by the evolution of “cytokine therapy” which implied that T cell-independent cytokine network was critical for RA pathogenesis. The latter theory led to the discovery of anti-cytokine therapies such as TNFi or IL-6Ri. On the other hand, success of CTLA4-Ig for the treatment of RA led to the reevaluation of “T cell centric theory”. Concurrently, progresses in T cell biology revealed novel T cell subsets, such as Th17, Treg, Tfh, and Tph, which together deepened our understanding for the role of T cells in RA. CTLA4-Ig selectively acts on T cell-immunity and does not affect innate immunity which play an important role for infection. Thus, CTLA4-Ig has less risk for opportunistic infection than other biologics or tsDMARDs. Even today when JAK inhibitors are developed, CTLA4-Ig is an essential therapeutic option for RA, in particular ACPA positive RA, RA-ILD, and elderly RA. In this seminar, past and recent progress in T cell biology will be presented and the role of CTLA4-Ig in RA will be discussed.

LS3

New horizon of interstitial lung diseases in patients with systemic rheumatic diseases

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Conflict of interest: Yes

Interstitial lung diseases (ILDs) are one of the main organ involvement in patients with systemic rheumatic diseases, or connective tissue diseases (CTD). CTD-ILD shows diverse histological, radiological and clinical characteristics, different response to treatment, and prognosis. CTD-ILDs are also not homogeneous even in patients with same rheumatic disease. Prevalence of ILDs are relatively high in patients with rheumatoid arthritis, systemic sclerosis, polymyositis/dermatomyositits, and ANCA-associated vasculitis. Two novel concepts regarding ILDs have been introduced into clinical research and practice; interstitial pneumonia with autoimmune features (IPAF) and progressive fibrosing-ILD (PF-ILD). The criteria of IPAF have been developed to extract and investigate interstitial pneumonia (IP) with characteristics of CTDs. The following four items are required to be classified as IPAF; 1) presence of IP by high-resolution CT or surgical lung biopsy, 2) exclusion of alternative aetiologies, 3) does not meet criteria of a defined CTD, and 4) at least one feature from at least two of clinical, serologic, and morphologic domains. Since items included in each domain are diverse, it is expected that patients satisfying these criteria are heterogeneous, which is supported by several studies of IPAF so far published. PF-ILD or chronic fibrosing ILDs with a progressive phenotype are recently proposed to describe a specific type of ILDs with poor prognosis; some patients with IIPs other than interstitial pulmonary fibrosis (IPF) or CTD-ILDs show progressive fibrosing change similar to IPF and do not respond to immunosuppressive treatments. The concept of PF-ILD was introduced along with the clinical development of nitedanib, a triple tyrosin kinase inhibitor. SENSCIS study for ILD in patients with systemic sclerosis and INBUILD study for PF-ILD promoted a better understanding of PF-ILD, but many questions are still remain unsolved and nintedanib poses several challenges to rheumatologists and pulmonologists treating CTD-ILD.

LS4

The inhibitory effect on bone erosion in Rheumatoid Arthritis

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Conflict of interest: Yes

The prevalence of osteoporosis is escalating with the increasing elderly population. Similarly, this trend is also seen in rheumatic diseases (eg, rheumatoid arthritis: RA) resulting in a potential increase in risk of fracture. The fracture risk in RA patients is also explained by both bone-related factors (underlying osteoporosis, medications to lower bone density, underlying diseases) and fall-related factors (including risk of falls and sarcopenia related to the locomotive syndrome). Erosion progression in the joints in RA patients led to significant morbidity, mortality, and decreased quality of life. Thanks to the advance of RA treatments, now, almost ten years have past since we called “Non-Erosive Era”. It is broadly understood and recommended in the treatment recommendations that if remission cannot be achieved with methotrexate, introduction of biologic therapy should be considered for RA patients, and can result in significantly better clinical and radiographic outcomes compared to routine care. However, biologic therapy continues to involve substantial barriers preventing all patients from receiving these benefits, including high costs, co-morbidity (ie, interstitial lung disease, renal and liver dysfunction, advanced age), adverse drug reactions including infection, and incomplete safety data in long-term administration. In these circumstances, phase three trial in RA patients with denosumab, anti-receptor activator of nuclear factor-kappa B ligand (RANKL) antibody, showed a significant inhibitory effect on erosion progression. In this session, we aim to introduce a recent advance in the management of osteoporosis and rheumatoid arthritis, especially focusing of denosumab. In addition, we would update glucocorticoid induced osteoporosis (GIO) management in daily practice.

LS5-1

Usefulness of tocilizumab in elderly patients with rheumatoid arthritis

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Conflict of interest: Yes

In Japan, which has become an aging society, the average age of rheumatoid arthritis (RA) patients is also increasing. Therefore, rheumatologists need to cope with an increase in the number of elderly patients including elderly-onset rheumatoid arthritis (EORA) who developed at more than 65 years old and RA patients who became older after developing at a young age (younger-onset RA, YORA). Elderly RA patients often have pulmonary and renal dysfunction as well as atherosclerotic lesions such as heart disease and hypertension. These comorbidities often limit anti-rheumatic treatment options, and their exacerbations often force changes in anti-rheumatic treatment. In addition, high number of medications for these comorbidities (polypharmacy) triggers further complications. On the other hand, it has been reported that EORA has significantly higher disease activity at the first visit and lower physical quality of life than YORA (Murata K, *et al, IJRD*, 2019). Elderly RA with high disease activity can also lead patients from frailty to irreversible disability with taking too much care of safety. From the above, as treatments for elderly RA, 1) to pay attention to adverse reactions such as infectious diseases and lymphoma, 2) to pay attention to drug interactions, and 3) to perform a tight controlled treatment with sharing an appropriate treatment goals with patients (shared- decision making), are required. The EULAR recommendation for the management of RA with synthetic and biological disease-modifying antirheumatic drugs (2019 update) clearly stated that "Treatment decisions are based on disease activity, safety issues and other patient factors, such as comorbidities and progression of structural damage". In this seminar, we would like to discuss anti-rheumatic treatment for the elderly RA patients, where safety is important, and shows the usefulness of tocilizumab, an IL-6 signal inhibitor.

LS5-2

Rheumatoid Arthritis Treatment Strategy to Increase Safety -In an Aging Society-

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Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), methotrexate (MTX) biologics (Bio) and JAK inhibitors (JAKi) has greatly improved the clinical outcomes. Tapering of treatment should be carried out based on the maintenance of disease activity control, but it is also important whether it can improve economic efficiency and safety. In the treatment of Bio and JAKi, the concomitant use of MTX is considered to be critical for good treatment results. When considering Tapering, from the perspective of improving economic efficiency, dose down or discontinuation of Bio and JAKi has a great impact. In daily practice, there are many safety problems associated with long-term use of MTX (Gastrointestinal symptoms, renal dysfunction, medication adherence due to cognitive decline, immunodeficiency-related lymphoproliferative disorders, etc). To avoid this problem, MTX dose down or discontinuation during Bio and JAKi treatment is also an option for Tapering. There have been many reports of the usefulness of monotherapy without MTX for tocilizumab. We conducted a multicenter joint study (funded by Chugai Pharmaceutical Co., Ltd.) at Nagoya University and related hospitals. We examined the maintenance of low disease activity after discontinuation of MTX during tocilizumab treatment (TReX study). Low disease activity was maintained in 76% (95% CI 61-87%) at 24 weeks and 69% (95% CI 55-82%) at 52 weeks after discontinuation of MTX (Mod Rheumatol 2020, Joint Bone Spine 2020). It shows a tendency to reduce gastrointestinal symptoms and is considered to be a useful method in daily clinical practice. We believe that strict control of disease activity over a long period of time is necessary to prevent the deterioration of frailty and locomotive syndrome, which are general indicators of physical function related to healthy life expectancy (Mod Rheumatol 2020). As patients become super-aged, increasing safety and maintaining disease activity control will become increasingly important in the future, together with interventions by exercise therapy.

LS6-1

Interstitial lung disease associated with polymyositis/ dermatomyositis

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Conflict of interest: None

Polymyositis/Dermatomyositis (PM/DM) is often accompanied by interstitial lung disease (ILD) which is one of the important prognostic factors. Recently, myositis-specific autoantibodies (MSAs) have been focused on their usefulness in subclassification of myositis. Among MSAs, anti-aminoacyl-tRNA synthetase (ARS) antibody and anti-melanoma differentiation-associated gene 5 (MDA5) antibody have the strongest association with ILD. In Japan, anti-ARS can be detected in about 40-50% of PM/DM-ILD patients and anti-MDA5 in about 25-30%. ILD with anti-ARS tends to show chronic disease course and respond well to initial glucocorticoid (GC) therapy but often recur. The 5-year survival of anti-ARS-positive patients is 90-95%, but 10-year-survival gradually falls down to 70-80%. This is mainly due to repetition of recurrence resulting in deterioration of pulmonary function. Moreover, activity of daily living (ADL) can also deteriorate because of side effects from long-term steroid use or necessity of home oxygen therapy. Thus, 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 recommended. Moreover, additional antifibrotic agents may give some benefits in patients with progressive fibrosing ILD. On the other hand, anti-MDA5-positive patients often show acute/ subacute ILD which is resistant to treatment, showing rapidly progressive respiratory distress. For these 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 has also been expected in terms of controlling interferonopathy. Thus, MSAs can be useful in prediction of clinical course and determination of treatment strategy in PM/DM-ILD.

LS6-2

Renal Injuries associated with Collagen Diseases

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Conflict of interest: Yes

Renal injuries are often associated with collagen diseases. Kidneys are directly injured by collagens diseases or subsequently injured by hypertension and diabetes mellitus, which are complicated with collagens diseases, and by drugs for collagen diseases. Lupus nephritis and ANCA-related nephritis are the typical renal injuries directly associated with collagen diseases. In this seminar, the treatment of lupus nephritis and ANCA-related nephritis will be focused on, and the future perspectives will also be presented. For the treatment of lupus nephritis, the "Systemic Erythematosus Clinical Practice Guideline 2019" was produced by the Japanese Society of Rheumatology in 2019, and treatment recommendations, including lupus nephritis, were presented. For first-line induction therapy, moderate to high doses of glucocorticoids (GC) with mycophenolate mofetil (MMF) or cyclophosphamide IV (IVCY) is recommended for Class III/IV, and moderate doses of GC and MMF are recommended for Class V. A combination therapy of MMF + tacrolimus (TAC) is also proposed as an alternative therapy for Class III/IV. TAC is proposed as an alternative therapy for Class V. For maintenance therapy, MMF or azathioprine (AZA) is recommended for Class III/IV, and TAC is also proposed. MMF, AZA, or calcineurin inhibitors are proposed for Class V. ANCA-associated nephritis is a renal injury complicated with ANCA-associated vasculitis, which pathologically causes pauci-immune crescentic necrotizing glomerulonephritis. Clinically, it often presents with rapidly progressive glomerulonephritis syndrome. The Japanese Society of Nephrology produced the "Evidence-based Rapidly Progressive Nephritic Syndrome RPGN Clinical Practice Guideline 2020", which provides treatment recommendations for

ANCA-associated RPGN. The content of the guideline will be introduced in the seminar.

LS7-1

New Era of Molecular Targeted Drugs Demonstrated by Upadacitinib Head-to-Head Studies

Kei Ikeda
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Conflict of interest: Yes

Advances in drugs for the treatment of rheumatoid arthritis (RA) have entered a new phase by the approval of JAK inhibitors that target Janus kinases (JAK). Upadacitinib, which was launched in April 2020 as the 4th JAK inhibitor, has been investigated in domestic and global clinical studies (SELECT program) targeting various patients. In particular, the head-to-head studies with biologics are valuable in considering the positioning of JAK inhibitors and upadacitinib in the RA treatment strategy. In SELECT-COMPARE trial, upadacitinib demonstrated greater efficacy in combination with methotrexate (MTX) than a TNF inhibitor adalimumab in head-to-head comparison in subjects with MTX-inadequate RA. Furthermore, in SELECT-CHOICE trial, upadacitinib demonstrated higher efficacy than non-TNF inhibitor biologics (CTLA4Ig, abatacept) for the first time in patients with inadequate response to biologics in head-to-head comparison. These studies have broadened the potential of molecularly targeted therapies to treat RA and have led to a paradigm shift. On the other hand, JAK inhibitors still have safety concerns and uncertainties in their mechanism of action. In this lecture, the positioning and possibility of upadacitinib will be discussed based on the evidence of JAK inhibitors including the above two studies.

LS7-2

Upadacitinib-monotherapy is one of the novel treatment strategy to achieve various remissions in rheumatoid arthritis. ~Ultrasound examination seek out the value of the real-efficacy of upadacitinib to the RA patient~

Kenta Misaki
Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

One decade has pasted after first-publication of RA-EULAR recommendation. We rheumatologists have experienced many paradigm shifts concerned with RA diagnosis and treatment during this 10 years, moreover can actually implement those to RA patients in clinical setting. ACPA is approved in medical insurance in terms of RA-diagnosis, however the diagnosis of seronegative RA has been become a major topic of discussion also in this new decade. The approval of musculoskeletal ultrasound examination (MSKUS) is also noteworthy for RA-diagnosis as one of the imaging procedures. MSKUS make it possible to depict the real-time pathological findings without harm nevertheless no findings by physical examination, and make a huge contribution to early seronegative RA-diagnosis. JAK inhibitors (JAKi) have been shared the spotlight with biologic agents since 2013 in our country. Upadacitinib (UPA) is a next-generation JAKi selective for JAK1 and has many novel RCTs. Especially the evidence of UPA-monotherapy is innovative and totally considered not only the clinical and structural remissions but also patient reported outcomes (PROs). Additionally, it is strongly expected that UPA-monotherapy is going to resolve the current issue about RA poly-pharmacy in this new era. In this session, I'm going to discuss about the strategy of UPA-monotherapy and real time RA evaluation by using MSKUS including our original case-reports under the treatment of UPA focused on both efficacy and safety.

LS8-1

Lung involvement in rheumatoid arthritis

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Conflict of interest: Yes

Lung involvement is one of the most common comorbidities in patients with RA. Among them, interstitial lung disease (ILD) and airway diseases (AD) are the mainstay of the diseases. Recently, "The Guide for the diagnosis and treatment of Interstitial Lung Diseases associated with Connective Tissue Disease 2020" and "Consensus statements for medical practice: Biological agents and lung disease for inflammatory diseases, 2nd Edition" were published by the Japanese Respiratory Society together with Japanese College of Rheumatology. In this seminar, the clinical presentation, diagnosis, and treatment for ILD and AD associated with RA will be discussed along with those new statements.

LS8-2

Role of T cells in rheumatoid arthritis and ILD

Hiroaki Niiro
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Conflict of interest: Yes

The pathogenesis of rheumatoid arthritis (RA) consists of autoimmunity, arthritis, and joint destruction. Autoimmunity already exists in the pre-arthritic phase, called at-risk individuals, and the lung is particularly important for the propagation of autoimmunity. In the lungs, inducible bronchus-associated lymphoid tissue (iBALT) is closely related to the production of autoantibodies such as anti-CCP antibodies (ACPAs) in the pre-arthritic phase through T-B cell interactions. In the arthritic phase, autoimmunity is further sustained by such T-B cell interactions at joints, and at the same time, arthritis is induced by neutrophils/macrophages and synoviocytes, and joint destruction is caused by osteoclast activation. Patients with RA often have various extra-articular complications including interstitial lung disease (ILD). T cells play a critical role in these processes. Abatacept (ABA), a CTLA4-Ig fusion protein, inhibits T cell activation by blocking co-stimulation from other cells. This biologic may be favorably used in seropositive cases, early-onset cases, elderly cases, and cases with ILD. On the other hand, given that T cells are also important for host defense against infection, the mechanism of action of ABA would raise concerns about its safety. This drug, however, has been used safely in both clinical trials and actual clinical practice. Along with a growing awareness of T cell subsets with different functions, ABA may not indiscriminately inhibit the activation of all T cells. In actual clinical practice, however, it is strongly recommended that ABA be used with careful consideration of the risk-benefit balance for each individual patient. Pathogenic autoreactive lymphocytes remain even in the stage of clinical remission in patients. Further studies are required to determine to what extent ABA, equipped with unique mode of action (a biologic like no other), can prevent the propagation of autoimmunity, the root of the pathogenesis of RA.

LS9-1

Importance of Introducing RA Early Remission-Based on Treatment Strategies for Young Female Rheumatoid Arthritis-

Atsushi Nakano
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Conflict of interest: None

In RA, the emergence of drugs targeting inflammatory cytokines by biologics / JAK inhibitors has made it possible to formulate therapeutic strategies premised on the induction of remission. However, there is a so-called "Window of Opportunity" in RA treatment, and the delay in the start of treatment limits the therapeutic effect. In recent years, it has been suggested that not only disease susceptibility genes but also epigenetic alteration are deeply involved in the onset and severity of RA. Persistent inflammation induces treatment resistance of RA. Recent studies on synovium suggest that long-term exposure to inflammatory cytokines may result in a more aggressive and refractory phenotype by altering the epigenome of resident cells in synovial tissue. The first half outlines the possible molecular basis for the relationship between synovial inflammation and epigenome alteration. From this point of view, it is important to determine the efficacy of the b/tsDMARDs as soon as possible and avoid continuous exposure to inflammatory cytokines until accurate biomarkers are established in RA clinical practice. Especially in young women with early-onset, it is desirable to avoid the acquisition of treatment resistance for RA in

order to prepare for subsequent life events. In this lecture, I would like to introduce the preliminary results of our ongoing clinical research and consider the optimization of RA treatment.

LS9-2

Treatment Strategies for Young Women with Rheumatoid Arthritis

Hiroaki Dobashi
Kagawa University

Conflict of interest: Yes

The treatment strategy of Rheumatoid Arthritis (RA) had greatly advanced with the development of many therapeutic drugs including csDMARDs, bDMARDs, and tsDMARDs. A lot of efficacy and safety evidence for such drugs has been established, which also contributed to this advancement. However, the RA treatment strategy should be decided for individual patients based on not only his/her disease activity, but also other factors such as comorbidities, as stated in the overarching principles of 2016 EULAR Recommendation for RA Treatment: "Treatment of decisions are based on disease activity and other patient factors, such as progression of structural damage, comorbidities and safety issues." RA is a common disease in women and one of the important life events in a woman's life is pregnancy / childbirth. Pregnancy / childbirth is a woman's right and not an obligation, but many women want to acquire motherhood and are no exception to RA patients. Therefore, establishing a treatment strategy for young female RA patients is an unavoidable problem for rheumatologists. Since it has been reported that the proportion of unplanned pregnancies is high in the younger generation, we practice preconception counseling for all patients regardless of whether or not they wish to have a baby, and confirm contraceptive method guidance and future pregnancy wishes. It is necessary to make a treatment selection after this. In addition, A treatment strategy for a young woman RA patient should be decided individually for each of the three pregnancy phases (preconception, during pregnancy, after pregnancy). This talk will present typical characteristics and necessary considerations in young woman RA patients and a proposal for the treatment strategy in such patients. As a result, this talk aims to discuss about "how to support RA patients who hope to become a mother." A patient wish is written down in the ACR draft guideline of reproductive health of ACR as "My rheumatologist knows me better than gynecologist." I hope this seminar will be helpful for the audience to meet this wish of young woman RA patients.

LS10

Latest trend of osteoporosis treatment - paradigm shift due to the arrival of anti-sclerostin antibody -

Kosuke Ebina
Department of Musculoskeletal Regenerative Medicine, Osaka University Graduate School of Medicine

Conflict of interest: Yes

According to the arrival of various new osteoporosis therapeutic agents (anti-bone resorption, bone anabolic, and dual effect agents), goal-directed treatment for osteoporosis has been recommended to reduce imminent fracture risk. In addition, it is of great interest to investigate effective sequential and combination osteoporosis treatment strategy considering whole lifespan. One novel anti-osteoporosis agent is romosozumab, a monoclonal anti-sclerostin antibody that promotes bone formation and inhibits bone resorption, which is called "dual effect". In this symposium, I would like to present latest evidences and discuss about the new goal-directed treatment strategy.

LS11

Long-term efficacy and safety of Tofacitinib

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

Conflict of interest: Yes

Eight years have passed since tofacitinib was introduced as a tsDMARD for the treatment of rheumatoid arthritis. As the first JAK inhibitor, Tofacitinib has contributed significantly to the history of JAK inhibitors. Due to its long-term use, EULAR recommendations now treat it at the same position as bDMARDs. In this seminar, I will talk about recent findings and long-term clinical data of Tofacitinib and other JAK inhibitors from a basic and clinical perspective. In terms of mechanism of action, Tofacitinib is a pan-JAK inhibitor. There are various debates about whether JAK selectivity make differences on efficacy and safety. Each JAK is involved in different cytokines, and since each cytokine is involved in its actions and side effects, there are advantages and disadvantages of various selectivity. However, it does not seem to make a big clinical difference so far. From a clinical point of view, Tofacitinib is as effective as biologics. In clinical trials for various patients in the background of DMARD inadequate response (IR) cases, MTX-IR cases, TNF inhibitor refractory cases, and monotherapy cases, the effectiveness of Tofacitinib has been shown. The major advantages of using Tofacitinib in daily practice is shown by the facts that the effect is exhibited from an early stage, that oral administration is possible, and that there is evidence of monotherapy. In RA treatment, various clinical issues remain, such as dealing with patients who do not remit and improving QOL. Since Tofacitinib improves PRO, it is expected to be effective in these respects as well. Regarding safety, Tofacitinib has been used in more than 10,000 patients in post-marketing surveillance in Japan, and data has been accumulated. The results of a 9.5-year long-term administration study have also been published, and evidence for long-term efficacy and safety has been established. In recent years, the risk of deep vein thrombosis with high doses of 10 mg x 2 times has been reported for patients with cardiovascular risk. The benefits of Tofacitinib can be maximized by using it while paying attention to safety.

LS12

Imaging for joints in rheumatoid arthritis

Isao Matsushita
Kanazawa Medical University, Japan

Conflict of interest: Yes

Plain radiographic examination is a basic tool to assess joint damage in RA. Radiograph shows pocket erosion in bear areas, joint space narrowing and roughness of subchondral bone in RA. Modified total Shrap score is a global standard method for the evaluation of small changes of joints in early stage of RA. However, only small joints in hands and feet are assessed by this scoring system. We developed ARASHI scoring system for the evaluation of large joint damage in RA. This scoring system is well related to Larsen grade and further detail of large joint changes can be evaluated. Ultrasonography (US) in RA is a very useful tool to make early diagnosis and to evaluate efficacy of treatment. Thickness of synovium and effusion are detected using gray scale method of US, and abnormal vascular signal can be detected by power Doppler method. Using US, sensitivity and specificity for detecting synovitis is as high as MRI. US is useful tool for early diagnosis of RA. MRI is more sensitive than conventional radiography in detecting bone erosions in early RA. MRI erosion is detected as a well-defined area of abnormal signal. MRI can identify bone edema in patients with RA which cannot be visualized by radiographic technique. Bone marrow edema has been described as an ill-defined area of abnormal signal intensity. The presence of bone marrow edema can be a marker of inflammatory activity of RA and be defined as a pre-erosive lesion which enables us to predict joint damage. HR-pQCT has been reported to be a more sensitive than MRI for the detection of bone erosion due to its high resolution. HR-pQCT can assess joint space narrowing with high accuracy using 3D reconstruction images. In this session, I will talk about the basics of imaging assessment and recent topics in RA.

LS13

Potential of Salilumab

Kensuke Oryoji
Center for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: Yes

Treatment of rheumatoid arthritis should be started with methotrexate if there are no contraindications, and biologics or JAK inhibitors should be used if inadequate response or adverse effects preclude their use and if

there are poor prognostic factors. IL-6R inhibitors have been shown to have an advantage among biologics, especially when csDMARDs such as methotrexate are not concomitantly available (Ann Rheum Dis. 2017; 76:960-). On the other hand, factors such as methotrexate-associated lymphoma and impaired renal function make the use of methotrexate more difficult in elder patients with rheumatoid arthritis. Patients with rheumatoid arthritis in Japan are aging, with 60% of patients over 65 years of age and 48% over 70 years of age in our hospital. The biologic agent whose efficacy is least likely to be affected by the presence or absence of methotrexate is tocilizumab, an anti-IL-6 receptor agent. We have also reported that the HLA-DRB1 genotype affects the efficacy of abatacept (Ann Rheum Dis. 2018;77:1234-1236.), but tocilizumab is more versatile in this aspect because of the lack of difference in efficacy by genotype. Sarilumab, an anti-IL-6 receptor agent similar to tocilizumab, has been approved in Japan and has been shown to have similar characteristics to tocilizumab in clinical trials and appears to have a rapid onset of efficacy. This presentation will review the pathophysiology of rheumatoid arthritis and the appropriate patient profile of sarilumab from both a basic and clinical perspective.

LS14-1

Diagnosis and management of SSc-ILD

Yasushi Kawaguchi
Department of Rheumatology, Tokyo Women's Medical University

Conflict of interest: Yes

Interstitial lung disease (ILD) complicates in >60% of patients with systemic sclerosis (SSc). Progressive ILD is seen in around 30% of patients with SSc-ILD, of whom therapeutic intervention is needed. However, early identification of patients with progressive ILD are as yet challenging. Generally, the following factors should be accounted for considering treatment indication; the extent of lung fibrosis, the severity of pulmonary dysfunction, progressive fibrosis over time, and known risk factors for progressive ILD. Cyclophosphamide (CYC) and mycophenolate mofetil (MMF) are included as main conventional medications for treatment of SSc-ILD, of those efficacy and safety were evaluated in phase III clinical trials named SLS-I and SLS-II, respectively. Nintedanib, a tyrosine kinase inhibitor with antifibrotic properties, has shown to have an inhibitory effect of SSc-ILD in SENSCIS trial which included mild SSc-ILD patients. The remaining issues to be clarified with nintedanib include timing of its use, additive effects on other medications, and its impact on long-term survival. In this session, we will discuss therapeutic strategies of SSc-ILD using immunosuppressive and antifibrotic agents as well as clinical unmet needs, and future perspectives of SSc-ILD management.

LS14-2

Management of SSc-ILD- role of immunomodulatory and anti-fibrotic therapies

Dinesh Khanna
University of Michigan, Ann Arbor, USA

Conflict of interest: Yes

Systemic sclerosis related interstitial lung disease (SSc-ILD) is leading cause of mortality. Lung fibrosis occurs in approximately 80% of patients with SSc; 25% to 30% develop progressive ILD. The pathogenesis of fibrosis in SSc-ILD involves cellular injury, activation of mesenchymal cells, and biological changes in epithelial and endothelial cells. Recent trials have shown beneficial effect of targeted therapies on attenuating and preserving the lung function in those with ILD and at-risk of progressive ILD. The symposium will discuss the recent data from large clinical trials on the management of SSc-ILD, including use of immunomodulatory and anti-fibrotic therapies and provide a practical overview of incorporating this in clinical practice.

LS15-1

Eli Lilly Sponsored Seminar: "Strategy for management of RA: Updated evidence from JAK"

Ulf Müller-Ladner
Department of Rheumatology and Clinical Immunology, Justus-Liebig University Giessen, Campus Kerckhoff, Bad Nauheim, Germany

Conflict of interest: Yes

The treatment goal of rheumatoid arthritis (RA) is to maximize long-term health-related quality of life through control of symptoms, prevention of joint damage, and normalization of physical function. The management of RA has been progressed in recent twenty years. New criteria for classification and remission, robust methods to measure disease activity status, setting of treatment target, development of innovative new drugs, and generating treatment algorithm, all contribute to the progress. The advent of molecular-targeting therapy has enabled us to follow the strategy more precisely. Biologic disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) are the two categories of molecular-targeting drug for the treatment of RA. In the treatment algorithm of European League Against Rheumatology (EULAR), these two types of DMARDs are indicated in patients who cannot achieve treatment goal with methotrexate or other conventional synthetic DMARDs (csDMRADs) within six months or who are intolerant to them. Evidence for efficacy and safety of tsDMARDs, JAK inhibitors, have been accumulated to date. Tofacitinib (2013), baricitinib (2017), peficitinib (2019), upadacitinib (2020), and filgotinib (2020), are approved in Japan. Baricitinib is a selective inhibitor of JAK1 and JAK2, which are involved in signal transduction of interleukin (IL)-2, IL-6, IL-15, interferon-gamma, and granulocyte-macrophage colony stimulating factor. In this session, I would like to discuss the positioning of JAK inhibitors with the updated EULAR Recommendations and the guidelines of German Society of Rheumatology. Also, as long-term evidence has been accumulated, benefit-risk balance and proper use of baricitinib will be discussed based on the latest evidence from clinical trials.

LS15-2

To achieve target of treating RA

Tatsuya Atsumi
Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Hokkaido University

Conflict of interest: Yes

The concept of Treat to Target (T2T) has been established as the treatment strategy with having clear treatment goals in daily practices. Today, we have many treatment options to treat Rheumatoid Arthritis (RA), which has enabled us to aim at various levels of treatment goals to meet different patient's needs. As discussed in the latest EULAR Recommendations, the treatment strategy has been changing. One example is that the descriptions related to targeted synthetic DMARDs (tsDMARDs), JAK inhibitors, has been updated. Compared to biological DMARDs (bDMARDs) that inhibits a single cytokine, JAK inhibitors inhibit multiple cytokines intermittently to control inflammation. As of November 2020, five JAK inhibitors has been approved for treatment of RA in Japan. Baricitinib is a selective inhibitor of JAK1 and JAK2, which are involved in signal transduction of cytokines such as IL-6, GM-CSF, and interferon-gamma. In this session, I would like to overview the roles of cytokines to discuss the positioning of tsDMARDs in the latest RA treatment strategy. The efficacy and safety profiles of baricitinib will also be discussed based on not only the evidence from clinical trials but also real-world evidence from post-marketing surveillance.

LS16-1

IL-6 inhibition in adult-onset Still's disease

Yuko Kaneko
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Conflict of interest: Yes

Adult-onset Still's disease is a rare, systemic inflammatory disorder of unknown aetiology that is characterised by high spiking fever, evanescent rash, and polyarthritis. The pathogenic mechanisms of adult-onset Still's disease are not fully understood, but the pivotal role of innate immunity involving macrophage and neutrocyte activation with hyperproduced interleukin-1β and interleukin-6 has been demonstrated. The mainstay of its

treatment has been glucocorticoid, and the response to glucocorticoid in adult-onset Still's disease is generally good, however, fatal complications refractory to high dose glucocorticoids and the frequent recurrence along with glucocorticoids dose reduction or discontinuation is still problematic in clinical practice. An IL-6 inhibitor, tocilizumab has been approved for rheumatoid arthritis and Catleman's disease. Progress in the understanding of the pathogenesis of adult-onset Still's disease has revealed the important role of IL-6, and the effectiveness of tocilizumab has been shown in many cases of adult onset Still's disease. And, a randomized, double-blinded, placebo-controlled trial has demonstrated the efficacy of tocilizumab in suppressing systemic inflammation and reducing the dose of glucocorticoids. In this session, I am going to discuss the role of IL-6 and IL-6 inhibition in the management of adult-onset Still's disease.

LS16-2

Interleukin-6 inhibition in patients with large-vessel vasculitis

Masayoshi Harigai
Department of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: Yes

Large-vessel vasculitis (LVV) involves aorta and its primary branches, and consists of Takayasu arteritis (TAK) and giant cell arteritis (GCA). The latest epidemiological study in Japan estimated the number of patients with TAK and GCA as 4882 and 2623, respectively. Corticosteroid and/or immunosuppressants were mainstay drugs for a long time, but tocilizumab (TCZ) has been approved in 2017 to change treatment strategies of these two diseases. TAKT study investigated efficacy and safety of TCZ-SC (162 mg QW) in patients with TAK. Time to relapse in the TCZ-SC group was longer compared to the placebo group albeit barely missing the significant level in ITT population, and a significant difference was observed in PSS population. In the long-term extension of TAKT study, CS dose continuously decreased throughout the study period, imaging evaluations showed improved or stable disease in 85.7% of the patients, and SF-36 improved in seven of eight domains. GiACTA study investigated efficacy and safety of TCZ-SC (162 mg QW or Q2W) in patients with GCA. Proportions of patients with sustained remission at week 52 were significantly higher in the two TCZ-SC groups compared to the placebo groups, and a significant CS-sparing effect was observed in the TCZ-SC groups. In patients with flare at baseline, only TCZ-SC QW group significantly suppressed flare of GCA than the placebo groups. Flares of GCA without elevation of CRP were observed in 33 of 36 patients (92%) in the TCZ-SC groups and in 20 of 59 patients (34%) in the placebo groups. SF-36 and FACIT-FATIGUE score significantly and clinically meaningfully improved in TCZ-SC QW group versus placebo groups. At week 52, health-related quality of life recovered to levels at least comparable to those of age and sex matched normative values, and exceed normative values in five of eight domains. In this seminar, treatment strategy will be discussed based on the latest evidence of IL-6 inhibition for LVV. 1. Ann Rheum Dis 2018;77:348-354 2. Rheumatology 2020;59:2427-2434 3. N Engl J Med 2017;377:317-28. 4. Arthritis & Rheumatology 2019;71:1329-1338 5. Arthritis Research & Therapy 2019;21:64

LS17-1

Significance of TNF inhibitor from the viewpoint of joint destruction mechanism in patients with rheumatoid arthritis centered on the proinflammatory cytokine tumor necrosis factor alpha

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Conflict of interest: None

One of the characteristics of rheumatoid arthritis (RA) is the excessive production of proinflammatory cytokines locally and systemically in the joint and the formation of osteolysis (bone erosion) occurs in juxta-articular sites. The bone erosion formation is caused by excess proinflammatory cytokines and results from an imbalance between osteoclast-mediated bone resorption and osteoblast-mediated bone formation. Osteoclast differentiation and bone resorption capacity are regulated by osteoclast differentiation factor (receptor activator of nuclear factor kappa-B ligand; RANKL) and proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6). Recently, we have discovered that cultured mouse bone marrow cells or human peripheral blood mononuclear cells (PBMCs) can be differentiated into TNF-α and IL-6-induced osteoclasts in the presence of the combination of TNF-α and IL-6. These cells are distinct from conventional osteoclasts. We further clarified that these TNF-α and IL-6-induced osteoclasts can absorb bone matrix both in vitro and in vivo and that they are RANKL-independent. We have also demonstrated that the numbers of TNF-α and IL-6-induced osteoclasts derived from PBMCs of RA patients are positively correlated with the bone destruction score (modified total Sharp score, mTSS) of the same patients, whereas the numbers of conventional osteoclasts were negatively correlated with the bone mineral density of the whole body. These data indicate that TNF-α and IL-6-induced osteoclasts are a novel class of osteoclasts and that they may play an important role in bone destruction and absorption in the affected joints of RA patients. In this seminar, we will discuss the significance of TNF inhibitor from the viewpoint of joint destruction mechanism by proinflammatory cytokines as a therapeutic strategy to prevent joint destruction in patients with RA, using the latest findings and our basic research data.

LS17-2

The mechanisms and countermeasure against bone and joint destruction associated with rheumatoid arthritis

Kosuke Ebina
Department of Musculoskeletal Regenerative Medicine, Osaka University Graduate School of Medicine

Conflict of interest: Yes

Major goal of the treatment in rheumatoid arthritis (RA) is obtaining both clinical and structural remission, preventing consequent physical disorders, and improving vital prognosis. In fact, it has been reported that most strong desire of RA patients is to obtain structural remission. However, in clinical practice, progression of joint destruction is frequently observed even in patients who obtained clinical remission assessed by laboratory test or composite measures. This may be due to 1) lack of understanding in high risk cases of joint destruction, 2) delay of obtaining clinical remission, 3) remaining synovitis of small joints such as fingers or toes which is not always reflected in laboratory tests, and 4) difficulty in the assessment of radiographic joint destruction in routine clinical practice. To improve these problems, 1) early identification of high risk cases with aggressive therapy, 2) careful assessment of both small joints and deep joints arthritis, and 3) routine radiographic assessment for joint destruction are required. On the other hand, after obtaining deep remission, tapering of glucocorticoids, csDMARDs, and biologics towards the reduction of side-effects and medical expense is gathering great attention (so-called, "beyond-remission"). This lecture aims to share the up-to-date information about 1) the risk of joint destruction and appropriate evaluation and 2) the evidence of "early and deep remission" and consequent tapering or discontinuation of biologics, which may lead to the optimization of RA treatment.

LS18

Role of TNF Inhibitors in Elderly-onset Rheumatoid Arthritis

Kimito Kawahata
Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine

Conflict of interest: Yes

The past two decades saw a significant change in management of rheumatoid arthritis with the advancement of therapeutic drugs and treatment approaches. As a result, the remission rate, which had been only about 10% around the year 2000, is now from 40% to 50%. In recent years, however, no great change has been seen in the remission rate. For further improvement, there are some challenges to overcome, for example: treatment in patients with refractory conditions, concurrent diseases, or complications. With the extreme societal aging, the patient age and onset age are remarkably increasing, and compounded with the fact that the remission rate in the elderly is slightly lower, this means that optimizing treatment for such patients is also a critical challenge. The advancing age of

onset is associated with various problems in clinical practice such as limitations to treatment due to concurrent diseases and complications; polypharmacy; management of adverse drug reactions; and ways of specialized treatment in community healthcare. These problems call for reflecting the advancement of recent therapeutic drugs, particularly molecular targeted drugs, on individual treatments in a safe and effective manner. Although TNF inhibitors have a long history among molecular targeted drugs, their characteristics have come to be recognized again with the launch of new drugs. In this lecture, I am going to describe the current practice for treating elderly-onset rheumatoid arthritis and the role TNF inhibitors should play in said treatment.

Afternoon Seminar

AS1

Simplifying RA management and preventing structural joint damage with filgotinib, a once-daily oral JAK inhibitor

Paul Emery
Leeds Institute Rheumatic and Musculoskeletal Medicine University Leeds, Leeds NIHR Biomedical Research Centre, The Leeds Teaching Hospitals Trust, Leeds UK

Conflict of interest: Yes

On behalf of Gilead K.K. and Eisai Co., Ltd., please join us for a dynamic virtual presentation by Prof. Paul Emery focused on contemporary management strategies for rheumatoid arthritis (RA) and the latest clinical data for filgotinib - a once-daily oral JAK1 inhibitor for the treatment of RA in patients who have had an inadequate response to conventional therapies, including the prevention of structural joint damage. The 2019 update of the EULAR recommendations for the management of RA reinforces that clinical remission and low disease activity are the optimal therapeutic targets for patients with RA, with the long-term goal of inhibiting progression of structural joint damage. In patients who have not achieved their treatment target with initial csDMARD therapy, EULAR recommends adding either a bDMARD or tsDMARD (ie, JAK inhibitor) based on the latest evidence regarding the long-term efficacy and safety of JAK inhibitors. Filgotinib is a newly approved JAK inhibitor that, in combination with methotrexate, demonstrated strong efficacy in preventing structural damage and achieving clinical remission in patients with inadequate response to methotrexate alone. Filgotinib 200 mg demonstrated superiority versus placebo for prevention of structural damage as measured by modified total Sharp score (mTSS). In addition, patients treated with the higher dose of filgotinib (200 mg) did not experience dose-dependent increases in the rates of JAK inhibitor-associated adverse events such as herpes zoster and venous thromboembolism during the 52-week trial. Data from ongoing long-term safety studies have further corroborated the safety observations from randomized controlled trials. The presentation will also discuss appropriate patient selection for filgotinib and ongoing patient management strategies.

AS2-1

Regulatory mechanism of bone remodeling by cytokines

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Conflict of interest: None

Bone is constantly renewed by the balanced action of osteoblastic bone formation and osteoclastic bone resorption both of which mainly occur at the bone surface. This restructuring process called “bone remodeling” is important not only for normal bone mass and strength, but also for mineral homeostasis. Bone remodeling is stringently regulated by communication between bone component cells such as osteoclasts, osteoblasts and osteocytes. During bone remodeling, resorption by osteoclasts precedes bone formation by osteoblasts. Based on the osteocyte location within the bone matrix and the cellular morphology, it is proposed that osteocytes potentially contribute to the regulation of bone remodeling in response to mechanical and endocrine stimuli. An imbalance of this process is often linked to various bone diseases such as Osteoporosis, Osteopetrosis and Rheumatoid arthritis. RANKL derived from osteocyte currently provides a paradigm that enables the molecular understanding of osteoclastogenesis. On the other hand, Sost is the key regulators of bone formation by suppressing osteoblasts. In excessive bone destruction and/or formation with Rheumatoid arthritis and Spondyloarthritis, inflammatory cytokines such as IL-17 have a great effect. Cytokines expressed in these osteocytes and immune cells have attracted attention as therapeutic targets and is currently bringing the gospel to the medical field. Furthermore, recently, the molecular basis of a new therapeutic strategy targeting the Semaphorin identified as a new bone remodeling regulator has been established, and future applications are expected.

AS2-2

New Insights for Clinical Practice in SpA

Denis Poddubnyy
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Conflict of interest: Yes

Spondyloarthritis (SpA) is a common term for a group of diseases sharing genetic background (e.g., an association with HLA-B27), pathophysiological mechanisms (e.g., a leading the role of the Th-17 pathway), and common clinical features both musculoskeletal such as involvement of the axial skeleton, peripheral arthritis, enthesitis, and dactylitis, and estra-muskuloskeletal such as psoriasis, acute anterior uveitis, and inflammatory bowel disease. Depending on the leading manifestation, SpA can be classified as axial (with predominant involvement of the axial skeleton - sacroiliac joints and spine) or peripheral (with arthritis, enthesitis or dactylitis as leading manifestations). There was a substantial progress in the field of SpA in terms of understanding disease mechanisms, early diagnosis, and improved treatment. Correct application and interpretation of imaging is a key to the improved diagnosis of axial SpA. In the last years, there is an increasing number of publications reporting a high prevalence of bone marrow edema on magnetic resonance imaging of sacroiliac joints in healthy subjects without back pain indicting a need for a better definition of SpA compatible findings. Tumor necrosis factor (TNF) alpha and interleukin (IL)-17 represent currently two major treatment targets in SpA, while other promising targets such as IL-23 or IL-6 failed in clinical trials. There is an unmet need for strategy trials to optimize and to individualize treatment in SpA. The role of Janus kinases and their blockade in SpA is still to be explored. TNF blockade showed efficacy in peripheral SpA, other targets (IL-17 and IL-23) should be investigated in clinical trials. Early, effective and long-term suppression of inflammation is currently the best method to prevent structural damage progression in the spine in axial SpA, while specific effects of IL-17 blockade and of nonsteroidal anti-inflammatory drugs on new bone formation are being still investigated.

AS3-1

Structure and functions of IL-6/IL-6 receptor and their pathophysiological roles in inflammatory conditions

Kei Ikeda
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Conflict of interest: Yes

Although interleukin-6 (IL-6) is primarily produced by hematopoietic cells, IL-6 has its effects on a wide range of cells via gp130 protein and influences not only immune/inflammatory responses but also broad tissue/organ systems. IL-6 is also involved in pathological immune/inflammatory responses and plays substantial roles in the pathophysiology of autoimmune/inflammatory/rheumatic conditions such as rheumatoid arthritis. Currently, anti-IL-6 receptor antibodies are the only clinically available molecular-targeted drugs that specifically block IL-6 signaling. In this short lecture, molecular mechanisms that provide rationale underlying IL-6 signal blockade will be discussed.

AS3-2

The Role of IL-6 in Rheumatoid Arthritis

Allan Gibofsky
Clinic for Inflammatory Arthritis, Hospital for Special Surgery, New York, USA

Conflict of interest: Yes

RA is a systemic disease driven by chronic joint inflammation that results in joint damage and loss of function. Integrated activation of the innate and adaptive responses is a requisite for chronic inflammation, and is mediated by cytokine signaling. IL-6 is one such cytokine, and is able to interact with virtually any cell based on its versatile signaling mechanism. Indeed, almost all cells of the innate and adaptive arms of the immune system, along with supporting stromal cells, respond to IL-6, and many of these cells also produce IL-6. As a result, elevated IL-6 levels may contribute to persistently activated innate and adaptive immune systems responsible for RA disease chronicity and pathophysiology. IL-6 facilitates not only communication among cells within the innate and adaptive immune arms, but also allows for interactions between the two. IL-6 produced by innate immune and supporting stromal cells can activate adaptive T and B effector cells. These effector cells also secrete IL-6, which then further influences the function of cells of the innate system. IL-6 also induces cells to produce other key cytokines that facilitate communication between the different cells of the immune system. In this way, IL-6 can be viewed as a key messenger in autoimmunity and, in cases of persistent elevation like RA, IL-6 contributes to a state of chronic inflammation. Continued research on the many functions of IL-6 may further delineate the pathological origins of RA. (1) 1. Calabrese L and Choy E: The Roles for IL-6 in Both Innate and Adaptive Immunity in RA. Sanofi Regeneron 2016.

AS4-1

Treatment strategy for psoriatic arthritis with metabolic comorbidities

Motomu Hashimoto
Osaka City University Graduate School of Medicine, Japan

Conflict of interest: Yes

Psoriatic arthritis (PsA) and rheumatoid arthritis (RA) are systemic autoimmune disease linked to metabolic comorbidities, such as obesity, diabetes mellitus, and hyperlipidemia. However, obesity and metabolic syndrome are more frequent in patients with PsA than in those with RA. In daily clinical practice, it is frequently observed that severe RA patients are cachexic while severe PsA patients are obese, accompanied by metabolic comorbidities. “Psoriatic march” is the concept of how severe psoriasis (PsO) and PsA accompany the risk of metabolic comorbidities and lead to cardiovascular events. Proinflammatory cytokines, in particular TNF-α, play a pivotal role in the pathogenesis of “psoriatic march”. TNF produced by adipocyte, together with TNF produced due to PsO/PsA pathogenesis, causes insulin resistance and endothelial dysfunction, leading to atherosclerosis and finally myocardial infarction or stroke. Epidemiological studies revealed that TNF inhibitors not only ameliorate PsO/PsA but also decrease the cardiovascular events. Therefore, TNF inhibitors can be a good treatment option for PsO/PsA with metabolic comorbidities. Obese patients are often resistant to conventional treatments. However, Pegylated TNF inhibitor, Certolizumab pegol (CZP), is reported to be equally effective for both normal weight and obese PsO/PsA patients. Pegylation may have allowed the maintenance of higher serum concentration of CZP and their accumulation to the inflamed tissue. In this seminar, the concept of “psoriatic march” and treatment strategy for PsO/PsA patients with metabolic comorbidities will be discussed.

AS4-2

Treatment strategy for the axial domain of psoriatic arthritis

Yuho Kadono
Orthopaedic Surgery, Saitama Medical University

Conflict of interest: Yes

Psoriatic arthritis (PsA) exhibits arthritis, enthesitis, or spondylitis with skin and/or nail psoriasis. The pathological condition is composed of chronic enthesitis in response to mechanical stress. Once inflammation occur in sacroiliac joint or spine, patients complain the inflammatory back pain (IBP). IBP is typically relieved by exercise, and worsened by rest. It is important that we do an interview and a medical examination appropriately to ascertain the difference with the general back pain. We should distinguish PsA from nonspecific lumbago or degenerative disease including disc herniation and spondylolisthesis. We should also distinguish it from pustulotic arthro-osteitis (PAO), osteitis condensans ilii (OCI), diffuse idiopathic skeletal hyperostosis (DISH) as well as ankylosing spondylitis (AS). We need to make a diagnosis with both clinical manifestations and images, but we sometimes need to follow up clinical findings for final diagnosis. PsA exhibits osteophyte formation around intervertebral disk space, which sometimes leads to ankylosis like AS. Unlike marginal syndesmophytes seen in AS, non-marginal syndesmophytes seen in PsA look chunky. In DISH, osteophytes look proliferrative Since PsA exhibits various symptoms, a treatment strategy depends on a targeted symptom. There is a few clinical trials which set an improvement of axial domain of

PsA as a primary end point. However, treatment recommendation for PsA is described based on the results of the studies, including clinical trial of biologics, which set improvement of axial domain as secondary end point. When an effect of NSAIDs, 1st choice drug, is insufficient, the biologics, such as TNF inhibitor and IL-17A inhibitor, should be considered. In this lecture, I discuss a treatment strategy for axial domain of PsA, and especially focused on differential diagnosis.

AS5-1

Targeting JAK in Rheumatoid Arthritis: Therapeutic Strategies and Future Prospects

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Conflict of interest: None

Rheumatoid arthritis (RA) is characterized by symmetric synovitis with bone destruction and production of autoantibodies due to a breakdown in immune tolerance caused by the interaction of genetic and environmental factors. EULAR Recommendation 2019 recommends early treatment, mainly methotrexate (MTX), and biologics (TNF inhibitors, IL-6 inhibitors, T-cell selective therapy) for refractory patients. The goals of RA treatment are broadly divided into clinical, structural, and functional remission. However, in clinical practice, it is often difficult to achieve or maintain all three types of remission due to the inaccessibility of MTX or the presence of multiple drug resistance to anti-rheumatic drugs. JAK inhibitors, which inhibit multiple cytokine signals simultaneously via inhibition of intracellular kinases, have been launched for rheumatoid arthritis with five drugs in the market (as of December 2020), and due to the convenience of being an oral drug, their share in clinical practice is expected to expand further. On the other hand, appropriate monitoring is important due to the presence of specific adverse events such as herpes zoster. In this talk, we will discuss the usefulness of JAK-targeted therapy, including the JAK1/2 inhibitor baricitinib, as well as cautions in management and future prospects.

AS5-2

Efficacy and safety of baricitinib in suppressing joint destruction revealed by the evaluation using mTSS

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Conflict of interest: Yes

Due to recent advances in the treatment of rheumatoid arthritis, not only clinical remission but also structural and functional remission have become a feasible therapeutic goal. EULAR recommendations 2019 update clearly stated that bDMARDs or JAK inhibitors (JAKi) should be added if patients with poor prognostic factors cannot achieve therapeutic goals with MTX. Unlike bDMARDs, JAKi have small molecular weights, can be administered orally, and can efficiently inhibit intracellular signal transduction of inflammatory cytokines. Among them, baricitinib mainly inhibits JAK1 and JAK2. The RA-BEAM study demonstrated that ACR20 at 12 weeks in patients treated with baricitinib proved to be non-inferior and superior to that in patients treated with adalimumab (N Engl J Med. 2017; 376 (7): 652-662.). In addition, not only inflammatory markers such as CRP and ESR and disease activity indices such as DAS28-CRP and SDAI, but also patient-reported outcomes including pain and fatigue were rapidly improved by baricitinib. Furthermore, in the evaluation of joint destruction using mTSS (modified Total Sharp Score), baricitinib was effective in suppressing joint destruction, similarly as adalimumab. At 24 weeks, joint destruction was completely inhibited in 81.3% of the baricitinib-treated patients (mTSS $\leqq$0). Subsequent follow-up data were presented at the ACR meeting in 2020, showing that baricitinib was effective in suppressing joint destruction over five years. In terms of safety, JAKi, including baricitinib, have been reported to cause more herpes zoster than bDMARDs. In addition, it is necessary to pay sufficient attention to the onset of malignancies and thrombosis. The author was directly instructed by Dr. van der Heijde, an advocate of mTSS, and has been involved in several clinical studies using mTSS. This seminar will focus on how to evaluate mTSS data and the effect of baricitinib on suppressing joint destruction.

AS6

Biosimilar in RA Treatment Strategies

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Conflict of interest: Yes

The introduction of Infliximab (IFX) and Etanercept (ETN) biosimilar (BS) has added options for biologics with clinical equivalence but at different NIH prices for RA treatment. This has facilitated access to biologics for patients and there is no doubt that the switch from branded biologics to BS provides medical economic benefits. “Basic Policies for Managing and Reforming the Economy2019” by the Cabinet states that “We will promote research and development of biologics and BS and accelerate the use of BS with better understanding of its efficacy and safety”. However, the knowledge and understanding of BS doesn’t seem to be adequate even though more than six years have passed since their introduction to the Japanese market in 2014. In this presentation, the data about the efficacy and safety of IFXBS and ETNBS, including switching studies, will be presented. Since IFX is a chimeric antibody, the production of neutralizing antibodies must be monitored carefully, and the same is true for BS. In addition, we must pay attention to the so-called nocebo effect. The nocebo effect refers to the reduced efficacy and side effects due to patient beliefs. Some abroad studies showed that patients who switched from ETN to BS had a significantly lower persistence rate, and patients who switched back to the branded drug had a greater change in PGA. On the other hand, the study that included 90 patients who switched from ETN to BS at total 14 RA institutions in Japan showed that there was no significant change in DAS28 and PGA. These results suggest that providing adequate information to patients by rheumatologists leading informed consent will contribute to reduce nocebo effects. In clinical practice, we know that there are patients who are hesitant to switch to BS because they are satisfied with the current biologic. Therefore, it is required to accumulate evidence regarding the switch from branded biologics to BS and among BSs and support patients to accept BS without concerns.

AS7

Basic Seminar for Spondyloarthritis 2021: The forefront of spondyloarthritis management: from pathogenesis to biologics

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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 disease and undifferentiated SpA. More recently, classification criteria for axial and peripheral SpA (axSpA & pSpA) have been developed by the Assessment of SpondyloArthritis international Society (ASAS); axSpA involves sacroiliitis and spondylitis, while pSpA predominantly presents with peripheral arthritis, enthesitis and dactylitis. In addition, axSpA is now 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 and are associated with MHC class I molecules, in particular HLA-B27. Activation of the IL-23/IL-17 pathway and the TNF-α proinflammatory cascade has been known to play an important role in the pathogenesis of SpA diseases such as psoriasis/PsA and AS/axSpA. IL-17 is now well defined as a major factor in inducing and mediating proinflammatory responses, including osteoproliferation as well as osteo-

clastgenensis. IL-17 production has been detectable in the skin and joints of AS and psoriasis/PsA, and of interest, this cytokine can be produced by the cells of the innate immune system such as γδ T cells, type 3 innate lymphoid cells and MAIT cells, in addition to $CD4^+$ T cells and $CD8^+$ T cells. It has been shown that SpA diseases can be greatly ameliorated by blocking the IL-23/IL-17 pathway, likely TNF-α, further indicating a significant role in disease development. In the seminar, speakers will cover the topics ranging from the pathogenesis of the SpA disease to the management of psoriasis/PsA and AS/axSpA.

AS8-1

Possibility of tremfya in PPP / PAO

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Conflict of interest: Yes

Palmoplantar pustulosis (PPP) is an intractable disease consisting of aseptic blisters and pustules that occur mainly on the palms and soles of the feet, and causes pustulotic arthro-osteitis (PAO). It may be merged to about 10-40%. Currently, there are no international guidelines for PPP / PAO and treatments are not well established. Murakami et al. (J. Invest Dermatol 2017) found that the onset of palmoplantar pustulosis is caused by the action of antibacterial peptides derived from eccrine sweat glands on keratinocytes after blistering due to some factor, IL-23, IL-17. IL. It is reported that cyst formation is completed by expressing inflammatory cytokines such as -8 and inflammatory cells such as neutrophils and Th17 cells, and finally filling the blisters with a large number of neutrophils. ing. Tremfya, the world's first insured for palmoplantar pustulosis in 2018, is a human anti-human IL-23p19 monoclonal antibody, the world's first biopharmacy with clinical efficacy against PPP / PAO. Is. In this seminar, I will mainly talk about the epidemiology, clinical symptoms, diagnosis, treatment, and the possibility of tremfya of PPP / PAO.

AS8-2

Update on treatment of psoriatic arthritis~IL23 inhibitor~

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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 for 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. 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 control PsA disease, as well as mitigate the risks of the many associate comorbidities that may accompany it. In this session, at first, we aim to review the new information in PsA including T2T, co-morbidity, the clinical features of PsA especially focusing on Axial PsA. Secondly, the treatment guideline and recommendation for PsA is changing constantly with the advent of new therapies in the EULAR, ACR, and GRAPPA internationally, and I would introduce a current treatment strategy "T2T" and its limitation. Furthermore, therapeutic strategies of how to set the treatment target should be determined through a shared decision making between physicians and patients in consideration of the disease activity and the characteristics (presence or absence of complications) of each patient. I will present a clear exposition of signification to choose bio-DMARDs in treatment of PsA including the new IL23-antagonist, Guselkumab. Finally, I would introduce it's mechanism of action and the clinical efficacy and safety data in PsA programs. **References** 1. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis. N Engl J Med 2017;376 (10):957-70. 2. van den Bosch F, Coates L. Clinical management of psoriatic arthritis. Lancet 2018;391 (10136):2285-94. 3. Gottlieb AB, Merola JF. Axial psoriatic arthritis: An update for dermatologists. J Am Acad Dermatol. 2020 Jul 31: S0190-9622 (20)30959-2. 4. Gossec L et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis. 2020 Jun;79 (6):700-712 5. Deodhar A, et al; DISCOVER-1 Study Group. Guselkumab in patients with active psoriatic arthritis who were biologic-naive or had previously received TNFα inhibitor treatment (DISCOVER-1): a double-blind, randomised, placebo-controlled phase 3 trial. Lancet. 2020 Apr 4;395 (10230):1115-1125.

AS9-1

Surgery for the rheumatoid hand 2021 - subcutaneous tendon rupture-

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Conflict of interest: Yes

There are still significant number of patients with "RA symptoms that are causing a reduction in quality of life (QOL), despite their well-controlled disease status", which is one of the definition of difficult-to-treat rheumatoid arthritis (D2T-RA) by European League Against Rheumatism (EULAR). The panel discussion will focus on the subcutaneous tendon rupture as a condition that markedly reduces QOL. Dr. Ikegami of Toho University will talk about multiple extensor tendon ruptures of the hand. He will discuss the preoperative evaluation of tendons and muscles of the ruptured and residual tendons, evaluation of the wrist joint, determination of tension of tendon sutures, and appropriate postoperative treatment. Surgical treatment of subcutaneous ruptures of the flexor tendon of the hand is generally challenging. Even if the ruptured tendon is reconstructed, progressive joint destruction of the affected finger may lead to a loss of overall finger function. Dr. Akita of Osaka Minami Medical Center will present cases of RA patients who underwent reconstruction of a subcutaneous rupture of the flexor tendon of the hand. He will also discuss the importance of inflammation control. In the special lecture, Dr. Ishikawa of Niigata Rheumatic Center will give a talk on "The significance of hand and finger reconstruction of patients with RA under disease control by bDMARDs". In this talk, he divided the cases of reconstructive surgery for rheumatoid hand and fingers into two groups: bDMARD-treated and non-bDMARD-treated patients, and reports the effectiveness of the surgery on patient reported outcomes (PRO), including physical function, quality of life, and psychological (depression) aspects, as well as disease activity, and reduction of medication. He will emphasize the importance of the control of disease activity by DMARDs, such as biologics, which are complementary to each other, in order to maximize the effectiveness of the surgery.

AS9-2

Significance of Rheumatoid Arthritis Hand Reconstruction under the use of Biologics

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Conflict of interest: None

In the era of biologics (bDMARD), the pathology of rheumatoid arthritis (RA) has improved dramatically, and approximately 60% of patients have reached clinical remission. However, there are many patients who have difficulty controlling disease activity due to comorbidities, extra-articular symptoms, insufficient effect for many drugs, and so on. Also, in the patients with clinical remission, remaining synovitis in the hand is often detected by ultrasonography, causing painless joint destruction and progressive of deformity as a silent destructor. Surgical reconstruction of the structurally damaged rheumatoid wrist and hand was performed at 137 sites in 119 patients, of which 39 sites in 30 patients were treated with bDMARD. As a result, DASH score before and 1 year after surgery was 45 →37, HAQ-DI was 1.15→0.89, patient VAS (mm) was 36→21, EQ-5D was 0.70→0.78, and BDI was 12.8→11.1. Improvement in physical function, QOL, and psychology (depression) was noted. DAS28-ESR decreased from 3.2 to 2.0, and steroid or csDMARD dose was possible to reduce in 8 patients (27%) during the follow-up. On the other hand, in 89 patients who were not treated with bDMARD, the similar favorable effect was observed. However, increased dose of steroid or csDMARD was required in 14 patients (16%). We have reported that a favorable outcome was provided by tight medical control throughout the course of RA; 1)

Postoperative pain, extension lag and subsidence of the implant in Swanson MP joint arthroplasty were related to high CRP or mutilating type of RA. 2) In the upper extremity surgery, a greater improvement in DASH score was expected in patients under the good control of RA. 3) Integrated disease activity for 10 years after the rheumatoid wrist surgery reflected postoperative joint deterioration. In order to maximize the surgical effect of rheumatoid hand reconstruction, it is extremely important to control disease activity by DMARDs, such as bDMARD which is complementary to each other.

AS10

Treatment strategy for CTD-PAH: Focusing on MCTD and Sjögren's syndrome

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Conflict of interest: Yes

Connective tissue diseases (CTD) occasionally complicate pulmonary arterial hypertension (PAH). According to the treatment flowchart of CTD-PAH in Japanese guidelines for treatments of pulmonary hypertension (2017), 1) diagnosis of CTD-PAH, 2) evaluation of CTD activity, and 3) risk evaluation of heart failure are important. However, it is difficult to determine the indications of immunosuppressive therapy and the treatment of occasionally overlapping group 2 or 3 PAH. In this seminar, I will discuss these problems with various case presentations of CTD-PAH, considering systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) as a basic course and primary Sjögren's syndrome (pSS) and mixed connective tissue disease (MCTD) as an advanced course. PAH is a rare complication of pSS (Launay, Medicine, 2007). It is easy to understand to divide pSS-PAH into 3 types: 1) SLE-like, 2) SSc-like, and 3) lung lesion-complicated. Some patients with pSS show extraglandular symptoms and high disease activity. PAH is interpreted as one of such extraglandular symptoms, and responsive to immunosuppressive treatment (Liu, Lupus, 2018). MCTD is characterized by anti-U1RNP antibody and overlapping syndrome (Sharp, Am J Med, 1972). However, it is difficult to distinguish MCTD as an independent disease from overlapping syndrome of 2 or 3 diseases. The presenter prefers "anti-U1RNP antibody syndrome" because it is simpler not to use MCTD as an independent disease. There are no specific treatment recommendations to MCTD-PAH. The indication of immunosuppressive treatment is determined by whether SLE component or SSc component is dominant in the case. It means that the disease is interpreted as overlapping of SLE and SSc.

AS11

Evaluation of matrix metalloproteinase-3 in clinical practice of rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis can be characterized by systemic synovitis with chronic synovial hypertrophy which can produce large amount of matrix metalloproteinase (MMP)-3. MMP-3 has wide substrate specificity including proteoglycan, collagens, fibronectin, gelatin, and so on. MMP-3 has been considered as the primary proteinase for joint destruction in RA. MMP-3 is a proteolytic enzyme, also known as stromelysin-1, and thought to play a pivotal role in joint damage in RA. MMP-3 is involved in the degradation mechanism of articular cartilage in RA by cleaving extracellular matrix proteins; collagen type 2, 3, 4, 9, and 10, and proteoglycans. MMP-3 is locally produced by synovial fibroblasts and chondrocytes in the inflamed joint and released into blood. Serum MMP-3 levels have been utilised as a valuable biomarker for assessing disease activity and predicting joint damage in RA patients. The multiple-biomarker disease activity (MBDA) comprises 12 serum biomarkers including MMP-3 and was shown to reflect disease activity and predict joint destruction. MMP-3 has been approved in RA patients by Japan national health insurance since 2001. MMP-3 has been mainly used for RA diagnosis, evaluation of RA disease activity and drug effectiveness, and prediction of long-term joint destruction. We previously reported the short-term improvement of MMP-3 can be an independent prognostic factor for the long-term drug effectiveness, using data from Japanese multicenter registry system (TBCR). We have found that percent improvement in MMP-3 levels was a significant predictor for clinical remission in RA patients treated with adalimumab or abatacept. Interestingly, the absolute value of MMP-3 was not associated with clinical outcomes of adalimumab. I would like to review the currently obtained evidence of MMP-3 to reconfirm its value in the clinical practice in RA.

AS12

Meet with Prof. Paul Emery -Potential of Filgotinib Considered from Global RA Treatment, Guidelines and Clinical Trials-

Paul Emery[1,2]
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Conflict of interest: YES

The outcome of treatment of patients with rheumatoid arthritis (RA) has qualitatively improved in recent years due to better and earlier treatment approaches, and new drugs. As one of new Janus kinase inhibitors (JAKi), filgotnib (JYSELECA®) has been approved for rheumatoid arthritis in Japan and Europe as results of Phase III clinical trials, FINCH-1, FINCH-2 and FINCH3, and safety and efficacy profiles of filgotinib have been characterized. In this session, Prof. Paul Emery, University of Leeds UK, introduces evidence-based guidance on the management of RA and the role of filgotinib, and discusses with 4 of Japanese RA Specialists about: 1) Updated guidance and implications for clinical practice and RA management; 2) Filgotinib, once a day oral JAKi, efficacy and role in clinical practice; 3) Characteristics of JAK pathway inhibition and clinical responses; hosted by Prof. Hiroaki Niiro, Kyusyu University.

Evening Seminar

ES1-1

Interleukin-6 as a key driver linking inflammation and structural bone changes in arthritis

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Conflict of interest: None

Rheumatoid arthritis (RA) is a systemic and inflammatory disease with substantial impact on the bone leading to local and systemic bone loss. Inflammatory cytokines lead to an imbalance between bone resorption and bone formation in RA. This imbalance, which is based on increased osteoclast-medicated bone resorption at the expense of osteoblast-mediated bone formation, triggers structural damage in the bone and joints, which drives functional impairment in patients with RA. Proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) are the main triggers for bone erosions by inducing an imbalance of local bone metabolism. The role of cytokines in this process is only partly understood, common concepts suggesting that a combination of TNF-alpha and IL-6 are responsible for the loss of bone in RA. Recent 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) induced the repair of existing bone erosions in patients with RA, while no such repair is found when inhibiting TNF-alpha with respective therapeutic antibodies. 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. Thus, apart from the anti-inflammatory action of IL-6 targeted therapies in RA, such approach also seems to restore bone homeostasis. In this symposium, I will focus on that these findings open new possibilities for tissue regeneration in inflammatory diseases.

ES1-2

Perspectives on tocilizumab

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an autoimmune disease with persistent inflammation of synovitis, progressive bone and joint destruction, and irreversible physical disability. Earlier diagnosis and rapid disease control as soon as possible are essential, since irreversible progression of joint destruction worsens quality of life. Appropriate disease modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) and biologic DMARD targeting on TNF and interleukin-6 (IL-6) can regulate immune abnormalities and improve disease activity in RA. Through treatment with these drugs, it is possible that we aim at remission, and regulate joint destruction and functional disability by sustainable remission. IL-6 is one of proinflammatory cytokine that affects production of autoantibody, formation of synovial pathology and so on. It is involved in the development of RA. Tocilizumab (TCZ), an anti-IL-6 receptor monoclonal antibody, was firstly approved to treat with RA in Japan. The PMS for all the patients with TCZ contributes to reducing almost all the concerns that physicians potentially had for the blocking of IL-6 signaling pathway. Currently, TCZ has been expanded for many diseases such as systemic juvenile idiopathic arthritis, adult Still's disease, Takayasu arteritis, giant cell arteritis and so on. TCZ is also able to shorten interval of administration for RA patients who have inadequate response to biweekly TCZ. TCZ has been used for RA patients regardless with or without MTX, and it is efficacious for them who have inadequate response to MTX and biological DMARD. Our data, which is named as "FIRST Registry", has been also confirmed efficacy and safety of TCZ as well as those of other biologic agents. Meanwhile, there are several issues for cost-effectiveness, work disability and difficult to treat RA. I will give an overview of the cumulative clinical evidence for TCZ and consider the future potency for the IL-6 signal blocking.

ES2

Current status and countermeasures for reactivation of hepatitis B associated with immunosuppressants including steroids

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Conflict of interest: Yes

It has been reported that hepatitis B virus (HBV) -infected patients with rheumatoid arthritis and collagen diseases are immunosuppressed as long as immunosuppressive therapy is continued, and are likely to have elevated HBV DNA levels. Fulminant hepatitis may occur in some cases, resulting in a fatal course. Once cured [HBs antigen (HBsAg) negative and HBc antibody (HBcAb) positive], the use of immunosuppressants may cause HBV reactivation and even de novo hepatitis B. Recently, a wide variety of biological drugs and five JAK inhibitors have become clinically available as immunosuppressants, which may change the risk of HBV activation. In addition, HBV reactivation occurs during or after dose reduction of steroids or immunosuppressants, and even if anti-HBV therapy is started after fulminant hepatitis develops, it often leads to death. Therefore, in the treatment of malignant tumors and autoimmune diseases, it is recommended to measure HBsAg, HBcAb, and HBs antibody (HBsAb), to administer nucleos (t)ide analogs to HBV carriers (HBsAg positive cases), and to administer nucleos (t)ide analogs to patients with a history of HBV infection (Patients who were negative for HBsAg and positive for HBcAb and/or HBsAb) at the time when HBV DNA is measured and becomes positive on a regular basis. Prevention of HBV reactivation can be sufficiently expected by assessing the risk beforehand and taking measures according to the risk based on the Guideline for Prevention of Hepatitis B Associated with Immunosuppressive Therapy/Chemotherapy. On the other hand, the this guideline for prevention of HBV reactivation has been mainly prepared for malignant tumors and autoimmune diseases. Until recently, there had been no clear guidances for risk management regarding the dose, duration of steroids treatmentat, and how often and frequency of monitoring for HBV reactivation in patients with a relatively low risk of HBV reactivation such as those in the "During steroid monotherapy" The Oto-Rhino-Laryngological Society, which frequently uses steroid monotherapy for a long time, prepared a new guideline on measures against HBV reactivation in collaboration with the Japanese Society of Hepatology last year. Since HBV reactivation may occur several months after completion of steroid monotherapy, cooperation with a hepatologist is espeically important in HBsAg-positive patients. In this seminar, the status and evidence of the latest guidelines on the risk of HBV reactivation after immunosuppressive therapy or chemotherapy including steroids are outlined, and future prospects are described.

ES3-1

When and who should be started with Hydroxychloroquine in Japanese patients with systemic lupus erythematosus

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Conflict of interest: None

Survival of patients with systemic lupus erythematosus (SLE) has dramatically improved over the last 50 years, possibly owing to earlier diagnosis and appropriate treatment schemes. However, SLE patients still display a high mortality rate compared with general population. Persistent disease activity is associated with increased organ damage which in turn is predictive of more damage and death. Several needs are still unmet among SLE population in that long-term prognosis remains poor and new methodological strategies should be found out aiming to prolong remission and minimize damage accrual. According to the treat-to-target strategy in SLE and 2019 update recommendation, remission or low disease activity should be a clinical goal and the lowest dose of glucocorticoid (GC) should be achieved. Hydroxychloroquine (HCQ) is a mainstay of therapy for SLE and has long been accepted as the standard therapy in foreign country. Given that HCQ was not approved in Japan until 2015, its therapeutic potential remains poorly understood. Recently, many investigators have examined the association between HCQ blood levels and clinical outcome. Some studies have reported taking an additional immunosup-

pressant other than corticosteroid was associated with higher HCQ concentration. In this review, we discuss "When and who should be started with HCQ in Japanese patients with SLE" by focusing on the background immunosuppressant use.

ES3-2

The role of hydroxychloroquine in long-term therapeutic strategies for SLE

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Conflict of interest: Yes

The pathogenesis of systemic lupus erythematosus (SLE) is characterized by immune complexes consisting of antigens, activation of dendritic cells and autoreactive T cells and overproduction of autoantibodies secreted from activated B cells. The prognosis of SLE has dramatically improved because of the widespread uptake of glucocorticoid and immunosuppressants, with survival rates reported to be 90% or higher after 5 years; however, 50%-70% after 20 years, given the age at onset, these survival rates are relatively low. In 2014, a task force of the EULAR, reported the treat-to-target (T2T) strategy for therapeutic goals. The therapeutic target was remission without any systemic symptoms or organ disorders, and the realistic therapeutic goal was the avoidance of relapse or organ disorders. As glucocorticoids and immunosuppressive drugs are non-specific therapeutic agents that cause many adverse reactions, the development of drugs aiming to control specific abnormal immune network is anticipated for the treatment of SLE. Antimalarial agents such as hydroxychloroquine (HCQ) have long been used as effective therapies for skin and joint symptoms, as well as for the malaise associated with SLE. Whereas HCQ has been generally given to most of patients from the beginning of the treatment during the remission-induction therapy in many countries, its effects on maintenance therapy have not been sufficiently supported by evidence. We evaluated the additive effects of HCQ in maintenance therapy for 1 year according to the standard of care (SoC) in 101 patients with SLE. The data indicated that addition of HCQ on the SoC improved SLEDAI scores and reduced the dose of steroids. The use of HCQ was a predictive factor for the prevention of SLEDAI flare. Therefore, HCQ may be considered a potential mainstay of maintenance therapy. In this seminar, we would like to discuss the role of HCQ in long-term therapeutic strategies for SLE.

ES3-3

Current status of ophthalmic monitoring of hydroxychloroquine retinopathy

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Conflict of interest: None

Five years have passed since hydroxychloroquine (HCQ) was approved in Japan, but there have been no reports of HCQ retinopathy in Japan. There are several possible reasons for this. That is, the screening function is working effectively, administration to at-risk patients is carefully considered, the incidence rate of Japanese people may be low, definitive diagnosis may be difficult, and patients might deviate from the cooperation system of prescribing physicians and ophthalmologists. Since these verifications are difficult, I will talk about the following from the perspective of an ophthalmologist at this seminar. 1. Reconfirmation of HCQ retinopathy test points, 2. Characteristics of Asian retinopathy, 3. Current status and problems of case tracking, 4. Proposal of medical care support program (H-SUPPORT), 5. Presentation of suspected retinopathy and diagnosed cases. 1. I want to check the timing of the inspection again. 2. I will introduce the characteristics of lesions in the peripheral areas, which are often found in Asians, and how to detect them. 3. I will introduce the side effect report and tracking system from Sanofi. 4. I will present the ophthalmologist's consultation desk and registry system for suspected cases. 5. Finally, I will present some specific cases I experienced and consider the current issues from the perspectives of 1-4. I hope that my talk will help audience and me to think together about the significance of cross-departmental collaboration and what we can do from each standpoint.

ES4-1

The Importance of Infection Control in Rheumatic Diseases

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Conflict of interest: Yes

The treatment of rheumatic diseases such as rheumatoid arthritis and systemic lupus erythematosus has made great progress in the last 20 years. In addition to methotrexate and other immunosuppressive agents, a number of biologics and JAK inhibitors have been used in recent years, making steroid-free treatment more feasible, but infections caused by immunosuppressive potentiation remain a challenge. Patients with rheumatoid arthritis have a higher incidence of pneumonia and mortality, and biologics have been shown to increase the frequency of severe infections. According to a domestic survey of all biologics, bacterial pneumonia was the most frequent infectious disease in Japan, and opportunistic infections such as tuberculosis, pneumocystis pneumonia (PCP), nontuberculous antacidosis, and herpes zoster also require attention. Risk factors for serious infections include old age, pre-existing pulmonary disease, and history of interstitial pneumonia, and these patients should be carefully screened, especially prior to the administration of biologic agents, for the appearance of symptoms such as fever and dyspnea after the start of treatment, and for the development of chest imaging findings and laboratory tests such as blood lymphocyte count, beta-D glucan, and KL-6. It is necessary to pay attention to the changes in It is also important to instruct patients to wear masks, to gargle, to wash their hands, to be alerted to respiratory symptoms, to see a doctor as soon as possible when they are sick, and to receive vaccines for prevention of infection. Reactivation of hepatitis B virus is also important in the treatment of rheumatic diseases. Screening for HBV infection should be performed in all patients with or without hepatic dysfunction prior to administration of biologics and immunosuppressive agents, as well as measures against de novo hepatitis, such as consideration of administration of nucleic acid analogs to HBV carriers and previously infected patients, and appropriate monitoring during administration.

ES4-2

Importance of pneumonia prevention in patients with rheumatoid arthritis

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Conflict of interest: None

While the treatment of rheumatic diseases has been changing due to the introduction of biologics and other immunomodulating agents into rheumatoid arthritis (RA), the complication of various infectious diseases has become a problem. As pneumonia is the most common reason for hospitalization in RA patients, respiratory tract infections occur frequently and often become severe. The diagnosis of respiratory infections in RA patients is sometimes difficult because they are complicated by pulmonary lesions such as interstitial pneumonia and alveolar hemorrhage, which occur regardless of the disease activity such as joint symptoms. Drug-induced pneumonia caused by methotrexate (MTX) or biologics is also known, and differentiation from such non-infectious respiratory lesions is also a problem. RA is a risk factor for infectious diseases by itself, but therapeutic agents are also risk factors, the largest of which is prednisolone. Biologics for RA are broadly divided into those that inhibit TNF-α, those that inhibit IL-6, and those that inhibit T cell activation. All of these preparations can induce opportunistic infections by reactivating latent infectious diseases. As mentioned above, the most common infectious disease in RA patients is pneumonia, and it has been reported that pneumococcus is the most frequently isolated causative agent in community-acquired pneumonia. One of the measures to prevent pneumococcal pneumonia is the pneumococcal vaccine. Currently, there are two pneumococcal vac-

cines that can be used by adults in Japan: the 13-valent pneumococcal conjugate vaccine (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23). In this talk, we will discuss topics related to vaccine prevention, along with findings on the pathogenesis and characteristics of respiratory tract infections in RA and other rheumatoid diseases, epidemiology, prevention, and diagnosis.

ES5-1

Prevention of sarcopenia in aged rheumatoid arthritis patients ~Importance of muscle~

Masahiro Tada
Orthopaedic Surgery, Osaka City General Hospital

Conflict of interest: None

Everybody has felt their physical decline. Especially, muscle mass comes to peak at 20-40 years, and decrease 10% in upper limb, 20% in lower limb at 60 years, moreover decrease 20% in upper limb, 40% in lower limb at 80 years. Rheumatoid arthritis (RA) patients that have joint destruction, are considered more decreasing of muscle mass. Actually, they have highly fallen rate and prevalence rate of femoral neck fracture compared healthy individuals. Falls and fractures account for 12.2% of requiring nursing care and are the fourth reason. It is important to prevent them that shorten the health expectancy. However, there is not enough study and evidence from the view of muscle. Sarcopenia, which is defined by low muscle mass, power, and quality, is classified in the ICD-10. Sarcopenia is recognized the disease, not aging change. If they suffer them, recovery is difficult, because there is no medicine to increase the muscle. Therefore, early diagnosis and intervention is only approach to prevent them. From this point, EWGSOP and AWGS advocated the new criteria at 2018 and 2019, respectively. We reported that muscle mass, exercise time, and energy intake of RA less than those of control from TOMORROW study. Prospective cohort study (CHIKARA study) has performed from 2016 to evaluate correlations between sarcopenia and disease activity in RA. Prevalence of sarcopenia, developing rate, correlation between muscle function and falls & fractures, relationship of disease activity and sarcopenia will be considered with new insight and evidence. We discuss the prevention of sarcopenia from exercise, nutrition, RA treatment, and team medical care. The aging of population is social problem, this phenomenon has already reached to RA. Rheumatologists need to deal with Increasing the side effect, poly pharmacy by comorbidity, and social estrangement by living alone. Even if aging occurs, most aged people want to look younger than they are by maintaining muscle mass and function.

ES5-2

Rheumatoid arthritis treatment in the elderly patients

Tomonori Ishii
Clinical Research, Innovation and Education Center, Tohoku University Hospital

Conflict of interest: Yes

In recent years, the incidence of rheumatoid arthritis has increased. Furthermore, the number of patients who develop rheumatoid arthritis at a young age is gradually increasing, and it is expected that the number of elderly patients with rheumatoid arthritis will continue to increase. In elderly patients, the probability of having complications such as hypertension and diabetes is high, and multiple drugs are often used for diseases other than rheumatoid arthritis. It is also likely that the patient has comorbidities affecting important organs such as the heart, liver, and kidneys. Infectious diseases, which are the most problematic adverse events associated with the treatment of rheumatoid arthritis, increase in frequency and severity owing to old age, regardless of the underlying disease. Therefore, individual patient-specific attention is more important when treating rheumatoid arthritis in the elderly than when treating it in younger people; personalized treatment that cannot be covered by the guidelines is often required, and treatment is generally restricted. On the other hand, a characteristic of rheumatoid arthritis that develops at an old age is that there are many systemic symptoms such as fever. In addition, the affected joints are often large joints. These characteristics are linked to the fact that the ability to move the body is greatly affected. If these symptoms are left untreated, the patient's condition progresses from frailty to disuse-related physical dysfunction. It is well known that for the elderly, not only rheumatoid arthritis but also immobility itself has a great effect on prognosis. Improving immobility quickly, in other words, improving rheumatoid arthritis quickly, is a more important goal in treatment of the elderly than in the treatment of young people. In order to prevent the progression of such physical dysfunction, it is becoming more important to fully utilize many prepared social resources such as long-term care insurance, regardless of the conventional treatment method for rheumatoid arthritis.

ES6-1

"Eosinophilic inflammation" in EGPA

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Conflict of interest: Yes

In response to type I allergic reaction, eosinophils increase in the tissue. Although this phenomenon has been well characterized in allergic disease and of interest to researchers, for decades, there has been a debate over whether accumulated eosinophils act to converge the inflammatory response or to increase inflammation, the so-called friend or foe theory. And even now, with the clinical application of biological therapy targeting IL-5, a factor known to prolong eosinophil differentiation and survival, the debate is far from settled. Recent studies have indicated that eosinophils possess a rather diverse set of functions. EGPA is often accompanied by marked peripheral blood eosinophilia. How do eosinophils contribute to the pathology? We need to know more about eosinophils themselves and their behavior at the site of inflammation. In the present talk, I will review the characteristics of eosinophils, their dynamics, activation, degranulation, and cell death in vivo, in light of our findings (especially with respect to extracellular traps and ETosis). The definition of "eosinophilic inflammation" in EGPA will be discussed.

ES6-2

Recent advances in the management of EGPA

Koichi Amano
Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University

Conflict of interest: Yes

The disease concept of EGPA was first defined by Jacob Churg and Lotte Strauss in 1951. Recent epidemiological studies revealed male-to-female ratio was 1:1.7 and ages of 30 to 60 years old are most susceptible to EGPA. In Japan, the diagnosis of EGPA is made by the diagnostic criteria by the Ministry of Health, Labour and Welfare of Japan but the American College of Rheumatology criteria or Lanham criteria is used for the classification of EGPA in the world. ANCA positivity in EGPA is as low as 30 to 40%. Clinical features are different between ANCA-positive and ANCA-negative cases. Genome-Wide Association Study has revealed ANCA-positive EGPA was related to HLA-DQ and ANCA-negative EGPA was related to IL-5 and GPA33 genes. High-dose steroids are a mainstay of the remission induction treatment of EGPA, and cyclophosphamide or azathioprine is used for steroid-resistant cases. Recently, mepolizumab, anti-IL-5 antibody, has proven to be effective for steroid-resistant non-severe EGPA and could reduce the dose of steroids, and mepolizumab has been approved for EGPA in Japan in 2018. The Research Committee of Intractable Vasculitis Syndrome of the Ministry of Health, Labour and Welfare of Japan will publish the treatment guide for EGPA, in which mepolizumab is strongly recommended in non-severe EGPA patients who have been refractory to the conventional therapies. In overseas, rituximab, anti-CD20 monoclonal antibody, is said to be a promising agent for EGPA but is not approved in Japan yet. The prognosis of EGPA is favorable in general but some have severe complications such as heart failure or gastrointestinal perforation. High-dose gamma globulin therapy can be effective for residual peripheral neuropathies.

ES7-1

Point of Interstitial Lung Disease associated with Connective Tissue Disease treatment -from a viewpoint of pulmonologist-

Yasuhiro Kondoh
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Conflict of interest: Yes

Interstitial lung disease associated with connective tissue disease (CTD-ILD) is a condition that affects the prognosis and is an important issue for both pulmonologists and rheumatologists. Underlying diseases are important in CTD, but in ILD, assessment based on imaging and histological classification is important. The clinical courses including treatment response in individual CTD-ILD cases are diverse, and it is not always easy to determine treatment choice. Corticosteroids and immunosuppressive drugs are thought as the basic treatment, but anti-fibrotic drugs are indicative for mainly fibrotic ILD; the former aims to improve and stabilize, while the latter to reduce disease progression and suppression. In addition to taking into account for underling disease, ILD needs to be distinguished not only from drug-induced lung disorders but also from opportunistic infections. Recently, it was reported that the disease-specific pathology is exhibited in the early stage, but the common progressive fibrotic pathology is exhibited in the advanced stage. Cases of ILD with progressive fibrosis are called the progressive phenotype of chronic fibrotic ILD or progressive fibrosing ILD (PF-ILD), for whom the efficacy of the anti-fibrotic drug (nintedanib) was reported and approved for insurance coverage. In the evening symposium, I would like to outline the points in the evaluation, diagnosis, and treatment of patients with CTD-ILD from the perspective of a pulmonologist.

ES7-2

Point of Interstitial Lung Disease associated with Connective Tissue Disease treatment -from a viewpoint of rheumatologist-

Shigeki Makino
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Conflict of interest: Yes

Interstitial lung diseases (ILD) is often associated with connective tissue disease (CTD) and has great influence on prognosis. There are chronic ILD like usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP), acute/subacute ILD like organizing pneumonia (OP) and diffuse alveolar damage (DAD). According underlying CTD the course and prognosis may be different even if they have same histology. In acute/subacute ILD, OP and DAD are frequently seen in rheumatoid arthritis (RA) and dermatomyositis/polymyositis (DM/PM). Prognosis and treatment responsiveness of OP and DAD associated with CTD are no different from idiopathic OP and DAD. Recently a new concept called progressive fibrosing ILD (PF-ILD) was proposed. The effectiveness of an antifibrotic drug nintedanib for PF-ILD was confirmed and an indication was obtained. Nintedanib may become a new treatment option for chronic CTD-ILD. In ILD associated with DM/PM (DM/PM-ILD), there are many cases in which the property of NSIP and OP coexist. In anti-MDA-5 positive cases, DAD often appeared and prognosis is poor. The combination therapy of high dose corticosteroid and calcineurin inhibitor and intravenous cyclophosphamide developed and their prognosis improved. A recommended treatment strategy of DM/PM-ILD has been proposed in the diagnosis and treatment guideline for CTD-ILD. ILD associated with RA (RA-ILD), there are OP, DAD, UIP, NSIP and unclassifiable chronic ILD. UIP associated with RA (RA-UIP) has poorer prognosis than NSIP of RA. Important causes of death of RA-UIP are acute exacerbation. Nintedanib can suppress acute exacerbation, so nintedanib may be useful for RA-UIP. In ILD associated with Systemic sclerosis (SSc-ILD), NSIP is predominant. MMF is primarily used to treat progressive case. Since SSc has a strong tendency for fibrosis, nintedanib can be expected. A recommended treatment strategy of SSc-ILD has been proposed in the diagnosis and treatment guideline for CTD-ILD.

ES8

Molecular Genetics of Behçet's Disease and Real World Data of Apremilast

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Conflict of interest: Yes

Behçet's disease (BD) is a recurrent autoinflammatory disease that presents with a variety of symptoms, including intractable oral ulcers, which can lead to a decreased quality of life. Various immune cells such as neutrophils and macrophages has been reported to play important roles in the pathogenesis of the disease by producing/releasing cytokines such as TNF-α and IL-1β. Analysis of data from an ongoing registry study revealed that BD patients still maintain high disease activity and require further therapeutic intervention. Apremilast, a small molecule drug with immunomodulatory effects, has been approved in Japan for the treatment of psoriasis and psoriatic arthritis as well as oral ulcers associated with BD for which topical therapies are inadequate. PDE4 inhibition by Apremilast increases intracellular cAMP levels resulting in phosphorylation of cAMP responsive element binding protein (CREB), which in turn modulates NF-κB and AP-1 mediated transcriptional activity of the immune system. Importantly, recent genome-wide association studies of BD and analysis of familial BD have revealed known therapeutic target pathways for apremilast, including IL-10, Th17 and NF-κB. My presentation will provide deeper understandings of BD pathogenesis from genetic perspectives and also will shed lights on the fundamental link between the mechanisms of action of apremilast and the pathogenesis of BD.

ES9-1

Importance of the pre-conception care in consideration of life plan of female patients suffering from rheumatoid arthritis: Survey in young female patients with rheumatoid arthritis

Taeko Takahashi
Sagawa Akira Rheumatology Clinic

Conflict of interest: None

Women aged from 18 to 45 are the age they experience various life events such as entering school, employment, marriage, delivery, and childcare, and also the age of susceptibility for rheumatoid arthritis (RA). Due to change of lifestyle, age of marriage and childbearing tend to late recently, current average age of first pregnancy is 30.7. In general, fertility is impaired 35 years old or later. In RA patients, fecundity is low and periods to achieve a pregnancy despite regular unprotected sexual intercourse is longer compare to healthy subjects. High disease activity of RA reduce fertility, and may lead high-risk delivery including preterm delivery and the low weight child born. Although RA patients must have deeper understanding of pregnancy and treatment of RA, they may hesitate to communicate on pregnancy and childbirth. Shared decision making with patients in consideration of pregnancy/childbirth is necessary to help patients to face their disease journey. Health care professionals need to be involved in disease management with clear understanding of patients' wish for life plan and knowledge of disease. Pre-conception care is the concept of "care before pregnancy", including improvement of health status and change of life style aiming to healthy pregnancy, childbirth, and child care in both mother and baby. We believe that definite disease control and preconception care from early stage bring better life planning. However, recognition of the pre-conception care in healthcare worker is low, and there is no consensus on the timing of preconception care. In addition, substantial cases consult after became pregnant. Pre-conception counseling for patients with rheumatic disease in EULAR recommendations was firstly described in 2017. In our hospital, some patients need pre-conception care, but patient care is not yet sufficient due to difficulty of aggressive information gathering of sensitive matters. Under these circumstances, we conducted patient survey on preconception care to identify issues which prevent implementation of preconception care.

ES9-2

Practice of preconception care in the internal medicine for pregnancy

Yuri Hiramatsu

Internal Medicine IV, Osaka Medical College

Conflict of interest: None

It is widely known that in the pregnancy of women with rheumatoid arthritis disease, pregnancy in a highly disease-active state is at very high risk for both mother and child. In recent years, the age of pregnancy has increased significantly in Japan. In patients with rheumatoid arthritis disease, if they become pregnant after controlling the underlying disease or treating infertility, the risk of pregnancy complications (chromosomal abnormalities, preterm birth, etc.) due to aging increases in addition to the risk of the disease. It is necessary to make an early pregnancy plan for WoCBA patients. Since 2013, our hospital has been providing outpatient clinics to support pregnancy with collagen disease in collaboration with obstetrics. At our outpatient department, we provide pre-conception care to patients of childbearing age from the aspects of both rheumatologists and obstetricians, and are working on patient education before pregnancy. First of all, it is important to eliminate the psychological anxiety of the person by consulting in advance about the physical constitution and treatment policy for the disease for general pregnancy from before pregnancy. On top of that, the aim is to obtain a good pregnancy outcome for both mother and child, hoping for pregnancy with sufficient disease control. Recently, the transitional medical care from pediatrics to internal medicine is also attracting attention. Adolescent and young adult patients, who are between childhood and adulthood, have "effects of illness treatment on reproductive function", "effects on schooling and employment", and "various effects of illness during sensitive periods". Although it has many problems such as "mental stress and anxiety about the future", the current situation is that the support system is not in place. Regardless of the disease, it is necessary to intervene for the independence of the patient's mind and body from an early stage, and to perform disease control and preconception care for future pregnancy from the time when the patient becomes pregnant after secondary sexual characteristics. is there. For WoCBA patients and their families, "uncertain vague anxiety" may have led to postponement of the decision to "get pregnant". It is very significant to cooperate well with other departments and provide pre-conception care so that all WoCBA patients who wish to become pregnant can think positively about pregnancy, childbirth, childcare, and even the next child pregnancy.

ES10

[Academic Society Co-sponsored Educational Event] Reviewing physician-patient communication: How to get the most from a time-pressured office visit

Kenta Misaki[1], Kei Ikeda[2], Naoto Azuma[3], Tadashi Okano[4], Takeshi Kashiwagura[5], Masaru Kato[6], Hirofumi Shoda[7], Hiroto Tsuboi[8], Natsuko Nakagawa[9], Shinji Fukaya[10], Yusuke Miyazaki[11]
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Conflict of interest: Yes

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 will focus on Module III: Practice Efficiency. Against the backdrop of time-pressured outpatient visits, it is difficult for rheumatologists to complete their many tasks and achieve their entire agenda quickly. The criteria that define care outcomes include "the quality of the interaction between the physician and the patient," "the time a visit actually took versus the time it felt like it took," and "the amount of clinical information." However, to improve practice efficiency, the goal is to find a way to improve tangible outcomes and actual outcomes without increasing the time required to do so. This will allow the physician to shorten the time spent on specific exchanges during visits and on each agenda item in some cases. Three communication techniques designed to improve practice efficiency are "utilizing examples/stories," "explaining the definitions of terms," and "setting the agenda." In this workshop, group discussions on selected topics will be followed by roleplaying to allow participants to learn ways to improve their practice efficiency that they could immediately put to implement in daily clinical practice.

ES11-1

Recent Advances in SpA Practice and Biologics

Hiroaki Dobashi
Kagawa University

Conflict of interest: Yes

Spondyloarthritis (SpA) can be broadly divided into two types: peripheral and axial. Psoriatic arthritis (PsA) is the most common form of spondyloarthritis with a focus on peripheral lesions. PsA has been thought to be rare in Japanese people, however, Kishimoto et al. reported that it occurs in about 15% of psoriasis patients in Japan, which is the same as in Europe and the United States. The main body of the disease is focused on enthesitis, which present with a great variety of symptoms, including finger inflammation and nail lesions, which are key to the diagnosis. On the other hand, ankylosing spondylitis (AS) is a typical example of a disease centered on an axial lesion. Recently, however, non-radiographic axial spondylitis (non-radiographic axial SpA), which does not meet radiographic criteria, has been recognized as a new disease category. As with PsA, there are various extra-articular features in this category of spondylitis. Although early diagnosis of SpA is desirable, differential diagnosis is crucial for the diagnosis of SpA that requires therapeutic intervention. Particular attention should be paid to the diagnosis of non-radiographic axial SpA. Advances in clinical immunology and the results of clinical trials of new drugs have led to therapeutic strategies based on the cytokine taxonomy, and there are now a variety of options for the treatment of SpA. Among them, TNF-alpha inhibitors were the first biologics to be approved for AS and PsA, and as with RA treatment. The treatment for PsA and AS using TNF inhibitor had a significant impact on physicians and SpA patients. Since then, further advances have led to the development of many agents that inhibit IL23-IL-17axis in addition to TNF-alpha inhibitors. Among them, that inhibit IL23-IL-17axis are proving to be particularly effective for axial SpA. The optimal use of many of these biologics has not yet been fully explored. In this seminar, I will discuss the importance of SpA diagnosis and the need for therapeutic interventions, using some cases in my institute.

ES11-2

TNF inhibition in patients with rheumatoid arthritis (RA)

Satoshi Ito
Niigata Rheumatic Center

Conflict of interest: None

In this seminar, I will show the effectiveness of infliximab (IFX) and golimumab (GLM). At Tsukuba University, we reported that joint destruction can be ameliorated by IFX using compact magnetic resonance imaging. The efficacy of IFX drew the interest of the clinical clerkship concerning its use for rheumatology. We reported the effectiveness of mizoribin pulse therapy for the secondary failure of IFX. Since dose escalation and shortening of the interval of IFX was approved in 2009, we reported its effectiveness regardless of the anti-cyclic citrullinated peptide antibody titer at Niigata Rheumatic Center. The nutritional state was improved by

IFX, and IFX was more effective than other biological disease-modifying antirheumatic drugs (bDMARDs) in patients with a high disease activity. We also reported the possibility of achieving a so-called "Bio-free condition (BF)" with IFX. When patients had flare-up after BF, dose escalation of methotrexate and/or adding conventional synthetic (cs) DMARDs was effective. However, when such treatments failed, introduction of GLM was very effective. One patient who achieved BF a second time after discontinuation of GLM received additional csDMARDs. We also reported the results of the long-term use of GLM. In some patients, GLM did not show an immediate response, but once it showed effectiveness, secondary failure was rare, possibly due to the lack of immunogenicity. We established a medical cooperation system to inject GLM in patients living in rural areas far from our rheumatic center. After the self-injection of GLM was approved, some patients switched to a self-injection approach or started GLM with self-injection. These patients tended to be younger with a shorter disease duration than those who received injections at the hospital. By using two TNF inhibitors (IFX and GLM) with consideration of their characteristics, effective treatment of rheumatoid arthritis is possible.

ES12-1

Positioning of TNF inhibitors in the treatment of spondyloarthritis

Kurisu Tada
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Conflict of interest: Yes

Ankylosing spondylitis (AS) is a prototype of spondyloarthritis (SpA), and is a chronicaly progressive rheumatic disease that affects the spine and sacroiliac joints. The main condition is inflammation that occurs at the insertion site of tendons or ligaments to bones, and in some patients, spinal ankylosis to kyphosis may progress and interfere with daily activities. Non-steroidal anti-inflammatory drugs (NSAIDs) have been used as conventional treatments for AS, but there have been some patients whose disease cannot be controlled by NSAIDs alone. With the approval of TNF inhibitors for AS in 2010 and their widespread use, the treatment of AS has made great strides. Furthermore, from 2018, IL-17 inhibitors have also been approved for AS, increasing treatment options then TNF inhibitors are inadequately effective or cannot be administered due to side effects. The efficacy of these biologics is maximized when administered at the right time with the correct diagnosis. Diagnosis of AS is often based on the modified New York criteria of 1984. Although the modified New York criteria was originally a classification criteria, it is also used as a diagnostic criteria due to its high specificity. In addition, the ASAS classification criteria for axial SpA of 2009 have been used. However, this is a classification criteria, and it is a mistake to use this criteria as a checklist for diagnosis. It is necessary to make a diagnosis after performing sufficient discrimination / exclusion diagnosis. It is also important to evaluate disease activity correctly in determining the necessity of strengthening treatment. Finally, attention should be paid to the selection of biologics. TNF inhibitors and IL-17 inhibitors can be used as biologics for AS, but it is recommended to use TNF inhibitors rather than IL-17 inhibitors. Because it is approved first and has a wealth of efficacy and safety information. In addition, patients with recurrent uveitis and patients with inflammatory bowel disease should use TNF inhibitors rather than IL-17 inhibitors. In this seminar, I will explain the points to be noted when using biologics for AS.

ES12-2

Skin manifestations of rheumatoid arthritis and spondyloarthritis and their treatment

Toshiyuki Yamamoto
Fukushima Medical University

Conflict of interest: Yes

Rheumatoid arthritis (RA) presents with a variety of skin manifestations, although these are not diagnostic of RA. These are classified as (i) specific lesions, (ii) lesions due to vascular impairment, (iii) lesions due to rheumatoid vasculitis, (iv) non-specific lesions, (v) lesions due to immune dysfunction, (vi) lesions due to RA-associated diseases, and (vii) drug-induced conditions. Lower leg ulcer is a frequent complication and its differential diagnoses include venous stasis ulcer due to circulatory disturbances, rheumatoid vasculitis, and pyoderma gangrenosum (PG) as an active form of neutrophilic dermatosis. Lower leg ulcer is often incorrectly diagnosed as a form of malignant RA (rheumatoid vasculitis) without a biopsy. PG is one of the common skin complications of RA, resulting in the formation of proliferative, gangrenous, perforated ulcers in the lower legs. It can also accompany other underlying conditions, such as inflammatory bowel disease, hematologic disorders, and Takayasu's arteritis. Its histopathological features include a dense neutrophilic and lymphocytic infiltrate and lack of vasculitis, without specific findings. Thus, the diagnosis is based on the exclusion of other differential diagnoses. While traditional treatments include corticosteroids and immunosuppressants, adalimumab has recently been covered by health insurance. Spondyloarthritis is a condition that must be differentiated from RA, and can be accompanied by psoriatic skin lesions, i.e. psoriatic arthritis (PsA). It presents with diverse symptoms, such as psoriasis, nail psoriasis, dactylitis, enthesitis, secondary synovitis, and peripheral and axial arthritis. It is well known that antibodies against TNF, IL-17 and IL-23 have been used for treating PsA. This presentation will focus on RA and PsA and their skin manifestations and treatment from a dermatological perspective.

Workshop

W1-1

Clinical characteristics of NinJa 2019 RA patients with CKD treated with Biologics

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Conflict of interest: None

[Objective] To clarify the characteristics of NinJa2019 RA patients with CKD treated with Biologics (BIO). [Methods] Data of 12155 patients registered to NinJa2019 with serum creatinine level (N19Cr) were used. Patients treated with infliximab (IFX), etanercept (ETN), tocilizumab (TOF), adalimumab (ADA), golimumab (GOL), certolizumab pegol (CZP), infliximab-BS (IFX-BS), sarilumab (SAR), etanercept-BS (ETN-BS) were extracted. DAS28 were compared between N19Cr and each BIO in total, or in three CKD stage groups, G1, 2, G3, and G4, 5. [Results] Patient numbers were IFX:194, ETN:495, TCZ:931, ADA:210, ABA:674, GOL:321, CZP:138, IFX-BS:60, SAR:50, and ETN-BS:113. Case number of CKD groups, G1, 2-G3-G4, 5 were 8869-3106-180/158-34-2/401-84-10/712-196-23/175-34-1/454-207-13/224-93-4/114-24-0/48-12-0/39-10-1/93-17-3. The percent of patients in CKD G3+G4,5 in each treatment was 27% in N19Cr, and 32.6% in ABA, 30.2% in GOL and 23.5% in TCZ. DAS28 was significantly lower in ADA, TCZ, and SRL than that in N19Cr in total, and significantly lower in TCZ than that in N19Cr in G1, 2 and G3. [Conclusions] The percents of patients of CKD G3+G4, 5 were higher in ABA and GOL than in N19Cr in NinJa 2019. In CKD G3, DAS28 was significantly lower in patients treated with TCZ than in those of N19Cr.

W1-2

Surveys of clinical practice for rheumatoid arthritis patients who complicated with malignancy from a large database (NinJa)

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Conflict of interest: None

[Objective] To investigate the clinical feature and treatment of patients with rheumatoid arthritis (RA) associated with malignancy. [Methods] RA patients information was collected using a national multicenter cohort database (NinJa2012-2018). The current status of disease activity and treatment was investigated in patients with newly complicated malignancies between April 1, 2012 and March 31, 2019. [Results] Of 28034 (101571 person-years) patients enrolled in NinJa 2012-2018, 1143 cases had malignant disease, 762 women (66.4%), average age 70.8 ± 9.8 years in the year when malignant tumor was diagnosed. The biologics usage rate for RA in patients with malignant lymphoma, the year before the onset of the tumor to 5 years after the onset, was 15.5% → 0% (TNF inhibitors), 2.2% → 30% (tocilizumab), 5.6% → 0% (abatacept). The usage rates of biologics for RA in other malignant tumors were 12.8% → 3.1% (TNF inhibitors), 8.5% → 6.3% (tocilizumab), 4.1% → 3.1% (abatacept). [Conclusions] Biologic agents used after the development of malignancies were more commonly tocilizumab, especially in malignant lymphomas. Other malignancies also had reduced use of TNF inhibitors after tumor development.

W1-3

The causes of death in deceased patients with RA by NinJa 2019 cohort

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Conflict of interest: None

[Objectives] The purpose of the present study is to evaluate the age at death and the cause of death in patients with rheumatoid arthritis (RA) in NinJa2019. [Methods] 135 Japanese deceased patients with RA, who were registered in the large cohort database (NinJa: National Database of Rheumatic Diseases by iRnet in Japan). We investigated the age at death, the causes of death of all patients. [Results] The mean age at death was 77.7 years old. The major cause of death in deceased patients was malignancy in 34 patients involving lung cancer or gastric cancer, next was infection in 39 patients involving in pneumonia in 28 patients. Next was cardiovascular disease in 21 patients respiratory dysfunction involving intestinal pneumonia in 10 patients. [Conclusion] The life expectancy of Japanese patients with RA was getting better. The major causes of death were malignancy and infection. It is important for us to risk management for elderly RA patients.

W1-4

Can early achievement of remission in early rheumatoid arthritis lead to improvement in 10-year survival rate? -results from the IORRA cohort-

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Conflict of interest: None

[Objective] To investigate whether early achievement of remission in early rheumatoid arthritis (RA) leads to good vital prognosis. [Methods] From the 2001 to 2009 IORRA cohort, patients with early and active RA (<2 years of disease duration and DAS28>3.2) at their first survey were identified. Of these, we enrolled patients who participated in at least one of the two surveys which were conducted 6 and 12 months after the initial survey, and observed them for 10 years. Patients who had achieved DAS28<2.6 at least once within 1 year after their initial survey were classified as Group A and the rest were as Group B. Primary endpoint was 10-year survival, which was analyzed by using the Cox model. [Results] The number of patients was 504 (80% female) in Group A and 1,265 (85% female) in Group B. The median age at baseline was 54 in Group A and 57 in Group B. Deaths were confirmed in 20 cases (4%) in Group A and 105 (8%) in Group B. The 10-year survival rate was 95% for Group A and 89% for Group B. Group B was identified as a risk factor for death within 10 years (adjusted HR 2.2, 95%CI 1.3-3.5: $p<0.01$) after adjusting for gender, age of onset, DAS28, and RF. [Conclusions] Early achievement of remission in early RA can lead to a better vital prognosis.

W1-5

The characteristics of rheumatoid arthritis patients with persisting moderate to high disease activity -based on the IORRA cohort

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Conflict of interest: None

[Objective] To examine characteristics of rheumatoid arthritis (RA)

patients with persisting moderate to high disease activity. [Methods] Patients with RA who participated in the IORRA surveys both in the April (baseline) and October 2019 were enrolled. Patients' background between the DAS28 < 3.2 group (the two consecutive DAS28-ESR < 3.2) and the DAS28 ≧ 3.2 group (the two consecutive DAS28-ESR ≧ 3.2) were compared. [Results] There were 280 patients in the DAS28 ≧ 3.2 group and 1789 patients in the DAS28 < 3.2 group. The patient background at baseline was as follows (DAS28 ≧ 3.2/ DAS28 < 3.2); % of female: 93.2/85.0 (p< 0.01), average age (years): 66.0/ 61.3 (p< 0.01), disease duration (years): 20.3/15.9 (p< 0.01), prednisolone (PSL) user (%): 40.7/17.8 (p< 0.01), average PSL dose (mg/day): 3.4/3.4 (p< 0.01), methotrexate (MTX) user (%): 65.4/78.5 (p< 0.01), average MTX dose (mg/week): 8.9/8.7, and biologics use (%): 28.6/30.6. The proportion (%) of the patients with any complications (52.0/37.3), concomitant heart disease (1.9/5.4), respiratory disease (4.6/10.8), and diabetes (5.0/10.9) were significantly higher in the DAS28 ≧ 3.2 group (p < 0.01). [Conclusion] The characteristics of RA patients with persisting moderate to high disease activity were revealed.

W1-6

Potential Immune-Mediated Diseases (pIMDs) with Pre-existing pIMDs, Allergies, and Reductions in Treatment Exposure in a Japanese Population: A Health Insurance-Claims Database Cohort Study (2014-2019)

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Conflict of interest: Yes

[Objective] We evaluated the incidence of pIMDs, and the proportion of patients (pts) with allergies and reduced treatment exposure prior to the onset of selected pIMDs of interest. [Methods] This was a retrospective cohort study using the JMDC claims database (2014-19). Incidence rates (IR) of subsequent, selected pIMDs were estimated after the onset of another initial, selected pIMD during the study period. The proportions of pts with allergies and reduced treatment exposure during the 12 months prior to the onset of any initial, selected pIMD were reported. [Results] The study included ~3.6 million pts. For each selected pIMD, the IR as a subsequent pIMD was generally higher than as an initial pIMD (e.g. Sjögren's syndrome: 733.9 vs 35.4 per 100,000 person-years). Before onset of any initial, selected pIMD, preexisting allergies were reported in 40.8% (Bell's palsy)-73.1% (mixed connective tissue disease) of pts, corticosteroid dose was reduced in 42.0% (1131/2692) of pts, and immunosuppressants and antineoplastic agents were discontinued in 19.9% (1086/5457) and 18.8% (79/421) of pts respectively. [Conclusions] There was high incidence of subsequent pIMD in pts with another preexisting pIMD. Some pts with pIMDs had preexisting allergies and prior reductions in treatment exposure.

W2-1

The survival rate, causes of death, and risk factors for death in RA: results from 10 years of observational study

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Conflict of interest: None

[Objective] To clarify the survival rate, causes of death, and risk factors for death in RA patients. [Methods] A cohort study. Subjects were consecutive RA patients who had visited our department in April 2010. We reviewed medical records. The survival rate and risk factors were determined using the Kaplan-Meier analysis. [Results] Subjects were 499 patients (134 males / 365 females) with an average age of 59.8 years. Biologics, MTX and glucocorticoid (GC) were administered to 183 (37%), 293 (58%), and 285 (57%), respectively. 164 cases were lost during the observation period. Five years- and 10 years survival rates were 93.6% and 87.6%, respectively. During the observation, 46 patients died; causes of death were infection of 13, pulmonary diseases of 10, malignancy of 9, and cardiovascular diseases of 8. The risk factors for death were male, age over 65 years, and the presence of pulmonary abnormalities. GC use was identified as a poor prognostic factor, while the use of MTX and biologics were factors for survival. [Conclutions] The 10-year survival rate in RA was 87%. Major causes of death were infection, pulmonary diseases, malignancy, and cardiovascular diseases. Glucocorticoid use was a risk factor for death, while the use of MTX and biologics was protective one.

W2-2

Risk factors for clinical fracture in patients with rheumatoid arthritis are low bone mineral density and use of glucocorticoid: Nine-year findings of the TOMORROW study

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Conflict of interest: None

[Objective] The present study aimed to prospectively determine the incidence of clinical fractures and the risk factors in the patients with rheumatoid arthritis (RA) in the TOMORROW study. [Methods] We evaluated bone mineral density (BMD), medication and the incidence of fracture during nine years in 202 patients with RA (mean age, 58.6 y) and 202 age- and sex-matched healthy controls (mean age, 57.4 y). Weanalyzed the risk factors for fractures. [Results] The incidence of fractures in patients was significantly higher compared to controls (27.5 vs 18.3%, p=0.04). Cox proportional hazard modelrevealed low BMD at thoracic vertebrae (< 0.7 g/cm2) significantly associated to the incidence of fractures (hazard ratio [HR] 1.86, p=0.02) in all participants, but RA morbidity did not (HR 1.47, p=0.10). In patients, low BMD was the most prominent risk factor (HR 2.66, p=0.02). Although medication with glucocorticoid (GC) at entry (HR 1.68, p=0.09) was not a significant risk factor, GC dose of only => 2 mg/day at entry increased risk for fractures in patients (HR 1.91, p=0.04). [Conclusions] The incidence of fractures in patients was significantly higher than controls during nine years. LowBMD and low GC dosewere significant risk factors for the incidence of fractures in RA patients.

W2-3

Relationship between falls and fall-risk-increasing medication in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Several studies have reported that patients with rheumatoid arthritis (RA) are more likely to fall than the general population. Many of these reports have found disease activity or physical ability, not concomitant drug use, as a risk factor. This study aimed to show the relationship between falls and fall-risk-increasing medication in patients with RA. [Methods] Data from patients with RA were collected in Showa University Hospital. Our outcome measure was the prevalence of fall incidents in the past year, determined by administering questionnaires to patients with RA. [Results] 303 patients were included in the analysis. The median age was 68 years and 78.5% were women. Of the 303 patients included in the study, 45 patients who used fall-risk-increasing medication, 18 experienced at least one fall in a year. Using Pearson's chi-square test, we examined the relationship between fall incidents and fall-risk-increasing medication (P<0.01, odds ratio [OR] 2.71, 95% confidence interval [CI]: 1.09-4.67). Using multivariable logistic regression, the adjusted OR of those who fall incidents and were using fall-risk-increasing medication

was 2.18 (P=0.02, 95%CI: 1.09-4.38). [Conclusions] Use of fall-risk-increasing medication may influence the likelihood of falls in patients with RA.

W2-4

Acute Kidney Injury (AKI) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] It is important to evaluate renal function in RA patients. Case reports of AKI have also been reported in RA patients due to drug administration. However, the frequency of AKI and the factors involved have not been investigated. Thus, we investigate the frequency of AKI and the factors involved in RA patients. [Methods] Two hundreds fifty three RA patients (211 females, 42 males, mean age 62.3 ± 12.5 years) diagnosed more than 3 years before if not followed for more than 5 years or more than 5 years were registered. Urinalysis, serum Cr, eGFR, BUN, other biochemical tests, serological tests, and disease activity were evaluated. The AKI during the observation period was evaluated. The criteria of AKI was that serum Cr increased by 0.3 mg / dl or increased by 1.5 times between consecutive visits according to the KIDIGO standard and the report of Leither et al. [Results] Twenty (7.9%) patients developed AKI, 22 times. The causes of AKI were 10 infections, 6 dehydrations, 2 enteritis, 1 urticaria, 2 hypercalcemia due to VitD administration, and 1 ureteral stone. Eight patients (40%) had eGFR less than 60 and 13 patients (65%) received MTX in AKI developed group. [Conclusions] It is necessary to pay attention to AKI from the viewpoint of drug treatment.

W2-5

Has the advent of biologics changed the association between depression, pain, and inflammation in patients with rheumatoid arthritis?

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Conflict of interest: None

[Objective] To examine the association between psychological factors in patients with rheumatoid arthritis and inflammation and pain before and after the advent of biologics. [Methods] A survey was conducted in 2003 and 2019 targeting RA patients who visited the outpatient department at the university hospital. A general linear model and multiple regression analysis were performed with adjustment of sex and age to compare the differences by year of study. [Results] The analysis subjects were 36 males (mean age 62.9 ± 11.7 years) and 161 females (59.1 ± 12.0 years) in 2003, 37 males (66.9 ± 9.4 years) and 216 females (64.7 years± 10.0 years) in 2019. CRP, DAS-28, and pain were all significantly lower in 2019 than in 2003 ($p < 0.001$), but the change in depression (BDI-II) was not significant ($p = 0.10$). For SF-36, the physical summary score was significantly reduced ($p < 0.001$), but the psychological summary score was not significantly different ($p = 0.10$). [Conclusions] It has been suggested that while the physical quality of life of patients with rheumatoid arthritis has improved significantly since the advent of biologics, the psychological burden may still be high.

W2-6

Incidence of malignant lymphoma in East Asian rheumatoid arthritis: A systematic review and meta-analysis of cohort studies

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Conflict of interest: None

[Objective] In order to meta-analyze standardized incidence ratio (SIR) and to examine heterogeneity of each study, we conducted a systematic review of cohort studies that reported the relationship between Rheumatoid arthritis (RA) and Malignant lymphoma (ML) in relatively homogeneous races in the East Asian region. [Methods] In August 2020, we searched literature for research on RA and ML conducted in East Asia using Pubmed, MEDLINE, and Cochrane databases. 432 documents were screened, and 6 articles which reported SIR, were subjected for the study. [Results] The SIR of ML compared to the general population of RA in East Asia was 4.34 [3.11-6.08] in the fixed effects model and 4.22 [3.01-5.92] in the random effects model. Cochran's Q test showed $p = 0.69$ and a heterogeneity scale I^2 was 0%. These results suggest no heterogeneity between studies. The Funnel plot did not show any publication bias. Analyses of the risk factors was performed in an article reported from Japan. Age, MTX, and tacrolimus were proven an risk factors, but biologics were not. [Conclusions] Studies reported in East Asia since 2010 showed that RA has approximately four times risk of developing ML, and that no heterogeneity was identified between countries.

W3-1

PD-1 regulates autoreactivity of peripheral helper T cells in the joint of rheumatoid arthritis

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Conflict of interest: None

[Objective] Recently, a subset of CD4 T cells that express high levels of PD-1 but are distinct from follicular helper T cells, peripheral helper T cells (Tph), were identified in RA joint. Since PD-1 is expressed on T cells chronically stimulated with the antigens, we hypothesized that Tph cells are the pathogenic autoreactive CD4 T cells in RA joint. [Methods] Mononuclear cells were isolated from the synovial fluid and peripheral blood of RA patients. TCR Vb repertoire were examined by a flow cytometer. In addition, TCR clone proliferation of Tph cells were analyzed by next-generation sequence analysis. Autoreactivity of CD4 T cells was investigated in vitro by an autologous mixed lymphocyte reaction (AMLR) assay. [Results] Tph cells showed biased TCR Vb usages compared to other CD4 T cells in the joint and peripheral blood. TCR clones of Tph cells had significantly lower similarity to peripheral blood memory CD4 T cells than PD-$1^{low/neg}$ CD4 T cells, suggesting that the clones proliferated locally in the joint. Tph cells exhibited AMLR activity, which was pronounced by blocking PD-1-signaling and required recognition of self-MHC class II molecules. [Conclusions] Tph cells might be the autoreactive CD4 T cells in RA.

W3-2

Analysis of regulatory T cell fractions in patients with rheumatoid arthritis treated with tocilizumab

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Conflict of interest: None

[Objective] We have reported that tocilizumab (TCZ) treatment increases the proportion of Treg in RA. It is well known that Treg mainly consists of three fractions with different inhibitory activity. The objective of this study was to identify the Treg fractions increased in RA patients treated with TCZ to clarify the mechanisms of efficacy of TCZ. [Methods] Forty RA patients who received TCZ as First-Bio from October 2011 to December 2014 and eleven healthy controls (HC) were enrolled in this

study. The proportion of $CD127^{low}$ Treg ($CD4^+CD25^+CD127^{low}$), resting Treg (rTreg; $CD4^+CD45RA^+Foxp3^{low}$), activated Treg (aTreg; $CD4^+CD45RA^-Foxp3^{high}$) and non-Treg (nTreg; $CD4^+CD45RA^-Foxp3^{low}$) in PBMC were analyzed by flow cytometry. [Results] Flow cytometry analysis revealed that the proportion of rTreg was lower in RA before TCZ treatment (0w) than in HC. $CD127^{low}$ Treg was elevated after 12w compared to 0w. In addition, rTreg increased at 52w, aTreg increased at 12w and 24w. On the other hand, nTreg decreased at 52w. No significant difference was observed in the proportion of each Treg fraction at 52w of TCZ treatment compared with HC. [Conclusions] Our data suggest that Treg fractions with inhibitory activity increased in RA patients treated with TCZ and that TCZ may normalize functional Treg.

W3-3

Role of TICAM-1 in IL-17 mediated inflammatory response and autoimmune disease

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Conflict of interest: None

[Objective] IL-17 is involved in autoimmune disease, but the molecular mechanism about underlying IL-17 mediated pathology is unclear. TICAM-1 is known as an adaptor molecule of TLR3, and its deficiency mice resulted in increased severity of autoimmune disease. Because TICAM-1 and 17RA share structural resemble domain, we hypothesized that TICAM-1 was involved in IL-17 signaling pathway. Then, we examined whether TICAM-1 was involved in IL-17-mediated inflammatory response and autoimmune disease. [Methods] We generated TICAM-1 knockout (KO) cells using the CRISPR-Cas9 system, and investigated their IL-17A-induced inflammatory response. We also investigated the molecular interactions among 17RA and its adaptor molecule, Act1 and TICAM-1. Next, we utilized EAE model and analyzed spinal cord in Wild type (WT) and KO mice. [Results] We found that 1) KO cells enhanced NF-kB dependent transcriptional activity and the expression of *Il6, Cxcl1, Ccl20* upon IL-17A stimulation as compared with WT cells, 2) TICAM-1 was co-immunoprecipitated with Act1 and inhibited the interaction between 17RA and Act1, and 3) KO mice had increased infiltration of pathogenic $CD4^+$ cells in spinal cord compared to WT mice. [Conclusions] TICAM-1 regulated autoimmune disease through suppressing 17RA signaling.

W3-4

Involvement of lung microbiota in interstitial pneumonia

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Conflict of interest: None

[Objective] The pathogenesis of interstitial pneumonia (IP) associated with collagen diseases is not well understood. We hypothesized that IP is possibly regulated by the lung microbiota through epithelial injury, which is one of the mechanisms for lung fibrosis. To test this hypothesis, we investigated whether the microbiota is involved in the pathogenesis of IP by using bleomycin (BLM)-induced IP (BLM-IP) mice. [Methods] Six-week-old C57BL/6 mice, orally pre-administered with antibiotics (ampicillin, vancomycin, neomycin, and metronidazole) for two weeks, were intratracheally instilled with BLM for IP induction. Two weeks later, the lung tissue was examined for HE and Masson trichrome stain and immunohistological analysis for cyclin-dependent kinase inhibitor 1 (p21). [Results] Lung fibrosis was significantly inhibited and there was a decrease in the number of p21-positive alveolar epithelial cells (AECs) in the Abx-treated BLM-IP mice compared to the untreated BLM-IP mice. [Conclusions] These results suggest that pulmonary microenvironments and the immune system regulated by the microbiota of the lung and gut may possibly contribute to the development and progression of lung fibrosis. The results also suggest that microbiota could contribute to the cellular senescence of the AECs.

W3-5

Microglial activation in the sensory circumventricular organs of the mice with collagen-induced arthritis

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Conflict of interest: None

[Objective] Neuropsychological symptoms such as hyperalgesia and depression are common among patients with rheumatoid arthritis (RA). However, it is unclear how peripheral arthritis affects the brain. The sensory circumventricular organs (sCVOs) that lack the blood-brain barrier located in three regions: the subfornical organs (SFO), the organum vasculosum laminae terminalis (OVLT), and area postrema (AP). They have high vascular permeability and cytokine receptors, and are rich in microglia. Therefore, substances in blood such as cytokines can affect microglia in the sCVOs. To clarify the pathway to brain thorough the sCVOs, we analyzed the brain of mouse model. [Methods] Mice with collagen-induced arthritis were transcardially perfused fluorescent dye. Immunostainings for c-fos, an activated neuronal marker, and Iba-1, one of the microglial markers, were performed on brain slices. [Results] Extravascular leakage of fluorescent dye showed locations of the sCVOs. In the AP, the Iba-1 expression increased and correlated with the c-fos expression. In the SFO and OVLT, there are no changes. [Conclusions] The differences between sCVOs in response to inflammation are not almost reported. Our findings estimated the possibility that the AP pathway is important under arthritis conditions.

W3-6

Imiquimod-induced psoriasis-like skin inflammation was attenuated in lowering uric acid model mice

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Conflict of interest: None

[Objective] High levels of serum uric acid (SUA) are frequently detected in patients with psoriasis. Some studies reported the correlation of severities of psoriasis with levels of SUA. However, the role of uric acid on the pathogenesis of psoriasis has not been clear. [Methods] We used one of lowering uric acid model mice, uricase transgenic mice (UOXTg) in which the metabolism of uric acid was increased and the amount of uric acid in the body was decreased. The psoriasis-like skin inflammation was induced by the application of imiquimod on the backs of UOXTg or wild type mice for five consecutive days. We used a modified PASI score for the evaluation of severity of the skin lesions. The expressions of inflammatory cytokines such as IL-17 or IL-23 in the skin lesions on Day 1 and Day 2 were evaluated by real-time PCR. [Results] The severity (PASI score) of skin lesions of UOXTg mice was significantly decreased than that of WT mice after Day 3 ($p = 0.03$). The expressions of IL-17A and IL-17F in lesions were significantly decreased in UOXTg mice (IL-17A; $p < 0.01$, IL-17F; $p < 0.01$). [Conclusions] Imiquimod-induced psoriasis-like skin inflammation was attenuated in lowering uric acid model mice. Uric acid may associate with the pathogenesis of psoriasis via IL-17A/F pathway.

W4-1

Plasticity and stability of regulatory T cells in adult-onset Still's disease

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Conflict of interest: None

[Objective] To investigate plastic differentiation and functional stability of regulatory T cells (Tregs) in adult-onset Still's disease (AOSD). [Methods] Peripheral blood samples were provided from 26 patients with

acute AOSD, 10 who achieved remission (remission AOSD), and healthy controls (HC). The expression of interferon-γ (IFN-γ), interleukin (IL)-17, and IL-4 in the population of CD4+CD25+FoxP3+, and suppressive function of Tregs were evaluated by flow cytometry. The obtained results were statistically analyzed with clinical findings. [Results] The expression of IFN-γ, IL-17, and IL-4 in Tregs was significantly higher in acute AOSD than in HC; notably, IFN-γ expression was significantly correlated with serum ferritin levels. The suppressive ability of Tregs was significantly reduced in acute AOSD than in HC. In remission AOSD, IFN-γ, IL-17, and IL-4 expression were significantly decreased, and not significantly different from HC. The suppressive ability of Tregs was also improved. [Conclusions] The plasticity and disability of Tregs were found in acute AOSD. Furthermore, IFN-γ expression in Tregs may be correlated to the disease activity. Meanwhile, dysfunction and plastic changes of Tregs were improved in remission, suggesting that Tregs stability is reversible.

W4-2

Subsets of synovial fluid derived fibroblasts in rheumatoid arthritis

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Conflict of interest: None

[Objective] The subsets of rheumatoid arthritis (RA) fibroblast-like synoviocytes in fresh human synovial tissue have the subsets characterized by the expression of PDPN, CD34, and THY1. The aim of this study is to investigate the subsets of SF-derived fibroblasts and the difference of subsets proportion in variety of clinical features. [Methods] We collected the SFs from RA patients at the onset or at the flare. The profile of cell surface markers expressed by SF-derived adherent cells were analyzed using flow cytometry performed by triple staining with PDPN, CD34 and THY1. [Results] We got the SFs from 10 patients. At the primary culture, $PDPN^+$ cells were lower than $PDPN^-$ cells (34.0 ± 4.5 vs 66.0 ± 4.5%). The proportion of $CD34^-THY1^+$, $CD34^-THY1^-$, $CD34^+THY1^+$ and $CD34^+THY1^-$ in the $PDPN^+$ cells were 66.0 ± 4.5, 34.0 ± 4.5, 6.4 ± 3.0, and 0.7 ± 0.1% respectively. 5 patients at the flare had more $CD34^-THY1^-$ cells (60.2 ± 12.6 vs 5.0 ± 0.6%). 3 patients who were pre-diagnosed pseudo-gout had more $CD34^+THY1^+$ cells (41.8 ± 10.1 vs 2.4 ± 1.0%). [Conclusions] These data show that $PDPN^+$ SF-derived fibroblasts have the subsets, and $CD34^-THY1^+$ cells would be major subsets. The difference proportion of SF-derived fibroblast subsets may be involved in a variety of clinical features in RA.

W4-3

Identification of osteoclast-inducer cells in autoimmune arthritis

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Conflict of interest: None

[Objective] In rheumatoid arthritis, inflammation and bone destruction in joints are mainly observed. Using collagen-induced arthritis resistant strain (C57BL/6), it was shown that synovial fibroblast-RANKL plays more important role than T cell-RANKL in joint destruction. To explore that pathogenic importance of synovial fibroblast-RANKL, we aim to evaluate it by generating CIA-sensitive DBA1/J RANKL cKO mice. [Methods] We generated RANKL cKO mice in which RANKL is specifically deleted in synovial fibroblast (Col6a1-Cre), T cells (Lck-Cre) and B cells (Mb1-Cre), respectively DBA1/J background and induced CIA, evaluated joint destruction by microCT. [Results] All the cKO mice exhibited inflammation at the maximal level. Under these inflammatory conditions, joint destruction is ameliorated in Col6a1-Cre Tnfsf11 cKO mice, but not in Lck-Cre or Mb1-Cre mice. [Conclusions] These results show that synovial fibroblasts, but not T cells or B cells are major cellular RANKL source in murine autoimmune arthritis. In RA, not only joint destruction but also periarticular and systemic bone losses occur. It will be important to examine osteoclast-inducer cells in the periarticular and systemic bone loss in the future.

W4-4

Effects of the filgotinib on human lung fibroblasts

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Conflict of interest: None

[Objective] Interstitial pneumonia is an important organ disorder in rheumatoid arthritis (RA). In this study, normal human lung fibroblasts (NHLF) were used to investigate the effects of the filgotinib on lung fibroblasts. [Methods] The expression of JAK1, 2, 3 in NHLF was confirmed by immunostaining. NHLF containing Filgotinib was stimulated with IL-6 / IL-6R, and cytokines in the culture supernatant were measured by ELISA. The expression and phosphorylation of JAK1, 2, 3 in cell lysate was measured by the Western brotting method. A proliferation assay and a chemotaxis assay were performed to investigate the effect of filgotinib on NHLF. [Results] JAK1, 2, 3 was highly expressed by stimulation of NHLF with IL-6 / IL-6R. The addition of filgotinib reduced the expression of total STAT in NHLF and increased the expression of phosphorylated STAT1, 3, 5. In the supernatant, the expression of CXCL16 was suppressed when filgotinib was added. In NHLF with filgotinib added, cell proliferation and migration were suppressed. [Conclusions] It was suggested that filgotinib suppresses cell proliferation and migration of lung fibroblasts and may suppress its inflammation.

W4-5

Antifibrotic agent, nintedanib ameliorates lung fibrosis in induced-rheumatoid arthritis-associated lung disease model

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Conflict of interest: Yes

[Objective] D1CC x D1BC mouse is a rheumatoid arthritis (RA) model which specifically expresses CIITA and B7.1 genes in chondrocytes and synovial cells. Chronic inflammatory arthritis like RA is induced by lower doses of bovine type II collagen than the CIA. Ankylosis following joint inflammation, also interstitial pneumonia (IP), which is characterized by non-specific interstitial pneumonia (NSIP) is observed (induced-RA-associated lung disease model). A therapeutic test with antifibrotic drug, nintedanib was performed. [Methods] Inflammatory arthritis is induced by injection of bovine type II collagen (0.02 mg/mouse). The onset of IP usually begins 35 weeks after the first injection of bovine type II collagen. Administration of nintedanib was started at this point and continued daily for two months. Histopathological analysis, fibrosis rate, and serum cytokine concentration were analyzed. [Results] In iRA-ILD, we found hyperplastic epithelial cells characterized as usual interstitial pneumonia (UIP). These epithelial cells have acquired invasiveness. Nintedanib improved fibrosis, and reduced the number of M2 macrophages and invasive epithelial cells. [Conclusions] Not only IP like NSIP but also UIP are observed in the iRA-ILD model. Nintedanib ameliorates IP in the model.

W4-6

The effectiveness of CX3CL1 inhibition to interstitial lung disease with rheumatoid arthritis

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Conflict of interest: None

[Objective] CX3CL1 is a chemokine involved in the migration of inflammatory cells and the activation of synovial cells. The humanized anti-CX3CL1 antibody to the rheumatoid arthritis (RA) reported the efficacy for 6 months, but the treatment on concomitant interstitial pneumonia

(ILD) has not been found. In this study, we investigated the effectiveness of CX3CL1 inhibition on RA-ILD model mice. [Methods] SKG male mice was intraperitoneally once injected Zymosan, and control antibody or anti-CX3CL1 antibody twice a week from the same time. After 12 weeks, Masson's trichrome staining of lung tissue and flow cytometric analysis of bronchoalveolar lavage fluid (BALF) were performed. [Results] SKG mice developed ILD with the expression of CX3CL1 at fibrotic area and CX3CR1 positive cell infiltration. In BALF, M1 and M2 macrophages increased significantly, the CX3CR1 positive rate were 78.5 ± 17.8% and 36.3 ± 17.8% (mean ± SD). Although anti-CX3CL1 antibody significantly reduced the number of M1, there was no improvement in the lung fibrosis and no significant change the number of M2. [Conclusions] Anti-CX3CL1 antibody more effectively suppressed the infiltration of M1 with high CX3CR1 positive rate, but that was not completely inhibited including M2, and lung fibrosis was not suppressed.

W5-1

Development of rheumatoid arthritis among anti-citrullinated protein antibodies positive asymptomatic individuals: A prospective observational study

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Conflict of interest: None

[Background] Anti-citrullinated protein antibodies (ACPA) are present in the serum for an average of 3-5 years prior to the onset of rheumatoid arthritis (RA) during an asymptomatic period. There have been no reports in which clinical courses of ACPA-positive asymptomatic individuals were investigated prospectively. [Objective] To determine the incidence of ACPA-positive asymptomatic individuals to develop RA and elucidate their clinical courses. [Methods] Asymptomatic volunteers without joint pain or stiffness were enrolled in this prospective observational study. The serum ACPA levels were quantified by anti-CCP enzyme-linked immunosorbent assay with levels > 4.4 U/mL considered positive. ACPA-positive subjects were followed clinically in our department. [Results] 92 out of 5,971 individuals had a positive ACPA test (1.5%). Of these, 19 (20.7%) developed RA. Their average age were 58-years, and women were 68%. ACPA-positive individuals who developed to RA had higher ACPA level than ACPA-positive individuals who did not. [Conclusion] Among ACPA-positive asymptomatic individuals, 20% developed RA.

W5-2

Factors related to anti-CCP antibody titer in patients with RA within 2 months after onset

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Conflict of interest: None

[Objective] In JCR 2018, we reported that in patients with RA within 1 year of onset, a-CCP-t was higher in patients with respiratory lesions (Resp-L). In this study, we tried to find factors related to a-CCP-t in patients with RA within 2 months of onset to know the relation more clearly. [Methods] Patients were 247 RA patients with the mean age of 58±14 years. Around the first visit, blood sampling and chest CT scan were done. Resp-L was divided into 2, i.e., ILD and airway lesion (AW-L), and was semi-quantified according to papers and a textbook (ILD 0-3, Resp-L 0-4). Other factors were checked up and multivariate analysis was done. [Results] By univariate analysis, smoking history, presence of AW-L, ANA titer, and IgG value were significantly related to a-CCP-t, whereas ILD tended to relate. A-CCP-t was divided into two, i.e., more or less than 15, and logistic analysis was done. Significant factors related to a-CCP-t of more than 15 were AW-L and ANA titer. Factors of $p < 0.2$ were IgG value and male gender. Almost the same result was obtained by multi-regression analysis. [Conclusion] At the onset of RA, a-CCP-t was higher in patients with AW-L and high ANA titer. This phenomenon may be related to high activity of acquired immunity.

W5-3

The association between cytoplasmic staining patterns of fluorescent antinuclear antibody and type of anti-ARS antibodies

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Conflict of interest: None

[Objectives] To evaluate cytoplasmic staining pattern of fluorescent antinuclear antibodies (FANA) for predicting the type of anti-aminoacyl-tRNA synthetase antibodies (anti-ARS antibodies), using EUROPattern. [Methods] We identified FANA patterns of 22 patients with anti-ARS antibodies-positive polymyositis / dermatomyositis (PM / DM) in our hospital. We assessed the association between cytoplasmic staining patterns and type of anti-ARS antibodies. [Results] 18 of the 22 patients of PM/DM were FANA positive, with showing cytoplasmic pattern. Furthermore, the researchers visually classified them into diffuse type (n=6), fine speckled type (n=7), and others (n=5). Among 6 patients of diffuse type, 4 patients were anti-PL-7 antibody positive and 2 patients were anti-PL-12 antibody positive. [Conclusions] In this study, all patients of anti-ARS antibodies-positive PM / DM with diffuse type of cytoplasmic patterns were positive for anti-PL-7 or anti- PL-12 antibodies, which are severe compared to anti-Jo-1 antibody. It may be possible to predict the clinical features and severity of anti-ARS antibody-positive PM / DM patients from the results of FANA by combining the results of EUROPattern and the visual classification of type of cytoplasmic staining patterns by skilled researchers.

W5-4

Examination of alkaline phosphatase as a prognostic factor in polymyalgia rheumatica

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Conflict of interest: None

[Objective] Some patients with polymyalgia rheumatica (PMR) present with high levels of alkaline phosphatase (ALP). The underlying pathophysiology has not yet been elucidated, but it has been proposed that abnormal liver enzymes are caused by inflammation of the hepatic arteries. We investigated whether the ALP value at the time of PMR diagnosis could be a predictor of treatment prognosis. [Methods] From October 2009 to October 2019, 48 patients who were diagnosed with PMR in our department and were able to follow up were included. Patient data was extracted from medical records and analyzed retrospectively. [Results] There were 24 patients in the group (remission group) who had a long-term continuation of PSL 2 mg or less without termination or relapse of PSL, and 24 patients who had relapse during tapering (relapse group). ALP value at diagnosis Was significantly higher in the relapse group ($p = 0.004$). In addition, ALP at diagnosis showed a positive correlation with CRP at diagnosis ($r = 0.452$, $p = 0.00127$). The higher the ALP value at diagnosis, the higher. The time required to reduce the dose to PSL 5 mg tended to be long. [Conclusions] It was suggested that higher ALP before treatment may relapse during PSL tapering, requiring longer-term PSL administration.

W5-5

Increased levels of serum Wisteria floribunda agglutin positive Mac-2 binding protein in rheumatic diseases

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Conflict of interest: None

Background: Mac-2 binding protein is a cell-adhesive glycoprotein of the extracellular matrix secreted as a ligand of galectin-3 (Mac-2). Recently, a Wisteria floribunda agglutinin positive-M2BP (M2BP) assay developed using a lectin-antibody sandwich immunoassay has shown promise

as a new fibrotic marker in liver fibrosis and interstitial lung disease to detect unique fibrosis-related glycoalteration. Objectives: The aim of this study is to evaluate the utility of serum Mac-2 binding protein glycosylation isomer (M2BPGi) levels in patients with rheumatic diseases (RD). Methods: We retrospectively measured serum M2BPGi levels in 68 patients with RD and 16 healthy controls (HC). We excluded patients of cirrhosis. Results: In patients with RD, the median age was 62.0 years. Serum M2BP levels were significantly higher in patients with RD than in HC. In patients with RD, a significant correlation was not found between serum M2BP levels and inflammation markers such as CRP or ferritin. Conclusions: Most of the rheumatic diseases in this study were considered to be type I interferonopathy diseases such as rheumatoid arthritis and SLE etc. So, it was suggested that serum M2BPGi may be a novel biomarker that indirectly indicates how much IFN is activated in rheumatic diseases.

W5-6

Relationship between chest CT findings and pulmonary function test (PFT) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] It has been reported that pulmonary function abnormalities such as reduced VC and airway obstruction are related to mortality. However, there are small number of reports dealing with the relation between chest CT finding and PFT findings, therefore we tried to study these relations. [Methods] Subjects were 163 patients with RA who underwent chest CT and PFT within 1 year of onset. Semi-quantification of ILD was done by our previous method (Nakashita BMJ open 2014) and graded as 0, 1, 2, and 3. Airway diseases were divided into bronchiectasis (BE) and bronchiolitis (Bron). Semi-quantification of airway diseases was done referring the textbook (High-resolution CT of the lung, Webb eds), and grades 0, 1, and 2 were given. [Results] %VC inversely correlated with BE grade, and ILD grade tended to do so. ILD grade tended to correlate inversely with %FEV1/FVC. BE grade inversely correlated with %V50. FEV1/FVC and %V25 showed no correlations with any of respiratory grades. [Conclusions] ILD contributes to restrictive abnormality to some extent and resists to obstructive abnormality. BE contributes to both pulmonary function abnormalities. Confounding among ILD, BE and Bron should be studied further.

W6-1

Association between ultrasound-detected inflammation and physical examinations in inflammatory arthritis

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Conflict of interest: None

[Objective] To clarify the associations between ultrasound (US)-detected inflammation and physical examination (PE)-based findings in inflammatory arthritis. [Methods] We enrolled patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA). We clinically assessed arthritis, enthesitis, and dactylitis of fingers. We also performed US and evaluated power Doppler signals for synovitis, tenosynovitis, and enthesitis. [Results] We enrolled a total of 100 patients. Synovitis was prevalent at wrist and knee. Enthesitis was prevalent at extensor digitorum insertions into 3rd middle phalanx and lateral epicondyle. Positive predictive value (PPV) for PE on synovitis was low at ankle and 4th MTP joints and negative predictive value (NPV) was low at wrist. PPV for PE on enthesitis was low at medial epicondyle and patellar tendon insertions and NPV was low at quadriceps insertion. Out of 36 regions with isolated tenosynovitis, 10 regions were clinically recognized as synovitis. Out of 38 joints with isolated enthesitis, 23 joints were clinically recognized as synovitis. [Conclusions] There are discrepancies between US-detected inflammation and PEs and their directions are different between regions. Enthesitis and tenosynovitis are frequently recognized as synovitis with PE.

W6-2

Comparison of ultrasound findings between TNF inhibitors and non-TNF inhibitors in first biologics patients

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Conflict of interest: Yes

[Objective] Clinically, there is no difference regardless of which biologics is used, but the effect for synovitis is unknown. We compared the difference in the improvement of ultrasound findings between TNF inhibitors and non-TNF inhibitors. [Methods] Fifty-four RA patients who started first biologics from September 2016 to December 2018 were included in this analysis. All the patients were performed clinical examination, blood tests and ultrasound examination of hand and foot at baseline, 4, 12, 24, 36 and 52 weeks. [Results] Among 54 cases, 32 patients were used TNF inhibitor and 22 were non-TNF inhibitor. Age and duration of RA were significantly higher in the non-TNF group, and MTX dose was significantly lower in the non-TNF group. The baseline inflammatory markers tended to be higher in the non-TNF group and the disease activity was also higher in the non-TNF group, but the ultrasound findings showed no significant difference between TNF and non-TNF groups in both GS and PD. There was no difference in the ultrasound findings improvement between the TNF group and the non-TNF group at 4, 12, 24, 36 and 52 weeks. [Conclusions] There was no difference in the ultrasound findings improvement between patients with TNF inhibitor and non-TNF inhibitor in the first biologics.

W6-3

Characteristics of functional enthesitis in anti-cyclic citrullinated peptide antibodies positive rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify the characteristics of functional enthesitis in rheumatoid arthritis (RA) patients with anti-cyclic citrullinated peptide antibodies (anti-CCP). [Methods] RA patients who were examined by power Doppler ultrasound from January 2019 to September 2020 were reviewed. Among them, RA patients who were positive for anti-CCP, within 1 year of RA onset, and had been untreated were included. Ultrasound analysis was done based on the JCR guideline. Functional entheses in bilateral dorsal metacarpophalangeal (MCP) joints was evaluated by ultrasound. The relationship between enthesitis and clinical features was analyzed. [Results] A total of 102 RA patients were included. The median age, median disease duration and mean DAS28-ESR were 58 years old, 1 months, and 4.4±1.4, respectively. Functional enthesitis was found in 33 (32%) of 102 patients and in 64 (6.4%) of 1020 MCP joints. The titer of anti-CCP was significantly higher in the RA patients with functional enthesitis ($p=0.016$, t-test). In 42 (66%) of 64 MCP joints with enthesitis, synovitis was not detected. [Conclusions] This study elucidates that functional enthesitis in MCP joint is observed in one-third of newly onset-RA patients with anti-CCP. High anti-CCP titer may be associated with functional enthesitis in RA.

W6-4

MASEI (MAdrid Sonographic Enthesitis Index) Reveals the Impact of Obesity on Psoriatic Arthritis

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Conflict of interest: None

[Objective] To evaluate the quantify the extent of sonographic entheseal abnormalities by MAdrid Sonographic Enthesitis Index (MASEI) assessment. [Methods] From November 2017 to October 2019, 47 PsA patients who visited Kindai University Hospital and performed MASEI score assessment. They were retrospectively divided into 32 obese patients with a body mass index (BMI) ≧ 25 kg/m2 and 36 non-obese patients with BMI<25 kg/m2. 3 of the obese and 4 of the non-obese patients were evaluated for MASEI score baseline and 24 and 52 weeks after. [Results] There were no significant differences in the visual analog scale scores, disease durations, and total MASEI scores. However, osteophytes and calcifications were observed in the proximal and distal patellar tendons in obese patients. The total score of the Achilles tendon was significantly higher in obese patients compared to that in non-obese patients. VAS, WPAI, and inflammatory score improved at 24 and 52 weeks compared with baseline, but the damage score remained unchanged. [Conclusions] Obesity contributes to structural changes such as osteophyte accumulation and calcification of tendons in the weight bearing joints and have a significant effect on enthesitis of Achilles tendon, as assessed using the MASEI.

W6-5

Relation of clinical course of Polymyalgia Rheumatica (PMR) and ultrasound (US) findings

Ikuko Onishi[1], Kentaro Susaki[1], Chie Fujisawa[2], Ai Tamagawa[2], Kaori Sadaoka[2], Taichi Miyagi[1], Miharu Izumikawa[3], Satoshi Tohdo[1], Masayuki Inoo[1], Noriyuki Kurata[1]
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Conflict of interest: None

[Objective] We considered that whether we could predict the response of corticosteroid (CS) for PMR patients by using US. Especially we compared between PMR and elderly onset rheumatoid arthritis (EORA) about US-detected synovitis, bursitis, tenosynovitis, tendinitis of fingers, wrists, knees, metatarsophalangeal joints, shoulders. [Methods] We picked up 18 patients of PMR and 12 patients of EORA with PMR-like onset. We observed from 2 to 6 years. We divided PMR patients into GC responders (13 patients), who could achieve drug free or decrease GC dosage under 5 mg within 2 years, and GC resistants (5 patients) who recured or have to take any other immunosuppressive agents. [Results] In PMR group, we found 95% biceps brachicsynovitis, 45% bursitis, 45%tendinitis and tenosynovitis of fingers, 15% wrists synovitis, 25% knee joints synovitis. Especially 5 patients in resistants group, we find knee joints synovitis or tenosynovitis of the ankle lesion. [Conclusions] We couldn't predict the response of GC with grade of power doppler (PD) or the location of PD. And we find that the grade of PD were higher in EORA than PMR in shoulder. The number of tendinitis or tenosynovitis of fingers and wrists were higher in patients of resistants group than responders group.

W6-6

Ultrasound of shoulders and knees can improve the accuracy of the 2012 ACR/EULAR provisional classification criteria for polymyalgia rheumatica

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the clinical characteristics and ultrasound findings of the shoulders and knees of patients with PMR. [Methods] We evaluated the characteristics and ultrasound findings of 141 patients at University of Yamanashi Hospital from January 2017 to December 2019 prospectively. We performed ultrasound examinations before and after treatment interventions prospectively. [Results] The distribution of patients were PMR60, PMR-mimic21 and RA60. The prevalence rates of US findings were highest in the PMR group for the long head of biceps tendon, the supraspinatus tendon, the subscapularis tendon, the medial collateral ligament, the lateral collateral ligament and the popliteus tendon. By multiple regression analysis, the following two items were important; both shoulders with biceps tenosynovitis, supraspinatus or subscapularis tendinitis, and both knee with popliteus tenosynovitis, medial or lateral collateral ligament inflammation. AUC of diagnosis increased by adding these criteria. [Conclusions] The ultrasound findings including tenosynovitis, tendinitis and ligament inflammation in the shoulders and knees increased the accuracy of the classification criteria.

W7-1

Temporal changes of finger joint cartilage evaluated by ultrasound (US) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] Cartilage damage in RA has been evaluated by X-ray, however, it is not a direct evaluation of cartilage. We aimed to examine the temporal changes of US cartilage evaluation in RA patients. [Methods] We enrolled 54 RA patients in whom the cartilage thickness of finger joints was measured at baseline and 1-year later. The cartilage thickness of MCP and PIP joints of 2nd to 5th fingers were bilaterally visualized and measured from a longitudinal dorsal view. Cartilage thickness was measured from the base of the cartilage to the interface artefact at the cartilage surface. [Results] The sum of total cartilage thickness from 16 joints per patient ranged from 3.1 to 9.1 mm (med. 6.5 mm) at baseline, and it was significantly correlated with disease duration (ρ=-0.38, p=0.005). There were no significant differences in the cartilage thickness after 1-year from the baseline. However, persistent moderate to high disease activity group (n=10) by the DAS28-CRP showed a greater decrease in the cartilage thickness than others (n=44) (med. -6.2% vs. -1.2%, respectively, p= 0.004). [Conclusions] This study demonstrated the progression of cartilage damage with sustained RA activity, supporting the validity and usefulness of joint cartilage thickness evaluation by US in patients with RA.

W7-2

Relationship between the tenosynovitis and serological profile or treatment response in early stage rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify the clinical significance of tenosynovitis, we investigated whether the presence of tenosynovitis in early RA patients was associated with serological profile and treatment response. [Methods] In all 139 patients, the serological profile related to RA, blood inflammatory markers and ultrasound (US) findings of both hands before and 1-year after the initiation of DMARDs were analyzed. [Results] Tenosynovitis was frequently observed in the MTP2, MTP3 and wrist joints. In seropositive patients (positive for RF or anti-CCP antibody), the group with tenosynovitis had higher values of RF, CRP and ESR, and higher scores of US examination, compared to the group without. Furthermore, the group with tenosynovitis showed lower achievement rate of US remission at 1-year after initiation of treatment (11% vs 37.5%, $p = 0.031$). On the other hand, in the seronegative patients, there was no significant difference in inflammatory markers and US findings regardless of the existence of tenosynovitis, and tenosynovitis was not related to the achievement rate of US remission (31% vs 18%, $p = 0.640$). [Conclusions] These results suggest that the influence of tenosynovitis on treatment response differs depending on the serological profile.

W7-3

Predictive factors for the progression of US-imaging remission in patients of rheumatoid arthritis

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Conflict of interest: None

[Objective] To examine 1 year - clinical outcome of patients with rheumatoid arthritis (RA) who reached to the ultrasound imaging remission (USIR). [Method] 73 patients with RA who referred to our institution, fulfilling following requirements were enrolled; disease duration≧6 months, maintaining same RA treatment at least 3 months, CRP value <0.5 mg/dl, USIR. USIR was defined as absence of power Doppler signal in bilateral wrist, 2nd-5th MCP and PIP joints. Clinical dates, including modified Total Sharp Score (mTSS), were collected as the baseline (BL) predictive factors. Change of treatment, USIR and mTSS was evaluated at 1 year. Progression is defined by either requirement: receiving additional treatment, ΔmTSS≧1, failure to reach USIR. BL predictive factors for prognosis was analyzed by univariate and multivariate logistic regression analysis. [Result] 64 patients maintain USIR, while 5 patients had radiographic progression, 10 patients received additional treatment at 1 year. Univariate analysis revealed an association of the disease duration, coexist of musculoskeletal pain disease, pain VAS, HAQ, and multivariate analysis revealed an association of HAQ (OR=58.1, p=0.026) on the progression. [Conclusion] This study revealed the predictive factors for progression in USIR patients.

W7-4

Comparison of joint ultrasound using SMI-Smart Sensor 3D imaging and conventional 2D Power Doppler imaging in rheumatoid arthritis

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Conflict of interest: None

[Objective] Three-dimensional (3D) ultrasound devices have become widespread because of their clinical utility for 3D imaging and quantitative 3D data acquisition. The aim of this study is to evaluate the usefulness of SMI-Smart Sensor 3D technology as a novel modality in synovitis in rheumatoid arthritis (RA) patients. [Methods] RA patients who were examined by Power Doppler ultrasound from April 2020 to August 2020 were reviewed. Among them, twenty-five RA patients (total 39 joints) who had tenderness or swelling at either the 2nd or 3rd in bilateral dorsal metacarpophalangeal (MCP) joints were included. 2nd or 3rd MCP joints with tenderness or swelling were evaluated by ultrasound using 2D imaging (PD semi-quantitative, 2D-PD quantitative) and 3D imaging (SMI-Smart Sensor 3D; 3D-SMI quantitative). [Results] In case of all joints (PD-Grade 1-3) and PD-Grade 3, quantitative analysis of 2D-PD correlated with 3D-SMI evaluation ($r = 0.575$, $p < 0.001$ and $r = 0.743$, $p < 0.001$, respectively). In PD-Grade 1/2 joints, 2D-PD didn't correlate with 3D-SMI ($r = 0.034$, $p = 0.882$). [Conclusions] In low PD-Grade synovitis, there was a discrepancy in the evaluation of synovitis between SMI-Smart Sensor 3D imaging and the traditional 2D-PD imaging.

W7-5

Examination of anti-CCP antibody (ACPA) and other factors related to carpal bone erosion confirmed by 2D / 3D images of HR-pQCT

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Conflict of interest: None

[Objective] In this study, we investigated the factors related to carpal bone erosion using HR-pQCT. [Methods] The subjects were 174 arthralgia cases, 118 ACPA negative (NG), 56 ACPA positive (PG). The wrist joints were imaged by HR-pQCT, rupture of the cortical bone in contact with the disappeared trabecular was defined as bone erosion. [Results] The number of bone erosions was 1.9 ± 1.8 in PG, which was significantly higher than that in the NG (1.0 ± 1.5) ($p = 0.0006$). The number of cases with bone erosion was also significantly higher in PG (40 cases) than in NG (54 cases) ($p = 0.002$). In PG, there was no significant difference in bone erosion in RA cases (1.5 ± 2.0) and non-RA cases (2.0 ± 1.6). With the number of bone erosions, age was positively correlated in NG ($p = 0.0003$), but not in PG ($p = 0.15$). The bone mineral density, microstructure, and geometry of the distal radius measured by HR-pQCT. NG showed a negative correlation with cortical bone mineral density ($p = 0.04$) and cortical bone thickness ($p = 0.04$). No correlation with the HR-pQCT mesurement was observed in PG. [Conclusions] Bone erosion in NG was considered to be caused by age-related fragility of cortical bone, while in the PG, bone resorption by ACPA was considered to be involved.

W7-6

Investigation of liver fibrosis in RA patients treated with MTX using Combi-Elasto and liver fibrosis scoring (Report 2)

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Conflict of interest: None

[Objective] MTX is an anchor drug in RA, but its long-term side effect is liver fibrosis. We previously reported that elastography and fib4-index were effective in assessing liver fibrosis in MTX-treated patients (JCR 2019). MTX-induced liver damage has been reported to be similar in histopathology to NAFLD/NASH. In the present study, we investigated fatty liver and fibrosis in RA patients receiving MTX. [Methods] Patients were RA patients receiving MTX. We measured ATT, Vs, LFI and other parameters to assess the relationship between liver function, disease activity and fib4-index. Statistical analysis was performed using PRISM ver.5. [Results] 338 patients (246 women), 61.0 years, MTX dose was 9.0 mg/w, and cumulative MTX dose was 0.44 g. Disease activity was well controlled with CDAI 3.66, SDAI 4.31, DAS28ESR 2.19, and mHAQ 0.15. ATT was 0.58, Vs was 1.28, LFI was 1.91, and fib4-index was 1.72. In multiple regression analysis, ALT was a significant contributor to ATT, ALT, DAS-28CRP and Vs were significant contributors to LFI and eGFR, DAS28ESR and Vs were significant contributors to fib4-index. [Conclusions] Elevated ALT is a risk factor for not only fatty liver but also for liver fibrosis, and patients with higher disease activity are more likely to develop liver fibrosis.

W8-1

Involvement of mTOR-phosphorylated CD8+ cells in pathology of rheumatoid arthritis and the effect of biological DMARDs

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Conflict of interest: None

[Objective] Role of $CD8^+$ cells in RA remained unclear. In this study, we focused on mTOR, which is important metabolic regulator, and assessed its functions and involvement in pathology of RA. [Methods] PBMCs were obtained from 17 healthy controls (HCs) and 86 RA patients. The expression of p-mTOR in $CD8^+$ cells were analyzed by FACS. In addition, we examined the function of mTOR in $CD8^+$ cells *in vitro*. [Results] (1) Proportion of HLA-DR^+CD38^+ cells and the expression level of p-mTOR in $CD8^+$ cell in RA were higher compared to those of HCs. They were correlated with disease activity scores in RA. (2) Proportion of HLA-DR^+CD38^+ cells in $CD8^+$ cells were decreased at 1 year after treatment with both TNF inhibitors and abatacept. Meanwhile, the level of p-mTOR

in $CD8^+$ cells were decreased after treatment with TNF inhibitors, but not abatacept. (3) *In vitro*, anti-CD3/CD28 Abs stimulation induced the expression p-mTOR in human $CD8^+$ cells, leading to induction of IFN-γ, Granzyme B, GNLY, but reduction of Granzyme K. (4) TNF inhibitors suppressed p-mTOR expression in $CD8^+$ cells, while abatacept did not change it. [Conclusions] Taken together, mTOR activation in $CD8^+$ cells may involve in disease activity, and TNF inhibitors and abatacept differently affect to the functions of $CD8^+$ cells in RA.

W8-2

Pathogenic role for peripheral helper T cells suggested by association with rheumatoid factor levels in ACPA (+) subjects both at-risk for and with classified RA

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Conflict of interest: None

[Objective] We explored T peripheral helper (Tph) cells and T follicular helper (Tfh) cells in the peripheral blood from ACPA (+) individuals both before and after development of RA. [Methods] 14 ACPA (+) individuals without arthritis but at-risk for future development of RA (ARI), 15 ACPA (+) RA patients, and 15 healthy controls (HC) were recruited from the Studies of the Etiologies of RA (SERA) population at University of Colorado. PBMCs were analyzed by flow cytometry to quantify $PD\text{-}1^{hi}CXCR5^-$ Tph cells and $PD\text{-}1^{hi}CXCR5^+$ Tfh cells. [Results] Circulating Tph cells and Tfh cells were significantly increased in RA (Tph, p=0.004; Tfh, p=0.008) but not in ARI compared to HC. The frequency of Tph cells was moderately correlated with serum IgM-RF levels in both RA and ARI (ρ=0.68 and 0.62, respectively), while no correlation was observed between Tph cells and serum ACPA levels in both study groups. [Conclusions] Circulating Tph cells were expanded in RA but not in ARI, suggesting their pathogenic role in the development of arthritis rather than serum ACPA status alone. Also, positive correlation between circulating Tph cells and IgM-RF levels suggests their potential role in both acquisition of IgM-RF by ACPA (+) individuals and future transition to RA.

W8-3

Glycosylation abnormalities in the serum IgG of RA patients

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Conflict of interest: None

[Objective] Previous studies have demonstrated the presence of glycosylation abnormalities in the serum IgG of RA patients (RA). We analyzed the sugar chain structure of IgG in RA using the novel technique, and examined its value as a marker for early diagnosis. [Methods] We analyzed the sugar chain structure of IgG in serum of unclassified arthritis (UA), RA, osteoarthritis (OA), and healthy individuals using liquid chromatography. We examined whether it was useful as a marker to predict the diagnosis of RA. Furthermore, the rate of sialic acid in RA was examined using mass spectrometry (MS). [Results] A marked increase in the rate of sugar chains lacking in galactose in serum IgG of RA patients, which was significantly higher than that in IgG of OA and healthy individuals. These changes were recognized from the early stage of onset, at the stage of UA, and were found to be useful as a diagnostic prediction marker for RA. Furthermore, MS revealed that marked increase in the rate of sugar chains lacking in sialic acid in serum IgG of RA. [Conclusions] Glycosylation abnormalities in the serum IgG is considered to be useful diagnostic marker for RA. Furthermore, it was suggested that these abnormalities might play a important role in the etiology and pathophysiology.

W8-4

In HR-pQCT Study, examination of bone structure (bone density, geometry, microstructure) in anti-CCP antibody-positive cases

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Conflict of interest: None

[Objective] Anti-CCP antibody (ACPA) is known to induced the mature osteoclasts. The bone structure of ACPA-positive cases was examined using HR-pQCT. [Methods] The subjects were ACPA-positive 43 women (PG) and ACPA negative 43 women (NG). The bone mineral density (BMD), bone microstructure, and geometry in the distal radius were measured by HR-pQCT. [Results] There was no significant difference in BMD between the two groups. The age of NG showed a positive correlation with cortical bone porosity, and the age of PG showed a positive correlation with cortical BMD and a negative correlation with trabecular BMD, trabecular number, and trabecular thickness. Cortical bone porosity was negatively correlated only with cortical BMD in NG, but was positively correlated with trabecular BMD and trabecular thickness in PG. Cortical BMD was negatively correlated with trabecular number only in PG. [Conclusions] In ACPA positive group, age and cortical BMD showed a positive correlation, and cortical porosity decreased and cortical bone mineral density increased as trabecular bone strength decreased. From this result, it is considered that cortical bone may compensate for the decrease in trabecular bone strength associated with ACPA exposure and the length of exposure period.

W8-5

Vascular endothelial cadherin is expressed on rheumatoid arthritis and concern with a disintegrin and metalloprotease-15

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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. Furthermore, it was reported that ADAM-15 and VE-cadherin were expressed in serum showed a positive correlation. In this study, we investigate whether ADAM-15 involved in shedding of VE-cadherin. [Methods] 1) RA synovial fibroblast cells (RA FLS) was stimulated with TNF-α, and we measured ADAM-15 in its serum. 2) VE-cadherin in ADAM-15 siRNA or control siRNA treated RA FLS was measured. [Results] 1) ADAM-15 stimulated TNF-α in RA FLS was increased compared with control (TNF-α 13.6 ± 2.26 pg/ml, control 0.35 ± 0.25 pg/ml). 2) VE-cadherin in ADAM-15 siRNA treated RA FLS was decreased compared with control siRNA treated RA FLS (ADAM-15 siRNA 559.9 ± 12.1 pg/ml, control siRNA 603.1 ± 7.8 pg/ml, respectively, $p<0.05$). [Conclusions] ADAM-15 may shed VE-cadherin in RA.

W8-6

Identification of disease pathway focused on oral microbiome (oral MB)-human acquired immunity interaction toward the development of ACPA-positive rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] ACPA production is observed in several organs even prior to the onset of RA, and oral mucosa is known as one of the important tissues. Saliva is considered to reflect the oral MB. We collected saliva samples from healthy subjects and analyzed the oral MB stratified by the presence or absence of RA and ACPA to determine the environmental and genetic factors that contribute to the production of ACPA. [Methods] We recruited residents who came to health checkups and obtained the medical questionnaire, their saliva and blood samples to examine ACPA, HTLV-1, HLA genotyping. The oral MB analysis is performed by the operational taxonomic unit analysis by using 16SrRNA gene by next-generation sequencing. [Results] Samples were collected from 1385 individuals between 2016 and 2018. The study included 191 female (61%), 42 samples positive for ACPA, 34 patients are diagnosed RA and 143 HLA-SE carrier (49.1%). In the ACPA-positive population of RA patients and in the RA population having HLA-SE, there was a bias towards the dominant cluster in the Neisseriaceae family. [Conclusions] We report here that *Neisseriaceae*, which is a high oral commensal bacterium in the healthy oral cavity, has an increased proportion in RA patients with the relevant literature.

W9-1

Treatment of rheumatoid arthritis with combination therapy using a biologic agent and methotrexate lower risk of decreasing kidney function compared to biologic agent monotherapy

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Conflict of interest: Yes

[Objective] Little is known about the DMARD on the risk of decreasing kidney function in RA patients. [Methods] We recruited 938 RA pts from ASHURA database. The following background factors were analyzed: age, sex, type of bDMARD, MTX and PSL dosages, use of csDMARD and NSAID, BMI, smoking history, diabetes, hypertension, dyslipidemia, Cr, CRP, MMP3 level and SDAI. We divided into two groups: bDMARD with MTX treatment group (461pts) and bDMARD monotherapy group (168pts). Patients who had primary and secondary failures, AE of drugs, and missing data and those who relocated or withdrew were excluded. Propensity scores were calculated based on the following factors: age, sex, PSL and MTX dosage, SDAI, Cr, eGFR, DM, HT, and DL. Overall, 115pts in each group were identified. The primary endpoints were the eGFR values before and 6 months and 1 year after treatment. [Results] The eGFR decreased from 81.7 ± 26.7 to 81.4 ± 25.6 and 77.7 ± 24.5 at 6 months and 1 year in the combination treatment group and from 73.0 ± 33.7 to 69.7 ± 34.0 and 68.4 ± 35.3 in the bDMARD monotherapy group. A significant difference was observed between the groups ($p = 0.011$) and during the treatment period ($p < 0.001$). [Conclusions] Conbination therapy may lower the risk of decreasing kidney function in patients with RA.

W9-2

The predictors for the safe reduction of methotrexate in the patients of rheumatoid arthritis under the golimumab treatment

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Conflict of interest: Yes

[Objective] Although MTX is a first-line therapy for RA patients, adverse events are reported. We aim to find factors of successful MTX reduction in patients receiving golimumab (GLM) + MTX. [Methods] Retrospective data from patients received GLM (50 mg) + MTX for >1 month were included. Definition of MTX reduction: ≧12 mg from the maximum dose in a 12-week period (≧1 mg/wk); relapse: DAS28-CRP score ≧3.2 or a sustained increase of ≧0.6 from baseline, evaluated at 3, 6, and 12 months post reduction. [Results] 41.7% (50/120) patients had MTX reduction. There was 18% relapse (9/50) in the reduction group; the time to relapse was 6.75mo (3-12mo). Between with and without relapse groups, no differences were found for age [49.3 vs 51.8yr (p=0.67)], disease duration [55.5 vs 30.1mo (p=0.20)]. Before reduction, MTX dose was 9.67 vs 9.88 mg/wk (p=0.88); DAS28-CRP was 2.56 vs 1.92 (p=0.06) for with vs without relapse group. The mean MTX dose was 4.11 vs 6.13 mg/w k (p=0.12); DAS28-CRP was 2.96 vs 1.64 (p<0.001) after reduction. [sc1] Predictors associated with no-relapse is ongoing with a second cohort. [Conclusions] With use of GLM, MTX dose reduction by 38% was observed in no-relapse group, indicating possibility to minimize potential AE.

W9-3

Decrease of neutrophil counts 1 month after initiating tocilizumab predicts clinical remission within 1 year in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Neutropenia is one of the common complications of tocilizumab (TCZ) in patients with rheumatoid arthritis (RA). This study aimed to examine whether TCZ-induced decrease of neutrophil counts predicts clinical remission within 1 year. [Methods] We reviewed medical records of RA patients who were treated with TCZ from May 2011 to September 2019 in our hospital. CDAI was evaluated before initiating TCZ and 1, 3, 6 and 12 months after administration. Clinical remission was defined when CDAI decreased ≦2.8. CDAI ≦2.8 after discontinuing TCZ was not regarded as remission. Ratio of neutrophil counts 1 month after initiating TCZ to those at baseline was assessed. [Results] 169 out of 255 TCZ-treated patients were enrolled. Mean age was 57 years, 79% was female, and ACPA was positive in 83%. Multivariate logistic regression analysis showed that the ratio was an independent factor predicting CDAI remission (OR 0.16, p<0.01). ROC analysis determined a cut-off value of the ratio as 0.8. Patients with the ratio ≦0.8 were more likely to achieve CDAI remission than those with the ratio >0.8 (Fisher's exact test, p=0.02). [Conclusions] Decrease of neutrophil counts 1 months after initiating TCZ can help identify patients who achieves clinical remission within 1 year.

W9-4

Examination of Predictors of Effectiveness of Sarilumab

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Conflict of interest: Yes

[Objective] To investigate the background factors for response to treatment in 38 patients with rheumatoid arthritis (RA) who have been

treated with salilumab. [Methods] Logistic regression analysis was performed to determine the factors contributing to the achievement of CDAI remission in patients initiated on sarilumab. Explanatory variables were selected using a stepwise approach with an emphasis on clinical relevance. [Results] The explanatory variables extracted as factors of CDAI remission attainment were bio naïve, age, and RF titer: CDAI remission rate for bio naïve/experience was 73.3%/34.8%, respectively (p=0.02). Two cutoffs were extracted for age: 63 and 72 years of age. 29.4%/66.7% (p=0.02) of patients under/over 63 years old achieved CDAI remission, and 37.9 %/88.9% (p<0.01) of patients under/over 72. The RF titer cutoff was 87 IU/L. The CDAI remission rate for patients under/over 87 IU/L was 31.3%/63.6% (p=0.04). The CDAI remission rate was 65.2%/26.7% (p= 0.02) in patients receiving less than or equal to 4 mg/6 mg or more. After 2 weeks of treatment, i.e., one shot of salilumab, CDAI decreased from 20.8 to 11.1 and MMP-3 from 415 to 126. [Conclusions] Sarilumab was effective in aged, bio naïve, low MTX doses, and higher RF levels. And the treatment response was rapid.

W9-5

Differences in Clinical Parameters and Laboratory Data of Rheumatoid Arthritis Patients in Remission or with Low Disease Activity Treated with Biologic Agents or Janus Kinase Inhibitors

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Conflict of interest: Yes

[Objectives] This retrospective study assessed differences in clinical parameters and laboratory data in RA patients who met the treatment goal with biologic agents (BIO) or Janus kinase inhibitors (JAK). [Methods] Participants were BIO- or JAK-treated RA patients with clinical disease activity remission or low disease activity categorized by BIO treatment with tumor necrosis factor (TNF) inhibitor (reference), interleukin-6 (IL6) inhibitor, or abatacept (ABT), and JAK treatment. Statistical analysis used the Dunnett test. [Results] For 171 TNF, 71 IL6, 50 ABT, and 18 JAK cases, parameters with statistical significance (means) were: TNF/IL6-ESR 34.5/14.0 mm/hr, MMP-3 47.5/71.9 ng/mL, WBC 6124/5404/μL, lymphocytes 2112/1646 μL; TNF/ABT-TJ 0.4/1.0, PtGH 13.3/20.0 mm, PainVAS 15.7/21.6 mm, PhGH 7.4/11.1 mm, CRP 0.1/0.4 mg/dL, ESR 34.5/44.2 mm/hr, MMP-3: 47.5/72.9 ng/mL, lymphocytes 2112/1816 μL, neutrophils 3364/4233 μL, eGFR 75.4/65.3 mL/min/1.73 m^2; and TNF/JAK-platelets 21.7/29.3 104/μL, lymphocytes 2112/1326 μL. [Conclusion] Clinical parameter and laboratory data differences result from differences in the targeted cytokine between TNF and IL6, differences in patient characteristics between TNF and ABT, and differences in the mode of action between TNF and JAK.

W9-6

Impact of shared epitope on response to treatment with tofacitinib or abatacept in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To compare effectiveness of tofacitinib and abatacept and to clarify impact of shared epitopes (SE) on response to these treatments in patients with rheumatoid arthritis. [Methods] After statistical adjustment by a propensity score matching, each 70 patients treated with tofacitinib or abatacept were extracted. Effectiveness of both drugs over 24 weeks and influence of SE on outcomes was investigated. [Results] There was no significant difference in DAS28-ESR remission between the tofacitinib and abatacept groups at week 24 (p=0.280). Analysis of EULAR response at week 24 showed that EULAR good response rate in tofacitinib group was not affected by number of SE copies (p=0.924), whereas in abatacept group it was increased significantly with increasing number of SE copies (p=0.0182). Multivariable logistic analyses showed significant association of SE with DAS28-ESR remission in patients treated with abatacept (OR=25.881, 95%CI=3.140-213.351, p=0.0025), but not with tofacitinib (OR=1.473, 95%CI=0.291-7.446, p=0.639). [Conclusions] Although Effectiveness of tofacitinib and abatacept was comparable at week 24, SE positivity was associated with DAS28-ESR remission rate at week 24 in treatment with abatacept, whereas had no effect on response to treatment with tofacitinib.

W10-1

Analysis of the impact of the age of disease onset on outcomes of the disease activity and functional measures of patients with rheumatoid arthritis by using the database of nation-wide observational cohort

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Conflict of interest: None

[Objective] To investigate the impact of the age of disease onset on outcomes of the disease activity and functional measures of patients with RA. [Methods] 16090 RA patients were registered in NinJa database. We focused on patients at 10 years after disease onset. The data including HAQ-DI, EQ-5D as well as DAS28, SDAI and CDAI was analyzed. Furthermore, we collected the records of surgeries that underwent due to RA. [Results] Totally 585 patients were included in this study and we divided into 2 groups. Group Y consisted of patients with onset below 50 years old (n=204, mean onset 39.5 y) and group O consisted of patients with onset above 51 years old (n=381, mean onset 60.8 y). In group Y, HAQ-DI was 0.26, EQ-5D was 0.81, DAS28 was 2.42, SDAI was 5.21, and CDAI was 4.95. In group O, the score was 0.45, 0.79, 2.74, 6.05, 5.57, respectively. Four total joint arthroplasty (TJA) were performed in 3 patients (1.5%) in group Y, and 39 TJA were performed in 32 patients (8.4%) in group O. [Conclusions] This study showed that patients of group O showed higher disease activity and lower functional ability in comparison with group Y. Moreover, TJA was needed in larger population of group O, suggesting that we should consider the possibility of TJA in RA patients with onset in older age.

W10-2

Urinary creatine/creatinin ratio among rheumatoid arthritis

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Conflict of interest: None

[Objective] To analyze urinary creatine/creatinin ratio (C/C ratio) among rheumatoid arthritis (RA). [Methods] We retrospectively studied 45 patients including 18 patients with RA who were mesured C/C ratio from Nov 2019 to Oct. 2020. [Results] The C/C ratio in RA patients (10.7 [2.07-30.44] %) was significantly higher than that of non RA patients (1.28 [0.67-3.01]; p=0.00153). In RA patients, C/C ratio was not correlated with age, sex, BMI, dose of prednisolone, duration of RA, class, stage, DAS28, serum CPK and creatinin clearance. There was significantly correlation between C/C ratio and HAQ (r=0.585, p=0.0168). [Conclusions] Muscle atropy could be progressed in the RA patients with functional disorder.

W10-3

Physician's global assessment at start of treatment is a predictor of attainment of treatment goals in early rheumatoid arthritis

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Conflict of interest: Yes

[Objective]: Early interventions for RA are important for achieving therapeutic goals. The aim of this study was to investigate drug treatment options and short-term treatment outcomes for patients with early-diagnosis RA in clinical practice, and to examine predictors of achieving remission. [METHODS] Of the 233 patients enrolled in the multicenter RA Inception Cohort *, 172 patients were followed up to 6 months. The effect of patient background at the start of treatment on achieving Boolean inception 6 months after the start of treatment was investigated using logistic regression analysis. [Results] MTX usage rate was 88→89→89% (0-3-6 months), MTX dose was 6.9→9.4→9.7 mg/week, DAS28-CRP was 4.13 →2.58→2.37, Boolean remission achievement rate was 0→28→35%. Physician's global assessment (PhGA) at the start of treatment (OR 0.84) and steroid use (OR 0.28) were independent predictors of Boolean remission at 6 months in multivariate analysis. [Conclusion] After RA diagnosis, good therapeutic effect was obtained in a short period of time by performing treatment centered on MTX. PhGA at the start of treatment and judgment on the necessity of glucocorticoid are useful for predicting the achievement of treatment goals. * This study is a doctor-initiated study funded by Eli Lilly Japan.

W10-4

Systemic immune-inflammation index in rheumatoid arthritis patients: Relation to disease activity (Ninja 2019 Databese)

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Conflict of interest: None

[Objective] To assess systemic immune-inflammation index (SII) in rheumatoid arthritis (RA) patients and compare between active cases and those in remission. [Methods] Using the data of NinJa (National Database of Rheumatic Disease in Japan) in 2019, a total of 16086 eligible RA patients were included in this study. Correlations of SII with the disease activity of RA were evaluated. SII was calculated by the following calculation formula; SII = Netrophils (%) / Lymphocyte (%) * Platelets (G/L). [Results] The mean age of patients was 66.9 years and the median of disease duration was 11 years. The DAS28-ESR was mean 2.81, and the SDAI was median 4.51. the median SII was 541.1. SII was significantly elevated as SDAI disease activity increased (median 475.6 in remission, 550.3 in LDA, 732.3 in MDA and 860.5 in HDA, respectively; P<0.00001). SDAI was recognized as an independent factor in the multiple regression analysis for LogSII, and LogSII was also a significant factor in the ordinal logistic regression analysis for each disease activity (remission / LDA / MDA / HDA) in SDAI. (Odds ratio 2.89 [2.50 - 3.36], P <0.0000001). [Conclusions] Based on the above results, SII was considered to be useful as an inflammatory marker for evaluating disease activity in RA.

W10-5

Association with frailty and patients global assessment in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] Patients global assessment (PtGA) in rheumatoid arthritis (RA) is an important indicator for patients to evaluate their clinical condition. Frail is a concept that indicates not only physical but also psychological and social frality. The aim of this study is to investigate the impact of flail on the PtGA. [Methods] 559 patients who were able to complete the Kihon Checklist for Assessing Frailty (KCL) were included. Multiple linear regression analysis was used to investigate the effects of the Frailty and scores of each domain on the PtGA. [Results] The patient's age was 67 years, disease duration 11 years, 73% female. Disease duration (partial regression coefficient (B)=0.03), swollen joints (B=0.09), tender joints (B=0.26), CRP (B=0.27), and Frailty (B=0.75) were independent factors for PtGA. When KCL was examined by domain, activities of daily life (B=0.23), motor function (B=0.36), social Withdrawal (B=0.49), and depressed mood (B=0.26) were independently associated with the PtGA. [Discussion] Frailty affects the PtGA of RA. It was found that not only physical frality (deterioration of activities of daily life and motor functions) but also mental and psychological frality (depressed mood) and social frality (social Withdrawal) affected the PtGA of RA.

W10-6

Factors related to satisfaction with medical care in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] A questionnaire survey was conducted to evaluate "medical care based on consensus between doctors and patients" and "satisfaction with the medical care provided" [Method] We investigated RA patients aged 40-79 years who visited a university hospital between March and July 2019 and agreed in writing to cooperate in the survey, using medical data at the time of their visit and a self-administered questionnaire. Background, disease activity, quality of life, and satisfaction with medical care were assessed, and treatment goals were divided into three groups: "have discussed", "have been briefed", and "neither". [Results] 441 people consented to cooperate in the survey. Multiple logistic regression analysis was performed with the top third of patient satisfaction as the objective variable and age, sex, presence of clinical and functional remission, and presence of discussion about treatment goals as the explanatory variables. The odds ratio (OR) for the group that had ever discussed treatment was 3.28 (P=0.005) based on the neither group. Other independent associated factors were age (OR1.05, P=0.001) and clinical remission (OR2.16, P=0.007). [Conclusion] It was suggested that physician-patient discussions about treatment goals were significantly related to patient satisfaction.

W11-1

A study on factors related to the development of interstitial lung disease (ILD) in the course of rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] We reported in JCR 2019 that the prevalence of ILD increases approximately 1% in the course of RA. In this study, we tried to find factors related to the development of ILD. [Methods] Subjects were 17 patients with RA in whom ILD developed in the course of RA. These patients showed no ILD in the first chest CT findings, but ILD was found in the later chest CT. Control group was patients with RA in whom chest CT showed no ILD taken after more than 8 years of RA development (n=214). In subjects, ILD development was found at the mean of 9.9 years after RA onset. In control group, the mean interval between RA onset and final chest CT was 16.6 years. We selected following factors and analyzed which are related to the development of ILD; age of onset, stage, class, gender, smoking Hx, anti-CCP-ab, RF, KL-6, ANA, CRP/MMP-3 /

DAS28ESR at the first visit, dose of MTX and PSL, presence or absence of bronchiectasis and bronchiolitis. [Results] Univariate analysis revealed that age of onset, RF, CRP and DAS28ESR were significant factors related to ILD development. Logistic analysis showed age of onset and the dose of MTX were significant factors and DAS28ESR tended to be significant. [Conclusion] ILD developed in elderly patients with RA activity.

W11-2

The risk factors for worsening of interstitial lung disease in rheumatoid arthritis during biological DMARDs

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Conflict of interest: None

[Objective] To identify the risk factors for worsening of interstitial lung disease (ILD) in RA patients under bDMARD therapy. [Methods] Subjects were consecutive 116 RA patients with ILD detected by HRCT at starting bDMARD therapy. Among them, we analyzed 73 patients who had a repeat HRCT after starting the therapy (mean interval: 2.71 years) and were free of Bio-switch in that period. The presence of and change in ILD were judged according to HRCT findings. We collected data on demographics, clinical features including disease activity and treatment. The risk factors were identified by logistic regression analysis. [Results] Between worsening and no worsening groups, no differences were found in gender, age, disease duration, the positivity for anti-CCP antibody and RF, smoking, disease activity, and levels of KL-6 and SP-D at the entry. Risk factors for worsening of ILD were identified as following: high titers of anti-CCP antibody and RF titer, use of tocilizumab, the presence of honeycomb, and the worsening of airway disease, particularly bronchiolitis. [Conclusions] ILD should be carefully monitored under the bDMARD therapy when RA- ILD patients revealed high titers of anti-CCP antibody and RF, honeycomb, and airway disease.

W11-3

TNF inhibitors for rheumatoid arthritis patients with interstitial lung disease (ILD) may exacerbate ILD

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Conflict of interest: None

[Objective] To examine aggravating factor of interstitial lung disease (ILD) in biological DMARDs users of rheumatoid arthritis (RA). [Methods] All cases that received biological DMARDs (bDMARDs) therapy for RA (n=67) in Okayama City Hospital from Jan 2013 to Nov 2018, were enrolled. We excluded in the following cases; (1) bDMARDs were initiated in other institutions, (2) a following duration was within 26 weeks (except cases discontinue bDMARDs due to exacerbation of ILD). Patients were divided into worsening ILD group and no change group with radiographic imagings. [Results] We analyzed 37 patients (27 females, mean age 69.7 years old, mean disease duration 71.8 months). Average of DAS28ESR and HAQ-DI was 26.2, 1.3, respectively. In all case, lung diseases were stable before initiation of bDMARDs. Mean following duration was 29.5 months, and We observed exacerbation of ILD among 8 patients. Ratio of TNF inhibitor users in worsening ILD group, was higher than in no change group. (75% v.s. 34%, p=0.0406). Patients' background, disease activity of RA, data of examination, other medications at introduction of bDMARDs, was no differentiation in each group. [Conclusions] We detected use of TNF inhibitors as aggravating factor in RA patients with ILD taking bDMARDs.

W11-4

Identification of pre-existing factors before the onset of acute exacerbation (AE) of RA-IP which predicts the prognosis of the AE

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Conflict of interest: None

[Objective] To identify pre-existing factors before the onset of acute exacerbation (AE) of RA-IP which associate with the prognosis of AE. [Methods] The subjects were 12 patients who were admitted to our department because of the AE and who had visited our department. We examined the relationship between the prognosis of AE and demographics, clinical features, and imaging and laboratory findings before the onset of AE. [Results] Between the survival (S) group (n=7) and the death (D) group (n=5), no differences were found in age, gender, arthritis activity, and treatment. There were no differences in CT findings before the onset of AE, including the extent of GGO, consolidation, reticular shadow, honeycomb, and traction bronchiectasis between the two groups. Serum SP-D levels 2-3 months before AE in the D group were higher than those in the S group (S:98.1 vs D:273.0, p=0.03). However, there was no difference in KL-6 levels between them. [Conclusions] Before the onset of AE, SP-D levels were elevated in patients with poor prognosis, which suggests that pulmonary injury was developing before AE in these patients.

W11-5

The influence of concomitant interstitial pneumonia on outcomes of rheumatoid arthritis -a longitudinal study using the IORRA cohort

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Conflict of interest: Yes

[Objective] To examine the influence of concomitant interstitial pneumonia (IP) on the achievement of remission and the occurrence of clinical events in patients with RA. [Methods]. Among the participants in the IORRA cohort from 2011 to 2012, patients not achieving DAS28 remission who reported concomitant IP including both incident and prevalent cases (IP group) and those who did not (non-IP group) were enrolled. We investigated associations of the presence of IP with time to achieving remission and developing clinical events (death, hospitalization, hospitalized infection, malignancy or CVD) for 5 years using the Cox regression models. [Results] We enrolled 242 patients in the IP group and 4,981 in the non-IP group. DAS28 remission was achieved in 55% and 76% in the IP group and non-IP group, respectively. IP was significantly associated with failure to achieve remission (adjusted HR: 0.81 [95% CI: 0.66-0.99]). The clinical events were observed higher in the IP group compared to the non-IP group (49% vs 15%), and IP was a significant factor associated with the clinical events (adjusted HR: 1.86 [95% CI: 1.42-2.44]). [Conclusion] Concomitant IP was a factor associated with failure to achieve remission and the occurrence of clinical events in patients with RA.

W11-6

Relation of anti-CCP antibody titer to respiratory lesions in patients with RA within 2 months of onset

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Conflict of interest: None

[Objective] In JCR 2018, we reported that in patients with RA within 1 year of onset, a-CCP-t was higher in patients with respiratory lesions (Resp-L). In this study, we selected RA patients within 2 months of onset to make the relation more clearly. [Methods] Patients were 247 RA patients with the mean age of 58±14 years. Around the first visit, blood sam-

pling and chest CT scan were done. Resp-L was divided into 2, i.e., ILD and airway lesion (AW-L), moreover AW-L was divided into 2, bronchiectasis (BE) and bronchiolitis (Br). Relation of a-CCP-t to each Resp-L was studied. [Results] A-CCP-t was significantly higher in patients with Resp-L than those without it (median 106 vs 17). When patients were divided into 4 groups, i.e., patients with ILD and AW-L (group 1), with AW-L alone (group 2), with ILD alone (group 3), and no Resp-L (group 4), the median of a-CCP-t of each group was 172, 105, 30, and 16, respectively. A-CCP-t of group 1 and 2 was significantly higher than that of group 4. There was no difference between group 3 and 4. A-CCP-t of group 1 and 2 tended to be higher than that of group 3. No difference was found between patients with BE and Br. [Conclusion] At RA onset, a-CCP-t was higher in patients with Resp-L, particularly with AW-L.

W12-1

Evaluation of muscle mass and function is able to predict falls in rheumatoid arthritis patients by the 4-year data of CHIKARA study

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Conflict of interest: None

[Objective] Prospective cohort study was performed to reveal the factors of falls and fractures in RA. We investigated whether the evaluation of muscle mass and function at baseline was able to predict falls and fractures during 4 years. [Methods] We used the 4-year date from prospective study. The correlation between muscle mass or function and falls or fractures were analyzed by survival rate and cox hazard ratio. The cut-off value of leg muscle score (max:100, min:0) and grip strength were calculated by ROC analysis to correlate falls. [Results] 100 RA patients (female rate:78%, mean age: 66.1 years) were entry. 35 patients had falls and 19 patients had fractures. Leg muscle score, grip strength, age, and fractures at baseline significantly correlated with falls. The cut-off value of leg muscle score and grip strength was calculated 84.5 points and 15.9 kg, respectively. The survival rate of falls as endpoint in both low group (35.3%) was significantly lower than other groups (P=0.002). The hazard ratio in both low group significantly increased 3.6-hold (95%CI:1.1-11.5) compared that at both high group. [Conclusions] Both lower leg muscle score and grip strength at baseline was high risk of falls during 4 years. Evaluation of muscle mass and function is able to predict falls in RA.

W12-2

Skeletal muscles atrophy is caused by systemic inflammation, and contributes to atherosclerosis and osteoporosis in RA patients

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Conflict of interest: None

[Objective] To clarify that skeletal muscles atrophy is caused by systemic inflammation, and contributes to atherosclerosis and osteoporosis in rheumatoid arthritis (RA) patients. [Methods] We performed cross-sectional study in which 168 patients with RA. Indicators of RA disease activity, systemic inflammation, bony destruction, skeletal muscle mass, osteoporosis and atherosclerosis were measured. [Results] Skeletal muscles mass index (SMI) was significantly correlated with Clinical Disease Activity index, Simplified Disease Activity index, erythrocyte sedimentation rate, and carpal-height ratio. Moreover, SMI was significantly correlated with indicators of osteoporosis and atherosclerosis such as bone mineral density, ankle-brachial index, brachial-ankle pulse wave velocity, and intima-media thickness. [Conclusions] Skeletal muscles atrophy is caused by systemic inflammation, and contributes to atherosclerosis and osteoporosis in RA patients.

W12-3

Teriparatide increase the bone mineral density irrespective of the concomitant medications and disease activity in patients with rheumatoid arthritis with osteoporosis

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Conflict of interest: None

[Objective] We evaluated the BMD change in patients with RA treated with teriparatide. [Methods] This study included 37 RA patients treated with teriparatide. BMD were evaluated by DXA at baseline and 6, 12, 18, 24 months after treatment. We evaluated the influence of disease activity, bDMARDs use and pretreatment of OP for BMD change. [Results] Improvement ratio of BMD at 6, 12, 18, 24 months after treatment at lumbar spine were 5.9% ($p<0.01$), 9.7% ($p<0.01$), 10.5% ($p<0.01$), 10.0% ($p<0.01$), at proximal femoral were 1.3% (p=0.35), 0.03% (p=0.76), 2.7% (p=0.27), 2.5% (p=0.09), and at femoral neck were 0.8% (p=0.79), -0.4% (p=0.5), 1.2% (p=0.65), 1.6% (p=0.44). There were no differences in improvement ratio of BMD at lumbar spine, proximal femoral and femoral neck between 13 patients with DAS28<2.7 and 13 patients with 2.7 ≦DAS28 (9.2vs10.7%: p=0.64, 2.5vs2.5%: p=0.76, 2.6vs0.5%: p=0.41), between 10 patients with bDMARDs and 16 patients without bDMARDs (5.7vs12.9%: p=0.11, 2.6vs2.4%: p=0.81, 1.6vs1.6%: p=0.69), between 15 patients with pretreatment of OP and 12 patients without pretreatment of OP (6.9vs14.8%: p=0.11, 5.1vs-0.5%: p=0.03, 1.2vs2.0%: p=0.59). [Conclusions] Teriparatide improved BMD at lumbar in patients with RA independently regardless of the disease activity, bDMARDs use, pretreatment of OP.

W12-4

Follow up of sarcopenia, locomotive syndrome and frailty in patients with rheumatoid arthritis from the CHIKARA study

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Conflict of interest: None

[Objective] To investigate the risk factors for new onset of sarcopenia, locomotive syndrome, and frailty in patients with rheumatoid arthritis (RA) and the course of each disease. [Methods] We used 2-year data from the rural group of the prospective observational CHIKARA study. Improvement was defined as cases with disease at baseline that no longer met the diagnostic criteria after 2 years. [Results] Eighty-one patients with RA (82.7% female), mean age 66.9±11.5 years, mean DAS28-ESR was 2.9±1.2, methotrexate use was 81.5%, glucocorticoids (GC) use was 22.2%. The new onset rates were 4.4% for sarcopenia, 15.4% for locomotive syndrome and 13.3% for frailty. Of the patients who had each disease at baseline, 36.1% had sarcopenia, 20.7% had locomotive syndrome, and 33.3% had frailty, with improvement at 2 years. The sarcopenia and locomotive syndrome new onset group had significantly higher rates of GC use (p=0.036, p=0.007) and significantly higher use (p=0.01, p=0.001) than the group without sarcopenia and locomotive syndrome new onset. [Conclusions] The new onset rates at 2 years were 4.4% for sarcopenia, 15.4% for locomotive syndrome, and 13.3% for frailty; the improvement rates were 36.1% for sarcopenia, 20.7% for locomotive syndrome, and 33.3% for frailty.

W12-5

Tocilizumab prevents progression of chronic kidney disease in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] This study was conducted to clarify the factor associated with chronic kidney disease (CKD) progression in patients with rheumatoid arthritis (RA) who treated with biologics. [Methods] We retrospectively selected RA patients who treated with the single biologics continued for more than 5-years from 2001 to 2018. They were divided into 2 groups according to CKD progression during 5-years observation. Clinical disease activity index (CDAI), c-reactive protein (CRP) level, and estimated glomerular filtration rate (eGFR) were collected every 0.5-years from the initiation of the biologics. Multivariate analysis was conducted to identify the independent factors associating with CKD progression. [Results] We examined 423 patients (196 of TNF inhibitors 190 of TCZ, 37 of ABT) and CKD was diagnosed in 35 (8.3%). Multivariate analysis revealed age (OR 1.06, p=0.037), NSAIDs use for more than 1-year (OR 4.83, p=0.018), TCZ use (OR 0.23, p=0.041), frequency of CRP > 0.14 mg/dL for 5-years (OR 2.55, p=0.024) were selected as independent factor associated with CKD progression. [Conclusions] Sustained high level of CRP may be associated with CKD progression and TCZ may prevent CKD progression in RA patients treated with biologics.

W12-6

Survey of Fibrosis 4 index in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] With the aging of RA patients, we need to pay attention not only to renal function but also to liver function. Therefore, we examined the effect of age and previously used csDMARDs on Fibrosis 4 index (Fib4) in RA patients. [Methods] We conducted a fact-finding survey of Fib4 using RA patinets' data (n=739) who visited our hospital from 2012 to 2019. We examined each factors which composed Fib 4, ChE and the complication status. Andmore, we collected patients' treatment history, if they had continued previous therapy (n=368). And, we analysed these data to clarify the actual condition of Fib4 in RA. [Results] We showed that Fib4 had an age-dependent increasing tendency and there was no tendency to depend on the number of lifestyle-related diseases. Fib4 in patients who had taken previous csDMARD was tended to be higher than in naïve patients. Patients who had taken MTX showed significant increase in all age groups after 50s compared to naïve patients. [Conclusions] Fib4, a surrogate maker for hepatic fibrosis, is age-dependently elevated in aging RA. Andmore, Fib4 in RA patients who had took MTX therapy was increased remarkably. We should necessary pay attention to Fib4's change when introducing or continuing RA treatment.

W13-1

Evaluation of MTX non -combination on Adalimumab or Golimumab treatment for rheumatoid arithritis patients using NinJa2019 database

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Conflict of interest: None

[Objective] To evaluate the necessity of MTX combination on Adalimumab or Golimumab treatment for rheumatoid arthritis (RA) patients. [Methods] RA patients treated with Adalimumab (n=258) or Golimumab (n=365) on the big datebase of NinJa2019 were divided into two groups; MTX combination group and non-combination group. We evaluated combinations of other drugs, CRP, DAS28-CRP, CDAI, and HAQ-DI between two groups in both agents, respectively. [Results] There was no stastically signifcant difference in use rate and dose of steroid, CRP, DAS28-CRP, CDAI, and HAQ-DI between two groups in both TNF inhibitors. [Conclusions] MTX cmombination is not always needed on Adalimumab or Golimumab treatment for rheumatoid arthritis patients.

W13-2

Determination of factors associated with optimal initial dose of Golimumab- Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER cohort) -

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Conflict of interest: Yes

[Objective] To determine patient's factors associated with optimal initial dose of Golimumab (GLM) for Rheumatoid Arthritis (RA). [Methods] We retrospectively analyzed RA patients who started GLM for 52 weeks. Patients were divided 4 groups: A) 50 mg/month, B) 100 mg/month, C) 50/100 mg/month (had a dose increase to 100 mg), D) 100/50 mg/month (had a dose decrease to 50 mg). Risk factors associated with time to increase (decrease) to 100 mg/month (50 mg/month) from 50 mg/month (100 mg/month) were determined with proportional hazards analysis. [Results] We analyzed 209 patients: 149 in A, 31 in B, 24 in C, 5 in D. DAS28CRP improved from A: 3.4±1.3, B: 4.5±1.2, C: 3.4±1.2, D: 2.0±1.6 at baseline, to A: 2.1±1.1, B: 2.3±1.4, C: 2.3±1.2, D: 1.8±0.54 at 52 weeks. We compared only with A and C, because the numbers of patients of B and D were not enough. Higher age (P value: 0.0227), higher body weight (P value: 0.0489), positive for anti-CCP antibody (P value: <0.0001), higher DAS28CRP (P value: 0.0014), higher HAQ (P value: 0.0159) were significantly associated with increasing to 100 mg/month from 50 mg/month. [Conclusions] We might have to start GLM 100 mg/month for RA patients with higher age, higher body weight, positive for anti-CCP antibody, higher DAS28CRP, higher HAQ.

W13-3

Reasons and Risk Factors for Discontinuation of Biologic Agents in Rheumatoid Arthritis Patients

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Conflict of interest: None

Background There are some rheumatoid arthritis (RA) patients who discontinue any biologic agent treatment due to various reasons. The objective of this study was to investigate the reasons and the risk factors for discontinuation biologic agents. Methods 758 patients who underwent biologic agent treatment over 10 years from starting at Tsurumai Biologics Communication Study Group were enrolled. We analyzed the retention rate of biologic agent treatment and the reasons for discontinuation. Baseline demographics were compared using cox hazard regression analysis. Results 758 patients were administered biologics continuously, 224 patients were withdrawn at last observation. The retention rate was 90.5% (number of discontinuation: 72) at least 1 year from starting biologics treatment, 84.6% (n=117) at 3 years, 78.2% (n=165) at 5 years, 71.2% (n=228) at 10 years. The reasons were adverse events in 140 patients, lack

of effectiveness in 43 patients, others in 41 patients. The risk factors were age (HR 1.04 [1.02-1.06], p<0.001]), concomitant methotrexate (HR 0.40 [0.26-0.61], p<0.001). Conclusion The most common reason for discontinuation was adverse events. Age and concomitant methotrexate were relative with discontinuation of biologic agents.

W13-4

Long-term evaluation of tocilizumab therapy in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate long-term efficacy and safety of tocilizumab (TCZ) therapy in RA patients. [Methods] 304 RA patients treated with TCZ therapy at our hospital were reviewed. [Results] Age: 60.0±13.6 years, disease duration: 17.1±14.7 years, Biologics or JAK inhibitors use: 61.5%, PSL use: 48.4%, MTX use: 41.1%, and DAS28-ESR: 5.4±1.4. The continuation rate of TCZ therapy was 83.4% at 1 years, 68.6% at 5 years, and 53.2% at 10 years by Kaplan-Meier curves. The continuation rate of TCZ therapy had no significant deference between the first TCZ use group and the previous use of Biologics or JAK inhibitors group, and between the MTX use group and the no MTX use group, respectively. 110 patients discontinued TCZ therapy because of insufficient efficacy (n=36), adverse events (n=66), remission (n=1), and others (n=7). Cumulative incidence for patients discontinuing TCZ due to insufficient efficacy was 6.1% at 1 years, 13.4% at 5 years, and 17.0 at 10 years, and adverse events was 9.5% at 1 years, 18.9% at 5 years, and 34.5% at 10 years. 29 patients received the shortening the dosing interval of subcutaneous TCZ therapy. The incidence rate of discontinuation of MTX use was 24% in patients with MTX co-therapy. [Conclusions] TCZ therapy in RA patients was well tolerated and effective.

W13-5

Long-term safety and effectiveness of abatacept in Japanese patients with rheumatoid arthritis: A 3-year follow-up of a postmarketing drug-use survey

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Conflict of interest: Yes

[Objectives] A postmarketing drug-use survey was conducted to assess the safety and effectiveness of long-term abatacept (ABT) treatment in patients with rheumatoid arthritis (RA). [Methods] Patients with RA who started treatment with ABT intravenous infusion between July 1, 2011, and October 31, 2012 were followed up for 3 years. The incidences of adverse drug reactions (ADRs) and serious ADRs were investigated during the observation period. The DAS28-CRP/ESR and HAQ were used to evaluate the effectiveness of ABT. [Results] The safety analysis set and the effectiveness analysis set included 647 and 596 patients, respectively. The incidences of ADRs and serious ADRs over 3 years were 22.87% and 6.65%, respectively. There was no increase in the incidence of ADRs due to long-term treatment. The 3-year incidence of serious infections reported as ADRs was 3.71% (1.95 /100 patient-years), and that of malignant tumors reported as ADRs was 1.08% (0.55 /100 patient-years). Disease activity decreased during the first year of treatment and this decreased disease activity was sustained in years 2 and 3 during the observation period. [Conclusions] This survey demonstrated the effectiveness of long-term ABT treatment in clinical practice, and there were no events requiring new safety measures.

W13-6

Impact of age on duration of first biologics in patients with rheumatoid arthritis and infection discontinuation: Examination of 203 patients

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Conflict of interest: None

[Objective] Few studies have examined the effects of age on the rate of continuation and the development of infections with respect to the administration of biologics to elderly patients with rheumatoid arthritis. [Methods] The course of cases in which the first biologic was administered to patients with rheumatoid arthritis 70 years or older by December 31, 2018 is retrospectively examined. [Results] The first biologic was administered to 203 patients with rheumatoid arthritis over 70 years of age. There were 85 cases between the ages of 70 and 74, 82 cases between the ages of 75 and 79, and 36 cases over the age of 80. 101 cases continued until December 31, 2018. There were 102 cases that were discontinued on the way. The cumulative continuation rate at 1 year after the start of administration was 63.3% for 70 to 74 years old, 61.0% for 75 to 79 years old, and 53.0% for 80 years old and over. Infectious diseases that cause discontinuation of biologics occurred in 12 cases aged 70 to 74 years, 10 cases aged 75 to 79 years, and 2 cases aged 80 years or older, 0.95, 0.88, 0.50 per 10 person years, respectively [Conclusions] The incidence of infections causing biologic discontinuation did not increase with increasing age.

W14-1

Response of patients with elderly onset rheumatoid arthritis to methotrexate compared with younger onset

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Conflict of interest: Yes

[Objective] To compare the efficacy of methotrexate (MTX) in elderly-onset rheumatoid arthritis (EORA) patients with that in younger-onset RA (YORA) patients. [Methods] This study was performed based on data from a multicenter inception cohort study*, and included 151 RA patients who could be followed up to 6 months after starting MTX (baseline). Patients were divided into two groups based on age at RA onset: the YORA (<65 years) and EORA (≧65 years) groups. [Results] Compare with the YORA group (n=82), the EORA group (n=69) was more likely to have a lower dose of MTX at baseline, 3 and 6 months. The DAS28-CRP and HAQ-DI were significantly lower at 3 and 6 months compared to baseline in both groups. The DAS28-CRP and HAQ-DI were significantly higher in the EORA group compared to the YORA group at baseline (DAS28-CRP: 4.4±1.3 vs. 3.9±1.1, P=0.014, HAQ-DI: 0.769±0.695 vs. 0.545±0.515, P=0.032), whereas no significant differences were observed between the EORA and YORA groups at 3 (DAS28-CRP: 2.8±1.2 vs. 2.4±1.2, HAQ-DI: 0.349±0.466 vs. 0.247±0.376) and 6 months (DAS28-CRP: 02.4±1.1 vs. 2.3±1.1, HAQ-DI: 0.306±0.512 vs. 0.196±0.306). [Conclusions] The efficacy of MTX in EORA patients is comparable to that in YORA patients. *This work was supported by Eli Lilly Japan K.K.

W14-2

Effectiveness of glucocorticoid combination therapy for MTX initial treatment in patients with rheumatoid arthritis-ANSWER cohort study-

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Conflict of interest: Yes

[Objective] To examine the effectiveness of oral GC combination therapy in the initial treatment of MTX for short and long terms in patients with rheumatoid arthritis (RA). [Methods] Five hundred fifty-three RA patients who newly introduced MTX from 2011 to 2020 were included. The disease activity, HAQ, and cumulative incidence of biologics (Bio) induction were compared for 5 years between a group with GC (GC) and a group without (No-GC). [Results] There were statistically significant differences between the GC group (n=131) vs No-GC group (n=422) in age, DAS28-ESR (DAS), SDAI, CRP, and HAQ. The median daily PSL dose was 5.0, 5.0, 4.0, 3.8, 3.0, 4.5 mg/day at baseline, 0.5, 1, 2, 3 and 5 years. There was no statistically significant difference between the groups in DAS for time-course changes in 5 years (P=0.22), but there was a significant difference in HAQ (P=0.02). PSL>5 mg/day was significantly associated withΔDAS for first 0.5y (vs No-GC, β=-0.85, P=0.01) in multiple linear regression model, and was a significant risk factor of Bio induction (vs No-GC, HR: 4.2, 95% CI: 1.4-12.4, P=0.01) in Cox proportional hazard regression model. [Conclusion] MTX+GC combination therapy was indicated in more severe cases and had dose-dependent efficacy, but was not sufficient to avoid induction of Bio.

W14-3

Liver injury and the amount of change in fibrosis-4 index (FIB4) in rheumatoid arthritis (RA) patients treated with methotrexate (MTX)

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Conflict of interest: None

[Objective] MTX has caused liver injury, and we should need to monitoring for AST/ALT. However, liver fibrosis associated with MTX was considered to be rare. Recently, FIB4 has been often used as an indicator of liver fibrosis, therefore we examined the amount of change in FIB4 for patients with the use of MTX. [Methods] We examined 150 cases diagnosed RA of MTX naïve. We evaluated the amount of change in FIB4 of those cases were divided into five different age groups of onset, from under 49 years old to the 80's. [Results] There was a significant difference for FIB4 in all observation periods (0M-18M), the results showed that the elderly had higher levels of FIB4. And, the amount of change in FIB4 (Δ0-18M) were compared among those groups using analysis of covariance; doses of MTX were used as covariates. The results showed a significant difference at only Δ0-6M, and the amount of change was significantly higher in the elderly. After six months of using MTX, there was a significant difference among all groups for he percentages that changed to FIB4>1.3. [Conclusions] We suggest that the amount of change in FIB4 before and after 6 months of MTX was higher in the elderly. FIB4 should also be an indicator for monitoring after MTX administration, especially in the elderly patients.

W14-4

Contribution of Tacrolimus concentration to the clinical efficacy to Rheumatoid Arthritis

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Conflict of interest: None

[Objective] The oral Tacrolimus (TAC) dose correlates just weakly to the serum concentration of TAC. We here compare serum concentration of TAC with the extent of arthritis and the progression of arthritic joint destruction in the patients with RA. [Methods] We measured serum concentration of TAC in 380 out-patients with RA and rheumatic diseases who visited our hospital during April 2019 to May 2019. We studied 153 out-patients with RA who newly started receiving TAC between Feb. 2016 and May 2019. [Results] There was a weak correlation between the dose of TAC and serum trough level; r= 0.35. The CRP, MMP-3 and ESR at 3, 6, 12 months later were improved compared at the start points. The median level of TAC was 2.53 ng/ml. The patients were divided into 2 groups; those with less than 2.5 ng/ml and those with more than 2.5. The CRP, MMP-3 and ESR at the start point, 3, 6, 12 months later were insignificant between 2 groups. The ratios of radiographic structural remission and radiological rapid progression for 1 year were not significant between 2 groups. [Conclusions] While it is commonly believed that the concentration of TAC should be around 5 ng/ml for successful treatment, our study shows that at least in RA, the TAC is effective irrespective of the serum concentration of TAC. [Objective]

W14-5

The additional effects of Tacrolimus and Iguratimod on inadequate response to biologics (ANSWER cohort)

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Conflict of interest: None

[Objective] To compare the additional effects of Tacrolimus (TAC) and Iguratimod (IGU) used for inadequate biologic effects in patients with rheumatoid arthritis. [Methods] The subjects were patients who had insufficient efficacy despite using the biologics for 8 weeks or more and added TAC (TAC group; N=39) or IGU (IGU group; N=94). Inadequate response to biologics (Bio-IR) was defined as CDAI>2.8 at the start of TAC or IGU, and the number of tender and swollen joints remained unchanged or worsened from 4-8w before. The additional effects at 8w, 16w and 24w was compared between the two groups in CDAI, DAS28-ESR, SJ, TJ, VAS, ESR, HAQ and MMP-3. [Results] CDAI (0w, 8w, 16w, 24w) was significantly improved in IGU group (12.4, 9.3, 7.0, 7.8; p <0.001) and TAC group (14.0, 12.2, 8.2, 6.4; p <0.001). The same tendency was observed in DAS-ESR, SJ, TJ, VAS, and MMP-3. The degree of improvement in DAS-ESR (ΔDAS-ESR) after 24w was significantly improved in the TAC group than in the IGU group (p = 0.397), but there was no difference in ΔCDAI between the two groups. [Conclusions] TAC and IGU showed almost the same efficacy against insufficient biological effect.

W14-6

Renal dysfunction caused by Iguratimod

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Conflict of interest: None

[Objective] Iguratimod (IGU) is a csDMARD, which was first developed as NSAIDs. IGU is possible to cause renal dysfunction due to decreased glomerular blood flow caused by COX inhibition. [Methods] We retrospectively studied cases of IGU administration in our hospital. [Results] 113 patients received IGU from July 2018 to August 2020. The mean age was 68.7 (20-99), 75 (66.4%) were female. The primary diseases were RA in 98 (86.6%), SpA in 9 (8.0%) and others in 6 (5.4%). Comorbidities of DMARDs were MTX in 56 (49.6%), SASP in 58 (51.3%), BUC in 14 (12.4%), TAC in 9 (0.8%) and biologic agents in 9 (0.8%). In 57 patients (50.4%), including temporary use, PSL was used. 18 patients were discontinued, two of which were due to renal dysfunction. In the 63 patients treated with IGU for 6 months, the eGFR was 67.6, 62.2, and 62.3 at the time of administration, after 3, and 6 months. There was a significant decrease in eGFR at 3 and 6 months ($p<0.001$ in two cases) compared to the baseline. There was no difference in eGFR reduction in gender, diabetes mellitus, and in the combination of NSAIDs or MTX ($p=0.76$, 0.72, 0.15, 0.18), but there was a difference in PSL ($p=0.007$). [Conclusion] IGU treatment reduced eGFR. Among patient backgrounds, PSL was significantly associated with lower eGFR.

W15-1

Comparison of the efficacy of abatacept on elderly and young patients with rheumatoid arthritis: 24 weeks results from ABT-ATS study

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Conflict of interest: Yes

[Objective] To clarify the efficacy of abatacept (ABT) in elderly and young patients with RA. [Methods] Refractory to csDMARDs and bionaïve patients were enrolled in a multicenter observational registry (ABT-ATS study group). 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) groups). Comparison was made between 4 groups of patients. [Results] A total of 202 patients who had been observed for 24 weeks were analyzed. The AO group showed higher EULAR good or moderate response than CO group at week 24 (83.6% vs 39.6%, $p<0.001$). The AY group also showed higher response than CY group. Moreover, the responses of AO group and AY group were comparable at 83.6% and 78.7%, respectively ($p=0.679$). Based on the cohort using propensity score matching, the AO group achieved higher EULAR good or moderate response than CO group (74.2% vs 45.2%, $p=0.038$). Whereas the response of AY group was comparable to that of CY group (64.0% vs 64.0%, $p=1.000$). The responses of AO group and AY group were similar at 76.3% and 76.3%, respectively ($p=1.000$). [Conclusions] The efficacy of ABT on elderly RA is comparable to that of young patients.

W15-2

Comparisons of effectiveness between tocilizumab and abatacept in rheumatoid arthritis patients without concomitant methotrexate: a propensity score matching analysis using data from multicenter registry system

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Conflict of interest: Yes

[Objectives] All biological DMARDs can be selected in the patients treated with methotrexate (MTX). However, in the patients without MTX, biological DMARDs other than TNF inhibitors are often used. We compared tocilizumab (TCZ) and abatacept (ABT) using multicenter registry study data. [Methods] Subjects were patients using TCZ (N = 110) and ABT (N = 220) without concomitant MTX registered in TBCR, and 51 pairs were extracted by a 1: 1 matching using a propensity score. Disease activities were compared using the CDAI score. [Results] Mean age of the TCZ and ABT groups was 60.2 and 59.7 years, disease duration was 9.9 and 8.8 years, the previous biologics history was 56.9 and 62.7%. The mean CDAI score at 52 weeks improved from 25.8 at baseline to 15.9 in the TCZ group and from 25.0 to 14.7 in the ABT group, with no significant difference between the groups at each time point. There was no significant difference between the groups in each component of CDAI and the MMP-3 and HAQ scores. [Conclusion] No difference in effectiveness was observed between TCZ and ABT in patients with matched background. Both agents can be considered to be a treatment option in the same line for the RA patients without concomitant MTX.

W15-3

The cost-effectiveness analysis of abatacept in rheumatoid arthritis using the IORRA cohort

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Conflict of interest: Yes

[Objectives] To investigate cost-effectiveness of abatacept (ABT) as the 1st line therapy in patients with rheumatoid arthritis (RA). [Methods] Effectiveness of ABT and TNF inhibitors (TNFIs) was calculated from RA patients who initiated these drugs in the IORRA cohort between 2010 and 2018, and medical costs were calculated from JMDC claims database between 2010 and 2019. Patients who used ABT at 1st line (ABT 1st) were matched with patients who used a TNFI at 1st line (TNFI 1st) or those who used ABT at 2nd line or later (ABT 2nd) using patients' background. We used the previously published ABT cost-effectiveness model. The primary endpoint was the medical direct costs per person to achieve ACR50 for 2 years. [Results] The costs per person to achieve ACR50 were ¥736,653 in ABT 1st and ¥745,636 in TNFI 1st. The cost-effectiveness doesn't differ between the two groups. The costs per person to achieve SDAI/CDAI remission were ¥385,866/¥405,159 in ABT 1st and ¥372,818/¥356,608 in TNFI 1st. The costs per person to achieve ACR50/SDAI remission were ¥867,630/¥365,318 in ABT 1st and ¥990,779/¥630,496 in ABT 2nd. [Conclusions] There was no difference in the cost-effectiveness between ABT 1st and TNFI 1st in patients with RA. Use of ABT at the 1st line was confirmed to be cost-effective.

W15-4

Experiences of Abatacept therapy in rheumatoid arthritis patients with pulmonary comorbidities

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Conflict of interest: Yes

[Objectives] We assessed the efficacy of Abatacept (ABT) in rheumatoid arthritis (RA) patients with pulmonary comorbidities (PD). [Methods] Ninety-one RA patients who had been treated with ABT were evaluated. These patients were divided into two groups; group A (G-A, n=12): pa-

tients without PD, group B (G-B, n=79): with PD. We compared the SDAI, ACR response, EULAR and response of G-A with G-B until 1-year treatment. [Results] There were no significant difference between groups in demographic characteristics at baseline. There were no significant difference in SDAI remission and low disease activity rate, ΔSDAI, EULAR good and moderate response rate, and ACR 20/50/70 response rate between groups. [Conclusion] ABT therapy is clinically effective for even RA patients with PD.

W15-5

Analysis of efficacy for abatacept treatment in early rheumatoid arthritis

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Conflict of interest: Yes

[Objective] It is reported that abatacept is effective for progressive RA which was positive for RF or anti-CCP antibodies. However it is unknown whether RF or CCP was related to the efficacy for early RA. We investigated those analyses in early RA of our clinic. [Methods] Early RA of 20 patients out of total 75 patients who underwent the abatacept treatment with mean age of 54 years, mean disease duration of 0.9 years, mean MTX usage of 6.3 mg/w, mean PSL usage of 1.5 mg/d, mean HAQ-DI of 0.67, mean RF of 53.7 IU/ml, mean anti-CCP antibodies of 333 U/ml was analyzed the 12 weeks efficacy of DAS28 (CRP) between group 1, RF (-) and CCP (-), and group 2, RF (+) or CCP (+) statistically. [Results] Continuation rate was 83% by Kaplan-Meier method in two years of 75 patients treated with abatacept in our clinic. DAS28 (CRP) in early RA cases of 20 patients was 4.12 at baseline to 2.17 at 12 weeks. DAS28 (CRP) in group 2 was 1.56 which was significant lower than in group 1 of 2.71. Patient VAS was also lower in group 2 at 10.4 mm compared with group 1 at 35.9 mm. delta DAS 28 (CRP) was 1.62 in group 1 and 2.34 in group 2. [Conclusions] RF or anti-CCP antibodies were possible for the clinical factor related to the efficacy in early RA treated with abatacept.

W16-1

Efficacy and safety of sarilumab in rheumatoid arthritis in clinical practice ~ including switched from biological DMARDs or Janus Kinase inhibitors ~

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Conflict of interest: None

[Objective] The aim of our study was to examine efficacy and safety of sarilumab (SAR) for rheumatoid arthritis (RA) in clinical practice. [Methods] We investigated the backgrounds and clinical courses of 37 RA patients treated with SAR from September 2018 to July 2020. [Results] At baseline, median age was 74 (33-85) years, 28 females, median disease duration 6.6 years, stage 3-4 15 cases, complicated ILD in 11 cases (30%), PSL usage 16 cases (43%), MTX naive 25 cases (68%). 21 cases (56%) were switched from biological DMARDs (Bio)/Janus Kinase inhibitors (JAK), 8 cases from TCZ and 4 cases from JAK. 22 cases could be analyzed, and there was reduction from baseline in DAS28-ESR and CDAI values at 4 and 12 weeks (the mean DAS 28-ESR 4.36/2.56/1.65, the mean CDAI 17.6/10.8/6.9). 3 of 4 cases switched from JAK showed improvement. The continuation rate of SAR after 52 weeks was 53% analyzed via Kaplan Meier Survival curves. SAR was discontinued due to 1 case remission, 6 cases ineffectiveness, 7 cases adverse events (the most was skin rashes. 1 of 2 cases of malignant lymphoma was dead). The correlation between neutropenia and anti SS-A antibody positive was not recognized. ALL ILD were continued without any deterioration. [Conclusions] SAR switched from Bio/JAK seems to be effective.

W16-2

Hemoglobin changes and disease activity in Japanese patients with rheumatoid arthritis treated with sarilumab

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Conflict of interest: Yes

[Objective] Rheumatoid arthritis (RA) is associated withinflammation-relatedanemia. This study investigated the potential effect of the anti-interleukin-6 receptor monoclonal antibody sarilumab (SAR) on anemia in Japanese patients with RA. [Methods] The KAKEHASI study (NCT02293902) randomized eligible Japanese patients with moderately to severely active RA to SAR 150 mg, SAR 200 mg or placebo (PL) every 2 weeks subcutaneously plus methotrexate. Change in Hb and percentage of patients with anemia over 24 weeks and the correlation of Hb levels with disease activity were included as endpoints for this post-hoc analysis. [Results] Approximately 50% of the 242 patients enrolled had anemia (WHO criteria) at baseline; of those, anemia resolved by 24 weeks in more than half of patients treated with SAR. Hb levels were raised from the beginning of SAR treatment. Greater Hb improvements were observed among patients treated with SAR than PL (mean change from BL at Week 16: -0.9, 7.4 and 6.1 g/L for PL, SAR 150 mg and SAR 200 mg, respectively). Changes in Hb were not correlated with disease activity and physical function. [Conclusions] SAR may increase Hb levels and may reduce the prevalence of anemia among Japanese patients with moderately to severely active RA.

W16-3

A retrospective study of rheumatoid arthritis (RA) patients treated with sarilumab (SAR) in our Departments

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Conflict of interest: None

Background In Japan, 8 biologics except for biosimilars and 4 JAK inhibitors are available for treatment of RA. To clarify the role of SAR in the treatment of RA, we retrospectively examined our cases. *Subjects* There are eighteen RA patients receiving SAR at Saitama Medical University Hospital and Japanese Red Cross Ogawa Hospital until October 2020. *Results* Concerning these 18 patients at the administration of SAR, the mean age was 56.4 years, the mean disease duration was 6.9 years, and the mean value of DAS28/ESR was 4.78. Eleven patients had a history of receiving biologics, including tocilizumab (TCZ) in 3 cases. Two patients experienced having baricitinib (BAR), a JAK inhibitor. Concerning 12 patients observed at least for 12 weeks, the mean values of DAS28/ESR were 4.62 at week 0 and 2.62 after 12 weeks. The mean values of DAS28/ESR of 6 patients observed for 52 weeks were 3.58 at week 0 and 2.09 after 52 weeks, showing a significant improvement. All of them had a history of receiving other biologics, including TCZ and BAR in 2 cases each. *Conclusions* Our study showed the early efficacy after the beginning of SAR treatment and the lasting efficacy for 52 weeks, and also showed the expected efficacy in the case of switching from other biologics including TCZ and a JAK inhibitor.

W16-4

Examination of the therapeutic effect of shortening the dosing interval of subcutaneous tocilizumab therapy

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Conflict of interest: None

[Objective] To investigate the clinical features of shortening the dosing interval of subcutaneous tocilizumab (TCZ) therapy in patients with rheumatoid arthritis (RA). [Methods] 37 patients (TCZ shortened group, M7, F30) who received shortening the dosing interval of subcutaneous TCZ therapy were recruited. The clinical features were examined at 0, 12, and 24 weeks after the administration. Randomly selected 37 patients (TCZ non-shortened group, M5, F32) who started normal administration of TCZ subcutaneous injection therapy were also recruited, and each item was compared respectively. [Results] The age of the TCZ shortened group was 57 ± 13 years, and the non-TCZ shortened group was 53 ± 13 years. CRP was 0.5±1.4 mg/dL, RF 85 (14-301) IU/mL, MMP-3 115 (69-176) ng/mL, DAS28-ESR 3.3 (2.3-4.3), CDAI 13 (9-18), and PSL 3 (0-4) mg/day at 0 week. After 24 weeks, DAS28-ESR and CDAI were improved, and PSL was reduced to 2 (0.25-3) mg/day. The median rate of decrease between 0 week and 24 weeks was CRP -50%, RF 0%, MMP-3 -20%, DAS28-ESR -26%, CDAI -19%, and PSL -20%. There was no significant difference between the two groups except CRP. [Conclusion] The shortening the dosing interval of subcutaneous TCZ therapy may be useful for the treatment of RA patients with high disease activity.

W16-5

Association factors with subcutaneous injection interval of tocilizumab in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We retrospectively studied the characteristics of rheumatoid arthritis (RA) patients in whom tocilizumab subcutaneous injection (TCZ-SC) interval was shortened or extended after the initial biweekly TCZ-SC administration. [Methods] Among 80 RA patients receiving TCZ-SC in our hospital, 57 patients in whom TCZ-SC was continued more than 6 months were examined. After the standard biweekly administration, patients were categorized by treatment optimization: the shorten group (19 patients, injection intervals <14 days), non-shorten group (38 patients, ≧14 days), extended group (17 patients, >14 days) and non-extended group (40 patients, ≦14 days). Then we retrospectively analyzed patients' clinical characteristics and concomitant medication. [Results] RF positive rate was higher in the shorten group than that of non-shorten group (94.7 vs. 68.4%, p=0.015). The rate of patients using other biological disease-modifying antirheumatic drugs previously tended to be higher in the shorten group compared to non-shorten group (88.0 vs. 45.0%, p=0.088). Concomitant steroid use was less frequent in the extended group compared to non-extended group (25.0 vs. 53.8%, p=0.047). [Conclusion] Factors associated with optimization of treatment upon continuation of TCZ-SC was suggested.

W16-6

Possibility of exacerbation of skin rash due to IL-6 blockade

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Conflict of interest: None

[Objective] To investigate the incidence of skin rash and to explore the feature of the gene expressions associated with skin rash after TCZ-Tx. [Methods] The medical record of 23 RA cases that was completely followed from the initiation of TCZ were checked to calculate the incidence of skin rash due to TCZ-Tx. Among them, 4 patients developed rashes (group S) and 10 patients without any side effects (group C) were selected for transcriptome analysis. The peripheral blood at just before (pre) and 3 months after (post) TCZ-Tx were subjected to the analysis. Total RNAs were analyzed with next-generation sequencing. [Results] The incidence of skin rash after TCZ-Tx was 9.25/100 person-years. Before TCZ-Tx, gene expression related to acute inflammation was activated in the group S. The genes associated with neutrophil migration were activated after TCZ-Tx no matter whether skin rash was developed or not. Particularly, gene expression related to cell adhesion and neutrophil migration were enhanced in the group S after TCZ-Tx. [Conclusions] We found the "paradoxical neutrophil activation" after TCZ-Tx. It should be noted that if RA patients have neutrophilic dermatosis, TCZ may lead to exacerbation of the rash.

W17-1

Real-world effectiveness of bDMARDs and tsDMARDs on clinical fracture reduction in patients with rheumatoid arthritis-ANSWER cohort study

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Conflict of interest: Yes

[Objective] The purpose of this study is to investigate whether biologic DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) suppress fractures. [Methods] Patients who firstly used bDMARDs and tsDMARDs in the Kansai multicenter cohort (ANSWER cohort) from 2009 to 2019 were included. The rate of fractures during the administration and that six months before the first administration of bDMARDs/ts DMARDs were compared. [Results] During the period, 3480 patients firstly used bDMARDs or tsDMARDs. In TNF inhibitors users (n = 2186), clinical fractures (CF) were 0.25 before administration and 0.17 after administration (/10,000 person-years), and major osteoporotic fractures (MOF) were 0.12 and 0.07, respectively. A 31% and 43% reduction in CF and MOF rate was observed (p <0.05, <0.05). With IL6 inhibitor (n = 574), CF was reduced by 43% and MOF was increased by 23%. With CTLA4-Ig (n = 628), CF was increased by 109% and MOF was increased by 4.7%. But, there were no statistically significant differences in fracture rate before and during the treatment of these drugs. No fracture patients were found with the JAK inhibitor (n = 92). [Conclusions] The use of TNF inhibitors in patients with rheumatoid arthritis can reduce fractures.

W17-2

Status of use of Tocilizumab, Abatacept and Golimumab 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, Abatacept and Golimumab for rheumatoid arthritis in our hospital with using the NOSRAD registry. [Methods] 493 patients of rheumatoid arthritis who introduced Tocilizumab, Abatacept or Golimumab until August 2019 were included in this study. The examination items consist of 1) Changes in DAS28 after the treatment, 2) Cumulative survival rate of Kaplan-Meier

method, 3) survival rate of bio-naïve and switch cases. [Results] The average age at the start of administration were 53.5±14.0 years old (Tocilizumab), 70.1± 10.7 years old (Abatacept) and 66.1±13.5 years old (Golimumab). Significant difference was found in each group. About DAS28, significant improvement was obtained after 12 months in each group. Survival rate of whole cases and bio-naïve cases in Tocilizumab was significantly higher than these cases in Abatacept or Golimumab. Significant difference wasn't observed between Abatacept and Tocilizumab in Survival rate of switch cases. [Conclusions] Tocilizumab was introduced to relatively young patients, but Abatacept was introduced to relatively elderly patients. Survival rate of whole cases and bio-naïve cases in Tocilizumab was good. However, survival rate of switch cases in Abatacept was no change compared to Tocilizumab.

W17-3

The effectiveness of biologic agents concomitant with tacrolimus in rheumatoid arthritis

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Conflict of interest: None

[Objective] The objective of this study was to investigate the efficacy of biologics agent concomitant with TAC with RA [Methods] All patients (n=2860) who underwent 5 biologics agent (etanercept: ETN, adalimumab: ADA, goliumab: GLM, tocilizumab: TCZ, abatacept: ABT) treatment at Tsurumai Biologics Communication Study Group were enrolled. In each biologics agent's analysis, patients were divided into three groups: (1) concomitant only MTX (MTX group) (2) concomitant only TAC (TAC group) (3) monotherapy (mono group). Kaplan-Meier analysis was used to estimate retention rates in each biologics agent group. [Results] Number of patients who administered each biologics concomitant with TAC were 142. Number of those were ETN: 47 ADA: 10 GLM: 14 TCZ: 27 ABT: 49. In each biologics agent's analysis, number of patients were, in ETN (MTX: 774 TAC: 27 others: 486), in ADA (MTX: 339 TAC: 10 others: 135), in GLM (MTX: 156 TAC: 14 others: 61), in TCZ (MTX: 272 TAC: 27 others: 207), in ABT (MTX: 213 TAC: 49 others: 178). Under multiple COX proportional hazard analysis, in ETN and TAC, the retention rate of TAC group was higher than others group. [Conclusions] We suspected that in ETN, ABT therapy, combination therapy with TAC are subsequent options for treatment to RA patient.

W17-4

Analysis of rheumatoid arthritis aged 80 years or older at the time of introduction of biologics

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Conflict of interest: None

[Purpose] In elderly rheumatoid arthritis (RA) cases, the frequency of complications and adverse events is high, and sufficient drug therapy may be a concern. We examined RA cases in which the biologic (BIO) was introduced was 80 years or older. [Methods] So far, 17 elderly RA cases aged 80 years or older who have been introduced BIO as a naive case were retrospectively examined. [Results] The breakdown of 17 cases was 5 males and 12 females, and the average age at introduction was 81.6 years. The drugs used were infliximab: 2, etanercept: 4, tocilizumab: 4, adalimumab 4, abatacept: 1, golimumab: 2. Twelve of the 17 patients were given subcutaneous injection, but no self-injection was given, and they were given by family members or by visiting the hospital. Because of dementia, lymphoma, cerebral infarction, pneumonia, cerebral hemorrhage, etc., 5 patients were discontinued therapy. Nine patients were transferred to another hospital. Currently, 3 patients are being continuously administered. [Discussion] There are various issues such as complications including dementia, family cooperation in hospital visits and treatment, but even in elderly RA cases, treatment using BIO is safe and effective if the conditions are met. It is considered possible to draw out.

W17-5

Real-world data of biologic and targeted synthetic DMARD usage in RA treatment

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Conflict of interest: None

[Objective] There is no standard for selection of bDMARD or tsDMARD in RA treatment It depends on physician's or patient's choice which is based upon their experience, situation and so on. The objective of this study is to clarify the tendency of bDMARD or tsDMARD usage in real-world patients with RA obtained from large cohort data base NinJa. [Patients & Methods] We used clinical data obtained from NinJa 2016 and 2017, which had been gathered from about 50 hospitals all over Japan. Study 1: The 427 cases, which were treated some bDMARD or tsDMARD in 2017 and treated without any bDMARD or tsDMARD in 2016 were selected. Study 2: The 358 cases which had been also listed on NinJa2018 were selected from Study 1. [Results] The rate of drugs were 1: TCZ24%, 2: ABT19%, 3: GLM14%, 3: ETN14%. The ratio of continuing same DMARD was as follows; BAR 100%, ABT 84%, GLM 76%, and percentage of remission (DAS-CRP) were BAR 85%, ADA 80%, CZP 75%. [Conclusions] This study revealed the difference in the bDMARDs and tsDMARDs usage in the real world. The detailed analysis would explain a proper treatment.

W18-1

Evaluation of efficacy and safety of Sarilumab in patients with previous Tocilizumab treatment

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Conflict of interest: None

[Objective] To clarify the question whether Sarilumab (SAR) could be used effectively and safely in patients with previous Tocilizumab (TCZ) treatment. [Methods] We retrospectively collected information of patients who were prescribed SAR for rheumatoid arthritis (RA) from April 2020 to September in our hospital. The information collected were histories of bDMARDs, and effectiveness, safety and persistence of SAR. We defined "partially effective", as 20% reduction of swelling and tenderness joints, and "effective", as none or 50% reduction of such joints. [Results] Twenty-one patients' data were collected. Ten patients used TCZ previously and 6 patients used TCZ just before switched to SAR. Seven patients experienced TCZ secondary failure, and 3 patients had adverse events. SAR was used effectively in 7 patients with previous TCZ treatment and in 10 patient without. SAR was partially effective in 2 patients with previous TCZ and in one without previous TCZ. In one patient who used TCZ before, SAR was not effective. No adverse event of SAR was observed among the patients. [Conclusions] We showed possibility of switch effectively between anti-IL-6R antibody agents after secondary failure of the fomar agent. We assume that binding properties to the antigen and pharmacodynamics cause this.

W18-2

Which DMARDs are better for RA patients who had inadequate response to IL-6 inhibitors?

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Conflict of interest: None

[Objective] To elucidate next better treatments for RA patients who had inadequate response to IL-6 inhibitors (IL-6i). [Methods] Among RA patients had received IL-6i in our hospital, the medical records of 79 RA patients who had received another DMARD due to inadequate response to IL-6i and had been followed up for more than 24 weeks were retrospectively evaluated. [Results] Background features at discontinuation of IL-6i were as follows; average age 63.0 y/o, mean disease duration 14.6 years, MTX usage rate 40.5% and the average CDAI and DAS 28-ESR 20.5 and 4.2. Next DMARDs after IL-6i discontinuation were as follows; TNF inhibitors (TNFi) 32 (40.5%), abatacept (ABT) 21 (26.5%), JAK inhibitors (JAKi) 23 (29.1%), another IL-6i 3 (3.9%). LOCF analysis revealed that the changes of CDAI from baseline to week 24 were from 22.3 to 14.3 for TNFi (P =0.0159), 21.5 to 10.3 for ABT (P =0.0001), 18.3 to 7.3 for JAKi (P < 0.0001) and 10.5 to 2.5 for IL-6i (P=0.0809), and the changes of DAS28 were from 4.4 to 4.3 for TNFi, 4.3 to 3.9 for ABT, 4.1 to 3.3 for JAKi and 3.4 to 1.8 for IL-6i. CDAI remission rate of TNFi, ABT and JAKi at week 24 are 12.5%, 0% and 30.4% respectively. [Conclusions] The switching to JAKi seems to be more preferable in RA patients who had inadequate response to IL-6i.

W18-3

Usefulness of sarilumab by stratifying patients by the preceding biologics

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Conflict of interest: Yes

[Objective] To clarify the usefulness of sarilumab (SAR) by stratifying patients by the prior bio. [Methods] Efficacy was assessed by CDAI using the LOCF method, and safety was assessed by investigating the reasons for discontinuation of SAR in consecutive RA patients treated with SAR in our hospital by July 2020. The 3 groups were compared in the preceding bio types (TCZ; TNFi; naïve). [Results] The study included 27 patients (18 women). Prior bio was TCZ in 10 cases, TNFi in 7 and naïve in 10. The mean age of all patients at the start of SAR was 70.5±13.7 years, the disease duration was 8.9±10.0 years, the treatment period at the last observation was 37.6±34.8 weeks, CDAI was 20.8±16.4; there was no significant difference among the three groups in each item. CDAI at SAR start (0w) and 12w was 21.2±15.8 to 11.7±10.4 (P=0.13 compared to 0w) in prior TCZ group, 17.4±7.8 to 4.6±3.0 (P=0.002) in prior TNFi group, and 22.7±21.7 to 7.7±5.0 (P=0.05) in naïve group. The rate of LDA+remission achieved at 26w was 60% in prior TCZ group, 100% in prior TNFi group, and 80% in naïve group (3 group comparison P=0.07). Of the 6 patients who discontinued SAR, all 3 who quitted due to inadequate effect were in prior TCZ group (P=0.03). [Conclusions] The prior TCZ group was more likely to have a poor SAR effect.

W18-4

Effects of Switching from Etanercept Originator to Etanercept Biosimilar on Disease Activity, Physical Function, and Patient-Reported Outcome Regarding a Self-injection Device in Patients with Well-Controlled Rheumatoid Arthritis

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Conflict of interest: None

[Objective] This retrospective study investigated the effects of switching from etanercept originator (ETN-OR) to ETN biosimilar (ETN-BS) on disease activity, physical function, and patient-reported outcome (PRO) regarding a self-injection device in patients with well-controlled RA. [Methods] We investigated disease activity, mHAQ, and patient characteristics in 42 RA patients that switched from ETN-OR to ETN-BS at least 6 months prior. Patients were also requested to answer the Toyohashi Self-Injection Assessment Questionnaire (T-SAQ), originally designed to assess PRO. [Results] All the patients were female. The mean age, RA duration, and ETN-OR treatment duration were 63.1 years, 18.3 years, and 3107 days, respectively. The disease activity and mHAQ after switching were as follows (baseline-3 months-6): DAS28-CRP (1.86-2.00-2.03), SDAI (4.3-5.0-5.3), and mHAQ (0.43-0.44-0.46). SDAI after 6 months was significantly elevated compare to baseline. T-SAQ scores before and after switching were 1.3 and 1.1 ($p < 0.01$), respectively. Ease of use, mental tension, and pain were especially improved after switching to ETN-BS. [Conclusions] Switching from ETN-OR to ETN-BS worsened disease activity in well-controlled RA patients, whereas the PRO regarding the injection device was improved.

W18-5

The addition of iguratimod to methotrexate reduces the need to switch to biological disease-modifying antirheumatic drugs in patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: Iguratimod (IGU) is generally used in patients with rheumatoid arthritis (RA) who inadequately respond to methotrexate (MTX). Clinically, we have found that add-on IGU can reduce the need to switch to biological disease-modifying antirheumatic drugs (bDMARDs), but no study has verified this finding. Therefore, we analyzed the efficacy of add-on IGU and discontinuation rates based on EULAR recommendations. Methods: Patients with RA who had started IGU therapy because remission or low disease activity was not achieved after at least 3 months of MTX administration were enrolled. We investigated the rate of discontinuation, as prompted by DAS28-CRP≧2.7 at 12 and 24 weeks or adverse events, of IGU + MTX therapy at 52 weeks using the Kaplan-Meier method. The factors associated with discontinuation were assessed. Results: In total, 60 patients with RA (10 males, 50 females) were enrolled. The survival rate of IGU + MTX therapy at 52 weeks was 30.0% (18/60 cases), and multiple regression analysis identified baseline DAS28-CRP as a factor that significantly influenced treatment discontinuation. Conclusion: The addition of IGU to MTX can decrease the need to switch to bDMARDs at 52 weeks.

W18-6

The trends of the dose reduction or dose increase of 6 biological DMARDs and 2 targeting synthetic DMARDs Japanese patients with RA by NinJa 2019 cohort

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Conflict of interest: None

[Objective] The purpose of this current study is to review the dose reduction or dose increase of 6 biological DMARDs (TCZ, ETN, ABT, IFX, ADA, CZP) and targeting synthetic DMARDs (Tofa Bari) in Japanese patients with RA by NinJa 2019 cohort. [Method and Results] The rate of dose increase of 722 RA patients medicated TCZ by subcutaneous injection is 8.0%, the rate of dose reduction is 16.2%. The rate of dose increase of 560 RA patients medicated TCZ by intravenous injection is 6.1%, the rate of dose reduction is 32.9%. The rate of dose reduction of 896 RA patients medicated ETN by subcutaneous injection is 42.9%. The rate of dose reduction of 387 RA patients medicated ABT by subcutaneous injection is 9.6%. The rate of dose increase of 513 RA patients medicated ABT by intravenous injection is 2.1%, the rate of dose reduction is 24.8%. The rate of dose increase of 454 RA patients medicated GLM by subcutaneous injection is 19.4%, the rate of dose reduction is 15.9%. The rate of dose reduction of 355 RA patients medicated Tofacitinib is 32.1% and 286

RA patients medicated Baricitinib is 31.8% [Conclusion] 3 bDMARDs, TCZ, ETN, ABT were widely used recently in NinJa2019 were selected the dose reduction. By the way, IFX and GLM were selected the dose increase.

W19-1

Impact of COVID-19 epidemic emergency declarations and stay home on RA patients

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Conflict of interest: None

[Objective] We investigated the effects of stay home in April-May 2020 due to the spread of COVID-19 on RA patients. [Methods] Disease activity score, laboratory test values, pain, physical function, body weight, and RA treatments were compared of January-March and June-August 2020 in 45 RA outpatients. [Results] SDAI were 5.1±5.4/4.8±4.8 (P=0.56), ESR were 28.0±23.5/26.8±26.5 mm/h (P=0.58), CRP were 0.6±1.0/0.51±0.15 mg/dl (P=0.14), RF were 234.4±739/337±1330 IU/ml (P=0.27), MMP-3 were 79.7±68.2/100.2±134.5 ng/ml (P=0.15), Alb were 4.0±0.3/4.0±0.4 g/dl (P=0.81), Hb were 12.3±2.8/12.5±2.0 g/dl (P=0.60), eGFR were 72.5±23.8/66.7±22.9 ml/min (P=0.00024), body weight were 53.7±11.3/53.7±12.1 kg (P=0.94), pain VAS were 24.3±24.3/25.7±27.0/100 mm (P=0.57), HAQ-DI were 0.9±1.1/0.9±1.1 (P=0.85) before/after the emergency declaration period. There were two cases (4%) who changed treatment according to medical condition, and one case (2%) whose condition worsens after discontinuing treatment at her own discretion. Weight gain or loss of 3 kg or more was observed in 4 cases (9%). [Conclusions] As a group, the medical condition and treatment did not change before and after the stay home period. However, careful support was required for the cases of condition worsening of or weight changes.

W19-2

Clinical features of outpatient consultations for RA patients during 2020 COVID-19 epidemic period-Ratio of cancellation and take less drug judging by one's ownself-

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Conflict of interest: None

[Objective] We investigated the outpatient consultation status of RA patients during 2020 COVID-19 epidemic period, especially the rate of cancellation of consultation and take less therapeutic drug judging by one's ownself. [Methods] Among RA patients who had made outpatient appointments before COVID-19 epidemic period with our department and rheumatism specialized clinic from April 6 to July 31, 2020, we investigated the rate of patients who canceled outpatient visits to avoid COVID-19 infection and the patients who had reduced the dose or stopped taking their therapeutic drugs judging by one's ownself. We also invested the status of consultations for other diseases. [Results] A total of 234 RA patients (RA group) (32 males, 202 females) and 548 patients with other diseases (non-RA group) (204 males, 344 females), 26 patients (11.1%) in RA group and 93 patients (17.0%) in non-RA group canceled their appointments other diseases even at once. In the RA group, 54 patients (23.1%) had their own doses or withdrawn from oral medications or Bio products. Two patients (0.9%) withdrew all oral medications and Bio, and 72 patients (30.1%) lost their dose. Of these, 9 (12.1%) had worse RA status. [Conclusions] It is necessary to grasp accurate information and provide advice.

W19-3

Survey of rheumatoid arthritis patients with severe renal insufficiency using MiRAi database

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Conflict of interest: None

Purpose: To elucidate the actual condition of treatment for RA patients with severe renal insufficiency in our hospital. **Methods:** Using the MiRAi database, we extracted the information of RA patients who had eGFR <30 for at least 3 months and could be observed for at least 6 months and examined the following 4 items, 1) survival rate, 2) changes over time in disease activity and eGFR, 3) dialysis induction rate, 4) continuation rate and reasons for discontinuation of Bio/ JAKi. **Results:** There were 46 patients including 2 patients with hemodialysis. The patient data were as follows; males/females: 14/32, Age: 72 [69, 78] years, disease duration: 14 [5.5, 32] years, RF/ACPA positive rate: 89/81%, SDAI: 12 [6.9, 17], mHAQ: 0.38 [0, 1.1], PSL/MTX/Bio or JAKi usage rate: 70/13/35%, and eGFR: 27 [25, 29]. 1) The 10-year survival rate is 58%. 2) There is no significant difference in disease activity and eGFR between the starting date and 3 years. 3) The dialysis introduction rate is 16%. 4) The 3-year continuation rate was 47% for non-TNFi and 30% for TNFi (p=0.09). Reasons for discontinuation were inefficacy (23%), infection (6.7%), and death (1.7%). **Conclusion:** There are few reports on the actual condition of treatment for RA patients with severe renal insufficiency, so we report here as valuable data.

W19-4

Effectiveness and safety of treat-to-target strategy for MTX-naïve late-elderly rheumatoid arthritis: Comparison of late-elderly and early-elderly in a prospective CRANE cohort

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Conflict of interest: None

[Objective] To clarify the effectiveness and safety of treat-to-target (T2T) for MTX-naïve late-elderly patients with RA. [Methods] The patients received T2T targeting low disease activity (LDA). SDAI remission, HAQ-DI, and serious adverse events (SAEs) were evaluated in patients aged ≧75 (late-elderly, n=98) and <75 years (early-elderly, n=99). [Results] Late-elderly (mean age 80.0±3.9) had higher HAQ-DI than early-elderly, but symptom duration, SDAI, and ACPA positivity were similar between the two groups. In the late-elderly, 70.4% started MTX and 34.1% received biologics at 52 weeks. At 156 weeks, 70.0% of the late-elderly received MTX and 37.1% biologics, and these were almost the same as early-elderly, while PSL use was quite different, and 24.6% of the late-elderly received PSL and 7.1% of the early-elderly. At week 52, 104, and 156, 27.6%, 28.6%, and 32.7% of the late-elderly achieved SDAI remission respectively, and 51.0%, 48.0%, and 37.8% achieved normal physical function. These were significantly lower than in early-elderly. The cumulative incidence rate of serious AEs was significantly higher in the late-elderly. [Conclusions] The late-elderly patients were difficult-to-treat RA in terms of poorer treatment response to T2T strategy by MTX and biologics and more serious AEs.

W19-5

How rapid should methotrexate dose be optimized in treatment-naïve rheumatoid arthritis?

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Conflict of interest: None

[Objective] To determine the relationship between duration for MTX

dose optimization and treatment outcome. [Methods] Patients with treatment-naïve RA were included, and remission at week 48 and adverse events were analyzed. [Results] A total of 65 patients were included. In patients with MTX monotherapy, the duration for optimization was significantly shorter in patients with remission achievement than those not in remission at week 48. Difference was not significant between patients who achived remission or not when combination therapy including MTX was introduced. Ten patients experienced adverse events during optimization, resulted in longer duration for dose optimization. [Coclusions] Rapid dose optimization resulted in better outcome in patients treated with MTX monotherapy, whereas adverse events should be paid attention.

W19-6

Observational study of changes in bone mineral density and bone erosion after denosumab discontinuation in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To investigate the changes in BMD and bone erosion after denosumab (dmab) discontinuation in RA patients without osteoporosis. [Methods] The patients who participated in the Phase 3 trial DESIRABLE were eligible for this study. The main inclusion criterion was completion of DESIRABLE. The main exclusion criteria were diagnosis of osteoporosis and administration of dmab or bisphosphonates after DESIRABLE. DXA and X-ray scans of the hands and feet were performed 30 months after the last dose of dmab, and changes of lumbar spine (LS) BMD and bone erosion score were evaluated. [Results] LS BMD after dmab discontinuation was similar to that at the start of dmab treatment (avg. % change was 0.10% (95%CI, -1.78-1.97)). Bone erosion tended to progress after dmab discontinuation compared with on-treatment although there was no statistical significance (p=0.0666). And the progression was significantly less in patients whose disease activity was remission than those not in remission (p=0.0195). [Conclusions] In RA patients without osteoporosis, dmab discontinuation is an option considering patient characteristics such as disease activity and fracture risk. Regular BMD and X-ray evaluation are necessary since the BMD decrease and bone erosion may progress after dmab discontinuation.

W20-1

Childbirth status and treatment of RA patients who desired for childbearing using the 2018 Ninja Database

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Conflict of interest: None

[Purpose] The purpose of this study was to assess the current status of pregnancy-related problems in RA patients. [Methods] Using the 2018 NinJa database, we assessed the number of pregnancies, the percentage of patients who desired for childbearing, and the current status of treatment for patients who desired for childbearing. [Results] Enrollment in NinJa2018 was 15440. Of the 1533 women under 50 years of age, 902 responded to pregnancy-related questions. There were 15 births and 2 miscarriages in one year. The expected birth rate was 73.1% [95% CI: 36.1-110.0]. Of the 743 respondents to the question of expected births, 12.8% wanted to have a baby. In the patients who desired for childbearing group, 32.6% of the patients were treated with steroids, 86.3% with anti-rheumatic drugs, 24.2% with methotrexate (MTX), and 45.3% with biologics, compared to 25.5% with steroids, 95.7% with anti-rheumatic drugs, 73.3% with MTX, and 34.0% with biologics in the patients who did NOT desired for childbearing group. [Conclusion] the number of pregnancies, the percentage of patients who desired for childbearing, and the current status of treatment for patients who desired for childbearing were identified.

W20-2

Impact of concomitant chronic kidney disease on occurrence of unfavorable clinical events in patients with rheumatoid arthritis -results from the IORRA cohort-

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Conflict of interest: None

[Objective] To examine the association between concomitant CKD and the occurrence of clinical events in RA patients. [Methods] RA patients in the IORRA cohort who had data for both eGFR and proteinuria were extracted. CKD was diagnosed by both 24th and 25th IORRA cohort data. They were categorized into non-CKD, CKD with normal eGFR, mild CKD, moderate CKD and severe CKD. To assess the association between concomitant CKD and the occurrence of clinical events (death, hospitalized infection and major adverse cardiovascular events) during a five-year observation, we used cox regression model to measure the HR after adjusting for sex, age, disease duration, obesity, smoking, DAS28-ESR, J-HAQ-DI and RF and/or ACPA positivity. [Results] CKD stages of 5,103 patients were as follows: non-CKD, n=4,417; CKD with normal eGFR, n=26; mild CKD, n=462; moderate CKD, n=164 and severe CKD, n=34. During 20,977 PYs, concomitant CKD was associated with hospitalized infection (aHR, 1.47, 95%CI [1.12-2.07]; p=0.03). After stratification by the CKD stage, the moderate to severe group (1.79 [1.04-3.06]; p=0.03) was also associated with hospitalized infection. [Conclusions] Our present study revealed that concomitant CKD was a risk factor for hospitalized infection in RA patients.

W20-3

Medical costs for patients with rheumatoid arthritis with or without concomitant diabetes mellitus

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Conflict of interest: Yes

[Objectives] To evaluate medical costs and resource use in rheumatoid arthritis (RA) patients with and without diabetes mellitus (DM). [Methods] We used the JMDC claims database. Patients with ICD-10 codes for RA who started csDMARDs after 6 months without csDMARDs from 2012 to 2017, were categorized as DM or non-DM groups based on ICD-10 codes and drugs for DM throughout the study period. To adjust baseline features, they were matched by sex, age, Charlson Comorbidity Index (CCI), months from the first RA codes, and medications. The primary endpoints were mean drug, treatment, and material costs per patient in the 12-month follow-up period. [Results] There were 128 patients who were observable for 12 months in each group. The medians of age and CCI were 59 years and 2.0 in both groups. Drug costs were significantly higher in the

DM group than in the non-DM group (DM/ non-DM: 246,405 JPY/ 127,249 JPY, $p < 0.05$). Biological DMARDs were more frequently used in the DM group (DM/ non-DM: 14.1%/ 5.5%). Treatment costs were also significantly higher in the DM group (304,284 JPY/ 259,142 JPY, $p < 0.05$), while material costs were not (14,076 JPY/ 25,516 JPY). [Conclusions] Medical costs were higher in the DM group, probably due to more frequent use of biological DMARDs.

W20-4

Clinical study of the administration of biologics (Bio) and Janus kinase inhibitor (JAKi) in rheumatoid arthritis (RA) patients with interstitial pneumonia (IP)

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Conflict of interest: None

[Objective] To investigate the clinical course of RA patients with IP treated with Bio/JAKi. [Methods] From 2011 to 2018, 72 RA patients received Bio/JAKi (33 TNF inhibitor [TNFi], 17 IL-6 inhibitor [IL6i], 18 CTLA-4Ig, 4 JAKi); of those, 16 (22.2%) had IP (excluding organizing pneumoniaOP) (5 TNFi, 6 IL6i, 5 CTLA-4Ig, 0 JAKi). [Results] Mortality (25.0% vs. 3.6%, $p = 0.02$) was significantly higher in patients with IP (25.0% vs 3.6%, $p=0.02$) than in patients without IP. Before the administration of Bio/JAKi, prednisolone use (100% vs 73%) and dosage (9.0 vs 4.9 mg/day) and DAS-28 ESR (5.0 vs 4.2) were significantly higher in patients with IP than those without IP, respectively. There was no significant difference in methotrexate use (75% vs 82%, respectively). Infectious pneumonia was noted in 20% and 40% of patients with IP treated with TNFi, and 40% of patients with IP treated with CTLA-4Ig, respectively, but not in patients those with IP who received IL-6i. Higher mortality rate was recorded in patients with IP who received TNFi (40% vs 7.1%, respectively, $p=0.09$) or CTLA-4Ig (40% vs 0%, respectively, $p=0.11$). T, but there were no deaths in the patients receiving IL-6i with or without IP. [Conclusions] In RA patients with IP, use of IL-6i is relatively safe.

W20-5

DMARDs therapy after the diagnosis of cancers in patients with RA

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Conflict of interest: None

[Background] There is a scarcity of reports about RA treatment after the diagnosis of cancers. A correlation between the severity of cancer and RA therapy is not well known. [Methods] RA patients diagnosed with cancer between April 2003 and November 2019 were included in this study. We analyzed a correlation between cancer stage /chemotherapy initiation and DMARDs continue. RA patients diagnosed with cancer separated into 2 groups. Continuing or Discontinuation group (continue or discontinue the DMARDs used before cancer diagnosis) [Results] 140 RA patients diagnosed with cancer. mean age: 68.3 years, female: 61.7%. RA treatment (MTX n=91, bDMARDs n=38, JAK inhibitor n=2). Cancer type (digestive system n=39, respiratory n=29, hematology n=28, genital organ n=18, urinary n=11, endocrine system n=9, Others n=6). Cancer stage (stage 0 n=4, stage 1 n=30, stage 2 n=24, stage 3 n=31, stage 4 n=25). Cancer treatment (chemotherapy n=73, surgery n=86, radiation n=21). On multivariate analysis, cancer stage 3 and 4 groups demonstrated association with the discontinuation of DMARDs used before cancer diagnosis, compared with cancer stage 0, 1 and 2 groups (OR: 3.58, 95% CI: 1.2-11.1). [Conclusions] After cancer diagnosis rheumatologists treated RA patients considering cancer treatment and stage.

W21-1

Medical costs and use of medical resources in rheumatoid arthritis patients treated with or without corticosteroids

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Conflict of interest: Yes

[Objectives] To evaluate medical costs and resource use in rheumatoid arthritis (RA) patients treated with and without corticosteroids (CSs). [Methods] Using the JMDC claims database, patients with ICD-10 codes for RA were enrolled at the first antirheumatic drugs (csDMARDs) prescription date (index date) from 2012 to 2017 after 6-months without csDMARDs. Patients treated with CSs (CS group) in 12 months after the index date (follow-up period) were compared with those without them (non-CS group). The primary endpoints were mean drug, treatment, and material costs per patient in the 12-month follow-up period. The incidence of hospitalization and RA-related surgery after that period were exploratory evaluated. [Results] A total of 1670 and 1487 patients who were observable for 12 months were extracted as the CS (median age: 51 years) and non-CS group (50 years), respectively. Costs and the proportion of resource use were significantly higher in the CS group (CS/ non-CS: drug: 295,875 JPY/ 197,611 JPY; treatment: 248,314 JPY/ 195,329 JPY; material: 11,768 JPY/ 8,126 JPY, all $p < 0.05$). The incidences of hospitalization and RA-related surgery were higher in the CS group. [Conclusions] RA patients with CSs in the first year of DMARDs have higher medical costs than those without CSs.

W21-2

Average glucocorticoid dose of only 1 mg/day was risk factor for clinical fractures - Nine-year findings of the TOMORROW study -

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Conflict of interest: Yes

Objective: The present study aimed to determine the effect of glucocorticoid (GC) dosage on the incidence of clinical fractures in the rheumatoid arthritis (RA) patients treated with GC. **Methods:** We evaluated bone mineral density, medication and the incidence of fracture during nine years in RA patients who participantthe TOMORROW study (UMIN000003876), which is a 10-years prospective cohort. Data on clinical fracture was self-reported on the questionnaires. In this analysis, the data of RA patients treated with GC at least once during nine-year period were evaluated. We analyzed the average dose of GC until the incidence of the clinical fractures. **Results:** During 9 years, in 67 RA patients treated with GC, the incidence of clinical fracture was 0.046/person-year. Cox proportional hazard analysis revealed that average GC dose of more than only 1 mg/day was a significant risk factor for the incidence of clinical fracture (HR: 2.80; $p=0.03$). **Conclusions:** In RA patients treated with GC, average GC dose of only 1 mg/day significantly increased the risk for the incidence of clinical fractures.

W21-3

Causes for methotrexate withdrawal in the treatment of rheumatoid arthritis

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Conflict of interest: None

[Objective] The causes for Methotrexate (MTX) withdrawal were examined to clarify the problems in MTX treatment in rheumatoid arthritis (RA). [Methods] We extracted cases of RA outpatients of our department who discontinued MTX, and investigated the causes for discontinuing MTX. [Results] There were 771 RA patients with MTX withdrawal. The most common causes for discontinuing MTX was 147 cases (19.1%) of infection. Respiratory disease was 74 cases (9.6%). Liver disorder 58 cases, gastrointestinal disorder 51 cases, hematological disorder 46, mucocutaneous disorder 39 cases, renal disorder 28 cases, heart failure / pleural effusion 20 cases, and 14 with fever. One hundred-ten cases (14.3%) of malignancy, 42 of which were lymphoproliferative disorders. Poor medication compliance 12 cases. There were 45 cases with refractory to MTX, 36 cases who changed to biologics, and 42 cases with remission. There were 35 cases of self-interruption and 39 cases of childbearing desire. Twenty-three cases were discontinued due to old age. The death was 22 cases, 15 of which were malignancy. [Conclusions] There were various causes for MTX withdrawal in RA treatment. Next to infection, MTX are often discontinued in malignancy, and the relationship between MTX and malignancy needs further investigation.

W21-4

Predictive value of NUDT15 codon 139 as a pharmacogenetic marker for thiopurine-induced liver dysfunction in patients with rheumatic deseases

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Conflict of interest: None

[Objective] Azathiopurine (AZA) has been widely used for rheumatic diseases and inflammatory bowel disease. In thes study, we investigated the association between the genotype of NUDT15 and AZA-related liver dysfunction (LD). [Methods] Twenty-nine patients with rheumatic diseases whom perfomed genotyping of NUDT15 were consecutively registered. Clinical and epidemiological information was collected from medical records. [Results] Among 29 enrolled patients (23 patients in Arg/Arg and 6 patients in Arg/Cys), seven patients (6 patients in Arg/Arg and 1 patient in Arg/Cys) developed LD (p=0.393). The duration from the start of AZA to the occurrence of LD was 61.8±36.9 (mean±SD) days (Arg/Arg vs Arg/Cys: 54.6±30.0 days vs 119 days, respectively). The underlying diseases of the patients were as follows: 5 ANCA-associated vasculitis (all patients with Arg/Arg), 2 IgG4-related disease (both Arg/Arg), 1 dermatomyositis (1 patient with Arg/Arg) and 1 relapsing polychondritis (1 patient with Arg/Cys). Doses of AZA at the diagnosis of LD was 52.8±36.2 (mean±SD) mg per day. In addition, leukocytopenia was observed in 2 patients and gastrointestinal symptoms in 2 patients. [Conclusions] No significant association was identified between NUDT15 and LD in patients treated with AZA.

W21-5

Multicenter Adherence Survey of Rheumatoid Arthritis Patients-Comparison between Facilities-

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Conflict of interest: None

[Objective] The effect of treatment of rheumatoid arthritis is closely related to medication adherence (AD). MAS was researched by using MMAS with several facilities. [Methods] Using MMAS4; MAS, the score was evaluated on a three-levels of "Disagree, Neither agree nor disagree, Agree". We also investigated the social support, patient background, complications, pathophysiology, history of side effects, adjustment of residual drug, AD evaluation by pharmacists, and utilization of medication notebooks. The relationship between patient evaluation of MMAS4 and other endpoints and pharmacists evaluation was examined and compared between facilities. [Results] A total of 194 patients were analyzed. Weak correlation between scored patient MMAS and pharmacist evaluation ($r=0.337$, $P<0.001$) and weak negative correlation between MMAS and patient age ($r=24.2$, $P<0.001$) was observed, with similar results among facilities. Age and morbidity did not correlate with other measures. [Conclusions] The AD evaluation of pharmacists linked to the evaluation of patients, and each facility was similar. However, the AD evaluation is better for the elderly. The aging of RA patients is not necessarily a factor that leads to a decline in AD.

W22-1

Evaluation of frailty in patients just prior to knee arthroplasty

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Conflict of interest: None

[Objective] Frailty is a concept that encompasses physical, psychopsychological, and social vulnerability due to a decline in physiological reserve in old age. In this study, we assessed the degree of frailty in patients who had just undergone knee arthroplasty (TKA). [Methods] All patients scheduled to undergo TKA at our hospital after July 2020 were assessed for basic attributes, clinical assessment (Knee Society Score: KSS), whole-body mode DXA, knee muscle strength by dynamometer and Japanese Cardiovascular Health Study criteria were evaluated. [Results] Thirty patients (27 women, mean age 74 years) were include. The distribution in frailty was 14.3% no, 57.1% pre-frailty and 28.6% frailty. A multivariate analysis was performed with frail as the objective variable, and the dependent variables were age, walking pain VAS, KSS, and quadriceps muscle strength, but no significant associations were found (p=0.29, 0.85, 0.45, and 0.16). In the analysis of each component of frailty, there was also no association except for gait speed and age (p=0.03). [Conclusions] Patients just prior to arthroplasty had a lower frailty frequency and was not associated with knee related functional assessments. Frailty appeared an inappropriate assessment of motor vulnerability due to knee joint dysfunction.

W22-2

Analysis of knee radiograph of rheumatoid arthritis patients treated with biological agents by KOACAD system

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Conflict of interest: None

[Objective] We aimed to investigate the radiographic feature of the knee joints in patients with rheumatoid arthritis (RA) treated with biological agents by KOACAD (knee OA computer-aided diagnosis) system. [Methods] We investigated 60 knees of 51 RA patients who underwent total knee arthroplasty at the University of Tokyo Hospital (63±10 age, all female). We measured minimum joint space width (mJSW), joint space area (JSA), osteophyte area (OPA), and femur-tibial angle (FTA) by KOACAD system and compared these items between the groups with/without biological treatments (n=30/30). [Results] There were statistical difference in medial mJSW, medial OPA; medial mJSW (3.5±2.1 mm, 2.2±2.3 mm, 0.026), lateral mJSW (1.3±1.8 mm, 1.1±1.8 mm, 0.638), medial JSA (37±35 mm^2, 23±28 mm^2, 0.09), lateral JSA (49±48 mm^2, 46±51 mm^2, 0.71), medial OPA (7.1±16 mm^2, 18±22 mm^2, 0.036), lateral OPA (1.1±3.0

mm^2, 4.2±13 mm^2, 0.19), FTA (174±8.1°, 178±14°, 0.30). Multiple logistic regression analysis adjusted with age, disease duration, BMI revealed a significant statistical difference only in medial mJSW. [Conclusions] We revealed the feature of knee radiograph of RA patient treated with biological agents by novel KOACAD system, which was characterized by an increase of mJSW.

W22-3

The patients' background of orhtopaedic surgeries for rheumatoid arthritis, An retrospective analysis of 1569 cases

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Conflict of interest: None

[Objective] To investigate the recent trends of patients' backgrounds who underwent the orthopaedic surgery for rheumatoid arthritis. [Methods] We reviewed the records of 1569 patients with RA who underwent orthopedic surgeries between 2004 and 2019 in our institution. These patients' data, such as age, disease duration, medication, type of surgeries, and preoperative serum CRP level, were collected. [Results] The mean age and disease duration of RA showed an increasing trend during the study period. Although the annual number of surgeries have not changed, the proportion of cases who performed TJR decreased dramatically (59.6% in 2011, 29.5% in 2019), and the surgeries for hand and foot increased significantly ($p<0.001$). The annual mean preoperative CRP level also decreased from 1.88±0.20 to 0.49±0.81. Compared to CRP positive group (n=1,113), the patients in CRP negative group (n=446) showed significantly younger age, shorter disease duration, lower late of GC use, and a higher rate of b/tsDAMRD use. The proportion of patients who underwent TJR was significantly higher in CRP positive group ($p<0.001$). [Conclusions] Along with the increasing use of b/tsDMARD, preoperative disease control, and the type of demanded surgeries have dramatically changed.

W22-4

Effects of Total Elbow Arthroplasty on disease activity of Rheumatoid Arthritis-Comparison between Use and Unuse of a Biological Agent-

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Conflict of interest: None

[Objective] We investigated the effect of biologic agent (BIO) use on changes in disease activity in patients with rheumatoid arthritis (RA) who underwent total elbow arthroplasty (TEA). [Methods] The study comprised 22 elbows of 20 people who underwent TEA for RA-associated elbow joint disorders. The mean age was 69.4±5.9 years, the mean duration of disease was 23.9±10.7 years, and the Larsen grade of the elbow was grade 3 in 1, grade 4 in 13, and grade 5 in 8 elbows. DAS28-CRP, MMP3, and elbow joint range of motion (ROM) were assessed and compared before and 1 year after surgery. Patients were divided into two groups according to the use of BIO; BIO group consisted of 11 elbows, whereas non-BIO group consisted of 11 elbows. DAS28-CRP improvement rate were compared between the BIO and non-BIO groups. [Results] DAS28-CRP was 3.65±0.95 before surgery and 2.92±0.91 after surgery ($p=0.01$). MMP3 was 182±137 ng/mL before surgery and 123 ± 84 ng/mL after surgery ($p=0.09$). ROM was 77±20 degrees before surgery and 105±23 degrees after surgery ($p<0.01$). The improvement rate of DAS28-CRP was 0.2±0.3 in BIO group and 0.2±0.2 in non-BIO group ($p=0.88$). [Conclusions] DAS28-CRP and ROM improved significantly after TEA. TEA reduced RA disease activity independently of BIO-use.

W22-5

Selection of optimal biologics using synovial immunostaining

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Conflict of interest: None

[Objective] Selection of optimal biologics using synovial immunostaining [Methods] There were 9 cases of shoulder joint surgery, 2 cases of knee joint surgery, 1 case of hip joint surgery, and 1 case of foot surgery. In the immunostaining of intraoperative synovial pathology, CD3, 20 predominance was defined as Lymphyoid type, and CD68 predominance was defined as Myeloid type. CD3 predominantly selected T cell-selective co-stimulation regulators, CD20 preferentially selected anti-IL-6 preparations, and CD68 preferentially selected TNF inhibitors according to their IH scores. [Results] Lymphyoid type was 6 cases, Myeloid type was 6 cases, and 1 case was mixed type. At the final postoperative observation, CRP averaged 0.35 (0.05-2.03) and DAS28 (CRP) averaged 2.49 (1.89-3.07), with 7 patients in remission and 6 patients with low disease activity. There were 2 cases of switching from TNF inhibitors to T cell-selective co-stimulation regulators and 1 case of switching to anti-IL-6 preparations. Two cases of Lymphyoid type were switched to JAK inhibitors due to diminished efficacy. [Conclusions] With more types of biologics and more options, in cases leading to surgery, examining the phenotype in synovial pathology seemed to lead to the prediction of effective biologics.

W22-6

Postoperative infection of joint / fracture surgery in patients with rheumatoid arthritis during administration of biologics and JAK inhibitors

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Conflict of interest: None

[Objective] The purpose of this study is to clarify the occurrence of postoperative infections. [Methods] The subjects are patients with RA who underwent joint surgery or open fracture surgery for 5 years and who are receiving biologics or JAK inhibitors. Basically, there was a drug suspension during the perioperative period. [Results] Of the 139 cases, TKA 30 cases, THA 17 cases, TEA 16 cases, TSA 6 cases, total MP joint arthroplasty 7 cases, TAA 1 case, finger / wrist joint surgery 19 cases, toe / ankle joint surgery 23 cases, fracture surgery 4 cases, and 16 other cases. The drugs were Etanercept 38 cases, Abatacept 30 cases, Tocilizumab 29 cases, Golimumab 15 cases, Certolizumab pegol 11 cases, Infliximab 5 cases, Adalimumab 4 cases, Sirukumab and Upadacitinib 2 cases each, and Infliximab BS, Etanercept BS, Tofacitinib 1 case each. Early infection was in only one case of TEA with Adalimumab who did not adhere to preoperative drug suspension. Late-onset infection was in two case, one was TKA and THA at the same time with Tocilizumab, and the other was TKA with Etanercept. [Conclusions] Joint surgery in RA can be performed safely during administration of biologics and JAK inhibitors with a drug suspension, but care should always be taken in the occurrence of late-onset infections.

W23-1

Efficacy of baricitinib in patients with moderate-to-severe rheumatoid arthritis with 3 years of treatment: results from a long-term study including Japanese subpopulation

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Conflict of interest: Yes

[Objective] To evaluate the long-term efficacy of once-daily Bari 4 mg. [Methods] Post hoc analyses of data from two Ph3 studies, RA-BEGIN (DMARD-naïve) and RA-BEAM (MTX-IR) for 52Wks, and one long-term extension (LTE) study for an additional 96Wks were conducted. [Results] At Wk24 in RA-BEGIN (N=584 including 104 Japanese), 62% of pts treated with Bari 4 mg or Bari 4 mg+MTX achieved SDAI LDA compared to 40% of the MTX group; the response rates were maintained

over Wk148. At Wk24 in RA-BEAM (N=1305 including 249 Japanese), 52% of pts with Bari 4 mg (+MTX) and 50% of pts with Adalimumab (+MTX) achieved SDAI LDA compared to 26% of the PBO (+MTX) group; the response rates were maintained over Wk148, even after pts switched from Adalimumab to Bari at Wk52. Similar trends were seen in Japanese subgroups. HAQ-DI showed similar efficacy patterns as SDAI did. The discontinuation rate from RA-BEGIN and RA-BEAM was 19.5% and 14.2%, respectively. In the LTE, the discontinuation rate was 13.7% for pts originating from RA-BEGIN; 12.6% for pts from RA-BEAM. [Conclusions] Long-term treatment with Bari 4 mg demonstrated the maintenance of clinically-relevant outcomes for up to 3 years. Discontinuation rates during the LTE were low and the risk-benefit of Bari long-term treatment was considered favorable.

W23-2

Safety of Baricitinib in Japanese Patients with Rheumatoid Arthritis (RA): the 2020 Interim Report from All-case Post Marketing Surveillance in Clinical Practice

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Conflict of interest: Yes

[Objective] To evaluate baricitinib (Bari) safety in RA patients (pt) in clinical practice. [Methods] An all-case post marketing surveillance (PMS) of Bari, that started in Sep 2017, collects safety and effectiveness for the first 24 wks of treatment and continues to collect serious adverse events (SAEs) for 3 yrs. We report patient (pt) baseline demographics and adverse events (AEs) up to 24 wks for pts whose case report files for 24-wk data were completed as of Jun 2020. [Results] Data from 3445 pts were analyzed (females=80%, mean age=64yr, mean RA duration 12yr). Bari dose regimen was as follows: 4 mg, 60%, 2 mg, 27%, 4 mg→2 mg, 5%, 2 mg→4 mg, 5%, and others, 2%. Concomitant use of MTX and glucocorticoid was 65% and 48%, respectively. 74% continued treatment for 24 wks. AE and SAE were recognized in 887 (26%) and 122 pts (4%), respectively. 6 pts died of pneumonia, aspiration pneumonia, bacterial pneumonia, cerebral infarction/ILD/aspiration pneumonia, adenocarcinoma, and colorectal cancer. Major AEs were as follows: herpes zoster=3%, liver dysfunction=3%, serious infection=1%, anemia=1%, hyperlipidemia=1%, malignancy=0.3%, interstitial pneumonia=0.2%, MACE=0.1%, and VTE=0.1%. [Conclusions] Data do not show new safety concerns, and encourage guideline-compliant use of Bari.

W23-3

Incidence rate and characteristics of herpes zoster in patients including Japanese with moderate to severe rheumatoid arthritis: an update from baricitinib clinical studies

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Conflict of interest: Yes

[Objective] To evaluate herpes zoster (HZ) in moderately to severely active RA pts including Japanese (JP) treated with baricitinib (Bari) [Methods] Incidence rate per 100 pt-years (IR) of HZ was calculated for Bari-treated RA pts pooled from Ph1-3 trials and long-term extension study. Risk factors for HZ were assessed by Cox proportional hazard models. [Results] HZ was reported in 323 of 3770 pts exposed to Bari as of Feb 2018 (IR=3.3). Of 323, 4% had a history of HZ, 3% had prior live HZ vaccination, 79% and 52% were on concomitant MTX and corticosteroids (CS), respectively. The median time to first HZ was 538 days. While the percentage of pts with HZ increased over time, the IR of HZ did not increase over time. Of 323, 8% were multidermatomal, 2% had involvement of the ophthalmic area, none had visceral involvement, and 3% had recurrent HZ during the study. A higher risk of HZ was associated with older age and Asia region but not with use of CS, history of HZ, or baseline lymphocytes. HZ rate for Bari in JP (81/514 pts, IR=6.8) appeared higher than overall pts. [Conclusions] IR of HZ in Bari-treated RA pts did not increase over time and the majority of HZ were monodermatomal and uncomplicated. HZ rate for Bari appeared higher in JP.

W23-4

Serious Infection Events and Associated Risk Factors in Patients including Japanese with Moderate to Severe Rheumatoid Arthritis Treated with Baricitinib, from an Update of Baricitinib Clinical Trial

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Conflict of interest: Yes

[Objective] To evaluate serious infection events (SIEs) in patients (pts) with moderately to severely active rheumatoid arthritis (RA) including Japanese (JP) treated with baricitinib (Bari). [Methods] Incidence rates (IRs, per 100 patient-years of exposure) were calculated for Bari-treated RA pts pooled from Ph1-3 trials and long-term extension study. Risk factors (RFs) for SIE were assessed using multivariate Cox models. [Results] 3770 pts (514 JP) were exposed to Bari as of Feb 2018. SIEs were reported in 283 pts (IR=2.7). Common SIEs (IR≧0.2) were pneumonia (0.5), herpes zoster (HZ) (0.3), and urinary tract infection (0.2). 11 pts had infections leading to death. In JP, SIEs were reported in 36 pts (2.8). Common SIEs (IR≧0.2) were HZ (1.2), pneumonia (0.6), and pneumocystis jirovecii pneumonia (PCP) (0.2). No pts had infections leading to death. As with other JAK inhibitors, HZ was more commonly observed in JP. Older age, JP, Asia region excluding JP, time from symptom onset of RA, HAQ-DI prior to dose of Bari, and corticosteroid use were observed as RFs for SIE. [Conclusions] While overall SIE IR was similar between JP and overall pts, HZ and PCP IR were higher in JP. Older age and Asia region were identified as two highest RFs for SIE from the multivariate analysis using COX model.

W23-5

Baricitinib is more effective for rheumatoid arthritis patients with ILD

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Conflict of interest: Yes

[Objective] To investigate the background factors that contribute to the response to treatment in 72 patients with rheumatoid arthritis (RA) who have been treated with baricitinib for at least 6 months. [Methods] Multiple regression analysis was performed to determine the factors contributing to the rate of decline in SDAI in patients who were started on baricitinib. Age, sex, disease duration, HAQ, TJC, SJC, gVAS, eVAS, CRP, ESR, SDAI, MTX dose, PSL dose, bio or JAKi naive (naive), ACPA titer, RF titer, aSS-A, with or without interstitial lung disease (ILD) was

used as an explanatory variable. A stepwise method was used to select explanatory variables in consideration of multicollinearity. [Results] The explanatory variables selected for the minimum AICc. Multiple regression analysis revealed ILD (n=22, p=0.02) and naïve (n=12, p<0.01) were factors for SDAI reduction. SDAI reduction rate in naïve/experience (baseline SDAI: 20.5/18. 6, p=0.60) was 94%/64% (p<0.01), respectively, and 80%/64% (p=0.03) for ILD/no ILD (baseline SDAI 20.0/18.5, p=0.62), respectively. All ILDs did not get worse. [Conclusions] Baricitinib was more effective in RA patients with ILD. In addition, Baricitinib was more effective in patients with Bio or JAKi naïve.

W23-6

Successful treatment with Baricitinib for 3 cases of refractory primary biliary cholangitis complicated with rheumatoid arthritis

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Conflict of interest: None

[Background] Primary biliary cholangitis (PBC) is a chronic progressive cholestatic liver disease of unknown etiology. Although autoimmune mechanisms are thought to be responsible for the pathogenesis, detail remains unclear and treatment strategies are limited. Here we report three cases of successful treatment with Baricitinib (BAR) for rheumatoid arthritis (RA) complicated by poorly controlled PBC. [Case 1] A 70-year-old man, who had been treated with ursodeoxycholic acid (UDCA) and bezafibrate for PBC and with various biologic agents for RA on account of high disease activity, improved ALP elevation and RA status after administration of BAR. [Case 2] A 58-year-old woman with persistently high ALP level in PBC treated with UDCA showed improvement in RA and rapid normalization of ALP level after the use of BAR. [Case 3] A 60-year-old woman, who took UDCA for PBC, had a poorly controlled ALP level. She developed seronegative RA and was treated with BAR, which improved her joint symptoms and rapidly reduced her ALP level to normal range. [Conclusions] We experienced three cases of PBC complicated with RA, successfully treated by use of BAR. This strategy might be effective for poorly controlled PBC complicated with RA. Additional investigations are needed for general clinical use.

W24-1

Upadacitinib Monotherapy in Methotrexate-Naïve Patients With Rheumatoid Arthritis: Results at 72 Weeks From SELECT-EARLY

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Conflict of interest: Yes

Objectives: To present the safety and effectiveness of upadacitinib (UPA) for MTX-naïve RA patients (pts) through 72 weeks (wks). Methods: SELECT-EARLY included 2 study periods: (1) a 48-wk double-blind, with pts randomized to UPA monotherapy 15 or 30 mg once daily or MTX; (2) a long-term extension (open-label treatment), up to 4 years. Results: Both UPA 15 mg and 30 mg as monotherapy was associated with statistically significant improvements in disease activity vs MTX monotherapy through 72 wks. The safety profiles of the UPA 15 and 30 mg groups were comparable for total treatment-emergent adverse events (TEAEs) and numerically higher than MTX. Serious TEAEs and TEAEs leading to discontinuation of study drug were comparable across all groups. Most AEs of special interest were comparable across MTX and UPA groups, with the exception of higher rates of herpes zoster, opportunistic infections, and elevated creatine phosphokinase among the UPA groups. Two, zero, and one pts with MTX monotherapy, UPA 15 mg, and UPA 30 mg experienced a venous thromboembolic event, respectively. There were 12 deaths (including 3 non-treatment-emergent). Conclusion: Through 72 wks, UPA monotherapy led to improvements in RA and showed the safety profile consistent with data reported through 48 wks.

W24-2

Upadacitinib as Monotherapy in Patients With Rheumatoid Arthritis and Prior Inadequate Response to Methotrexate: Results at 84 Weeks From the SELECT-MONOTHERAPY Study

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Conflict of interest: Yes

Background: Upadacitinib (UPA) demonstrated greater efficacy compared to continuing methotrexate (MTX) in patients (pts) with rheumatoid arthritis (RA) and prior inadequate response to MTX. Objectives: To describe the long-term safety and efficacy of UPA monotherapy in an ongoing long-term extension (LTE) of the SELECT-MONOTHERAPY. Methods: Pts on stable MTX were randomized to either continue MTX (cMTX) or switch to UPA 15 (UPA15) or 30 (UPA30) mg monotherapy for 14 weeks (wks). Then, pts could enter a blinded LTE and continue to receive UPA15 or UPA30. Results: Of 648 pts randomized, 598 (92%) completed 14 wks and entered the LTE on blinded UPA. The most frequently reported Treatment-emergent adverse events were urinary tract infection, creatine phosphokinase increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, bronchitis, herpes zoster, and alanine aminotransferase increase; the most common serious AE was pneumonia. Rates of serious infection and malignancy appeared comparable between doses. Pts who switched from cMTX to UPA15 or UPA30 demonstrated comparable efficacy responses to those initially randomized to UPA. Conclusion: Through long-term follow-up, the in long-term exposure to UPA15 or 30 as monotherapy was no new safety signals identified.

W24-3

Safety and efficacy outcomes by age following peficitinib (PEF) treatment of rheumatoid arthritis (RA): Pooled analysis from clinical studies

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Conflict of interest: Yes

[Objective] To analyze safety and efficacy outcomes by age in RA patients using pooled data from PEF studies. [Methods] Incidence rates (IR) of adverse events (AEs) and special interest AEs were calculated using two pooled datasets: Phase 3 (P3) studies (RAJ3-4) and P2/3 studies (RAJ1-4). Efficacy for RAJ3-4 included ACR20 response at week 12. Patients were categorized according to age: <50, ≧50-<65 and ≧65 years old. [Results] Pooled P3 studies included 1025 patients. For the age categories of 50, ≧50-<65 and ≧65 years old, 12-week AE incidence was 55.9% (38/68), 49.6% (65/131) and 64.3% (45/70) with PEF100 mg; 57.7% (45/78), 53.9% (69/128) and 64.3% (45/70) with PEF150 mg; and 46.3% (38/82), 52.6% (60/114) and 53.3% (40/75) with placebo. Pooled P2/3 studies included 1052 patients. IR per 100 patient-years by age category were 3.7, 6.4 and 11.2 for herpes zoster; 0.8, 2.6 and 4.7 for serious infections; and 0.0, 0.9 and 2.0 for malignancy. ACR20 responses in RAJ3 were 84.4% (27/32), 69.8% (30/43), 70.4% (19/27) with PEF100 mg, and 47.1% (16/34), 63.3% (31/49), 61.9% (13/21) with PEF150 mg. [Conclusions] Efficacy of PEF was unaffected by age, but IRs of special interest AEs increased with age. A multivariate analysis adjusting for prognostic factors (e.g. renal function) will be conducted.

W24-4

Incidence and Risk Factors for Herpes Zoster in Rheumatoid Arthritis Patients Receiving Upadacitinib

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Conflict of interest: Yes

Background: Upadacitinib (UPA) is an oral JAK inhibitor approved for the treatment of rheumatoid arthritis (RA). Patients (Pts) with RA receiving JAK inhibitors have been reported to have an increased risk of Herpes Zoster (HZ). Objectives: To evaluate the incidence and risk factors for HZ in pts with RA receiving UPA relative to active comparators in the Phase 3 trial. Methods: The incidence rate of HZ was determined in pts receiving UPA in 5 randomized Phase 3 trials. Risk factors for HZ were assessed using univariate and multivariate Cox regression models. Data cut-off was 30 June 2019. Results: Overall, 2629 pts who received UPA 15 mg, 1204 pts who received UPA 30 mg, 579 pts who received ADA, and 314 pts who received MTX mono were analyzed. HZ (n/100 PY [95% CI]) occurred in 142 pts (3.1 [2.6-3.7]) with UPA 15 mg, 126 pts (5.5 [4.5-6.5]) with UPA 30 mg, 8 pts (1.0 [0.4-2.1]) with ADA, and 5 pts (1.1 [0.4-2.6]) with MTX mono. Most of the HZ cases (~71%) with UPA and all cases with ADA and MTX mono involved a single dermatome. In multivariate analyses, prior history of HZ and Asian region were associated with an increased risk of HZ in both the UPA groups ($p \leqq 0.01$). Conclusion: HZ events in pts with RA receiving UPA were more common in both groups compared with the ADA and MTX groups.

W24-5

Clinical manifestations of upadacitinib: Part 1 Short-term efficacy and safety

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Conflict of interest: None

[Objective] To study the clinical manifestations of upadacitinib (UPA). [Methods] Data from 21 patients who were treated with UPA in our hospital after the launch of UPA till October 2020 were analyzed (21 showed inadequate response to multiple biologic drugs and/or multiple JAK inhibitors; 4 chose UPA 7.5 mg due to financial reasons). The assessment items included CDAI, SDAI, morning stiffness (MST), fatigue (FVAS, 0-100 scale), neutrophils real number, lymphocyte count, hemoglobin, platelet, creatinine and creatine kinase. [Results] CDAI, SDAI, MST, FVAS rapidly improved 1 week after introduction of UPA treatment. Improvement and maintenance in efficacy were also observed during the subsequent courses. As for safety, abnormal decrease in neutrophils real number, lymphocyte count, hemoglobin was not observed, also abnormal increase in platelets, creatinine, creatine kinase was not observed. [Discussion] UPA showed efficacy at an early introduction, and it was shown to be effective in patients with insufficient effect even after multiple biologic drugs introduction and multiple JAK inhibitor introduction. UPA 7.5 mg may be one of the options. [Conclusions] Short-term results suggest that UPA may be guaranteed efficacy and safety.

W24-6

Use of biological agents (bDMARDs) for rheumatoid arthritis (RA) in patients before and after treatment with JAK inhibitor (JAKi): a single-center experience

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Conflict of interest: None

[Objective] To clarify the usage of bDMARDs for RA before treatment with JAKi and after withdrawal of JAKi in patients who had shown an insufficient response. [Methods] Among RA patients who had been treated with JAKi and followed up for more than 3 months at our hospital, we retrospectively examined the usage of bDMARDs before JAKi treatment, and then after the JAKi treatment had been discontinued as of October 2020. [Results] Fifty-six patients were treated with JAKi. The number of bDMARDs used before JAKi was zero in 12 patients, 1 in 21, 2 in 12, 3 in 7, and 4 in 4. As of October 2020, 40 of the 56 patients (71.4%) had been treated with JAKi [8 of 12 previously untreated patients (66.7%), 16 of 21 who had received one drug (76.2%), 10 of 12 who had received two drugs (83.3%), 5 of 7 who had received three drugs (71.4%), and 1 of 4 who had received four drugs (25%)]. Among 14 patients who had discontinued JAKi because of insufficient effect, the number of bDMARDs used before JAKi was zero in 4, 1 in 4, 2 in 2, 3 in 1 and 4 in 3. The bDMARDs used after JAKi were IL-6i in 7 patients, TNFi in 4 and others. TNFi and IL-6i were effective in some patients in whom JAKi had been ineffective. [Conclusion] JAKi was effective for patients treated with fewer than 3 bDMARDs before treatment.

W25-1

Comparison of the efficacy and safety of tofacitinib and baricitinib in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To compare the efficacy and safety of tofacitinib (Tofa) and baricitinib (Bari) treatment in rheumatoid arthritis (RA). [Methods] A total of 242 patients were enrolled in the study. 81 patients were treated with Bari and 161 patients were treated with Tofa. After propensity score matching based on the clinical characteristics such as MTX use, ACPA positivity, 80 Bari-treated patients and 57 Tofa-treated patients were statistically extracted. Clinical disease activity and AEs were evaluated during 6 months. [Results] The mean ΔDAS28-ESR from baseline to 6 months were -1.46 (Bari), -1.64 (Tofa), respectively. Repeated measures ANOVA analysis revealed that there was no significant difference in the efficacy among two drugs during 6 months. 66 patients (82%) in Bari group and 45 patients (79%) in Tofa group continued each treatment for 6 months. AEs were experienced by 14 patients in Bari group and 11 patients in Tofa group. As described, discontinuation rate and safety were almost equal in both groups, however the incidence rate of herpes zoster was slightly different among these two groups (Bari: 3.8%, Tofa: 8.8%). [Conclusions] The comparison using propensity score matching revealed that the efficacy and safety was almost equal among Tofa and Bari treatment in RA.

W25-2

The add-on effectiveness and safety of csDMARDs in patients with rheumatoid arthritis who showed an inadequate response to JAK inhibitors-Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER cohort)-

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Conflict of interest: Yes

[Objective] To evaluate the effectiveness and safety of add-on csDMARDs in RA patients who showed an inadequate response to JAK inhibitors. [Methods] Fourty-four RA patients who showed an inadequate response (IR) to JAK inhibitors (29 tofacitinib and 15 baricitinib with treatment duration 8.8 months, 33 women, age 58.6y, disease duration 13.1y, concomitant MTX 8.3 mg/week [34.1%] and PSL 5.6 mg/day [47.2%], DAS28-CRP 3.6) were treated with additional non-prescribed csDMARDs (bucillamine [n=4] or iguratimod [n=16] as an immunomodulator group [group M], and tacrolimus [n=9] or MTX [n=15] as an immunosuppressant group [group S]) were enrolled in this 12-week, multicenter, retrospective study. Longitudinal change between baseline and at 12 weeks was examined by Wilcoxon signed rank test. [Results] Outcome measures improved as follows (4-8 weeks before IR→baseline→12 weeks): DAS28-CRP ([group M; 3.1→3.5→2.6 (P=0.004)/group S; 3.2→3.6→3.0 (P=0.15)]), CDAI ([group M; 14.4→16.2→10.8 (P=0.08)/ group S; 14.4→18.0→11.4 (P=0.02)]), and serum MMP-3 levels (ng/ml) ([group M; 159.8→198.3→111.8 (P=0.0006)/group S; 248.3→277.5→ 224.9 (P=0.22)]). Eighty-five % patients of group M and 91.7% of group S continued JAK inhibitors at 12 weeks. [Conclusions] Adding csDMARDs may be an alternative treatment option.

W25-3

The efficacy of JAK inhibitor for treatment to rheumatoid arthritis after inadequate response to at least two bDMARDs (D2T-RA)

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Conflict of interest: None

Objective: If a bDMARD (Bio) failed for rheumatoid arthritis (RA) patients, treatment with another Bio or JAK inhibitor (JAKi) should be considered. However, difficult to treat RA (D2T-RA) patients with inadequate response to at least two Bio or JAKi exist in daily clinical practice. The aim of study is to evaluate about the efficacy of JAKi for D2T-RA. Method: In this retrospective study, we evaluated 16 D2T-RA patients about the background and clinical course. Result: In D2T-RA 16 cases (93.8% of women, average age 61.6 years old, average disease duration 11.5 years, and JAKi; tofacitinib (n=9), baricitinib (n=7)), 13 cases (81.3%) were continuously administered until week 24. Mean SDAI was 22.53 at starting time of JAKi and 6.65 at week 24. SDAI remission rate was 31.3% and low disease activity rate was 81.3%. Mean SDAI at starting time of JAKi did not detected significant difference with effective and resistant cases (23.92 vs 16.5). In addition, MTX combination rate was 61.5% in effective cases, but 0% in inadequate response for JAKi. Conclusion: JAKi is regarded as effective treatment to D2T-RA.

W25-4

The study of predictive factors for clinical response to baricitinib and tofacitinib in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Four JAK inhibitors for patients with rheumatoid arthritis (RA) were approved in Japan, and there is no consensus on the proper use. We clarified the predictive factors for clinical response to baricitinib (BAR) and tofacitinib (TOF) in RA patients at our hospitals. [Methods] We enrolled the RA patients that were newly introduced BAR (n=59) or TOF (n=26) in 3 hospitals. Multiple regression analysis was performed using anti-CCP antibody (ACPA) titers, RF, and MMP-3 before treatment which are clinical parameters related to the JAK-STAT pathway, as independent variables for predicting ΔDAS28-CRP at 4, 12, and 24 weeks after treatment. [Results] There were no significant differences in the background factors of both groups such as age, gender, and disease activity. Both agents showed a significant improvement in DAS28-CRP during the entire observation period. In multiple regression analysis, we showed high ACPA titers was a significant related factor for improvement in DAS28-CRP by BAR (4w: β=0.50, p=0.006, 12w: β=0.44, p=0.036, 24w: β=0.41, p=0.035). On the other hand, no tendency was found in the TOF group. [Conclusion] Although ACPA titers were not associated with TOF efficacy, it was suggested that BAR may be particularly effective in RA patients with high ACPA titers.

W25-5

IL-6 inhibitor and JAK inhibitors in RA treatment: Is there any rationale for switching among these agents if one of these treatments resulted in lack of efficacy?

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Conflict of interest: Yes

[Objective] Seeking a rationale for switching among IL-6 and JAK inhibitors if one of these treatments resulted in lack of efficacy. [Methods] Total of 38 RA cases were analyzed, including TOF (n=15), BAR (n=10:) and TCZ (n=13) treatment groups. Transcriptome of peripheral blood drawn at just before (pre) and 3 months after (post) treatments was analyzed with using next-generation sequencer. From the comparison of post- vs. pre-treatment, differentially expressed genes (DEGs) were selected. [Results] The DEGs seemed to be discrete depending on the treatments. The hierarchical clustering also showed the influence of these treatments over the transcriptome seemed to be disparate. Different GO terms were enriched in each group of DEGs. Genes relevant to viral defense including 'response to type I interferon (IFN)', phosphorylation process such as 'IL-7 signaling' and wound healing including 'platelet activation' were enriched in the down-regulated genes of TOF, BAR and TCZ treatment, respectively. [Conclusions] Although the upstream of biological cascade for TOF, BAR and TCZ treatment might be shared, our findings will support a rationale for switching each other if one of these treatments resulted in lack of efficacy.

W25-6

Postoperative course after orthopedic surgeries in patients with rheumatoid arthritis under treatment using JAK inhibitor

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Conflict of interest: None

[Objective] The effect of JAK inhibitor on the postoperative course after orthopedic surgeries for patients with rheumatoid arthritis (RA) has not been elucidated. [Methods] A total of 39 cases with RA under treatment using JAK inhibitor had underwent orthopedic surgeries in three facilities. Among them, 35 cases could be matched for cases treated with csDMARDs in terms of type of surgery, age and sex. Between two groups, body temperature (BT), blood CRP levels, white blood cell (WBC), neu-

trophil and lymphocyte counts, postoperative complications were compared in the postoperative course of two weeks. [Results] JAK inhibitors being used were tofacitinib for 31 cases and baricitinib for 4 cases. Preoperative discontinuation periods were 6.5 days in average. No complications was observed in JAK group. JAK inhibitor showed no influence on the postoperative transition of BT and CRP level. The number of lymphocyte demonstrated increasing tendency in csDMARDs group while decreasing tendency in JAK group postoperatively. [Conclusion] Orthopedic surgeries had been performed safely in RA patients under treatment using JAK inhibitor. A postoperative decrease in the number of lymphocytes recommends surgeons to decide when to resume JAK inhibitor depending on individual cases.

W26-1

Safety Profile of Upadacitinib Up to 3 Years of Exposure in Patients With Rheumatoid Arthritis

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Conflict of interest: Yes

Background: The safety and efficacy of upadacitinib (UPA) was evaluated in the phase 3, which included 5 trials across a spectrum of rheumatoid arthritis (RA) patients (pts). Objectives: To describe the long-term integrated safety profile of UPA relative to active comparators in pts with RA treated in the SELECT program up to a cut-off date of 30 June 2019. Methods: Treatment-emergent adverse events (TEAEs) were summarized for the following: methotrexate (MTX), adalimumab (ADA), pooled UPA 15 mg and UPA 30 mg. Results: 3833 pts received ≧1 dose of UPA 15 mg [n=2629] or 30 mg [n=1204]. The exposure-adjusted event rates of overall SAEs and AEs leading to discontinuation on UPA 15 mg were comparable to MTX and ADA. The most common AEs reported with UPA were upper respiratory tract infection (URTI), nasopharyngitis, urinary tract infection (UTI), bronchitis, increased CPK, increased ALT (15 mg), and herpes zoster (30 mg). Overall rates of serious infections and opportunistic infections were comparable between UPA 15 mg, MTX and ADA groups. Rates of VTE were comparable across treatment groups, as were rates of adjudicated MACE and malignancies. Conclusion: Through long-term follow-up, the integrated safety profile of UPA remained consistent with previous analyses, with no new signals identified.

W26-2

Comparison of the change of the number of the lymphocytes and eGFRcys for 54 RA patients treated with TOF and 550 RA patients in our hospital for 3 years

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Conflict of interest: None

[Purpose] As we weighed a change of the number of the lymphocytes for 3 years against 54 RA patients treated with TOF (A) and 550 RA patients (B) in our hospital for three years, we report it. [Method] In the background of the A group mentioned above, a biological preparation (following BIO) use career had 42 of 54 cases for 13.2 years during average age 66.5 years old, a mean contraction of a disease period. As for the number of the use of BIO before the TOF dosage, an average of 1.9 drugs, the disease activity at the time of the TOF dosage start are DAS28ESR: 4.3, DAS28CRP: It was 4.0. I divided both A, B groups into a 64 years or younger example (1 group), examples (2 group) less than 65~74 age, a 75 years or older example (3 group) and weighed a change of the number of the lymphocytes for 3 years. [Result] The change of number of the mean lymphocytes (/mm³) is A group: 1737 → 1391 (80.1%), B group: 1654 → The number of the lymphocytes decreased 1637 (99.0%) and A group, and, as for the number of the lymphocytes drop ratio in the A group, 1 group <2 group <3 group and elderly person group were big. [Consideration and Conclusion] In this examination, it was thought that it was necessary to warn an infectious disease including the herpes zoster enough.

W26-3

Comparison of drug tolerability and discontinuation reasons of Baricitinib, Tofacitinib, and Sarilumab in patients with rheumatoid arthritis -Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER cohort)-

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Conflict of interest: Yes

[Objective] To compare the drug tolerability and discontinuation reasons of Baricitinib (BAR), Tofacitinib (TOF), and Sarilumab (SAR) in RA patients. [Methods] 413 treatment courses (BAR=166, TOF=185, SAR=62; Bio/JAK switched cases 78.4%, age 61.0y, female 80.9%, disease duration 11.1y, DAS28-CRP 3.6, CDAI 17.7, combined MTX dose 8.8 mg/week, rate 58.4%, and combined PSL dose 5.3 mg/day, rate 47.0%) were included in this multi-center, retrospective study. Reasons of discontinuation was classified into 4 major categories (lack of effectiveness, toxic adverse events, non-toxic reasons, and remission). Data was adjusted by potent confounders (age, sex, disease duration, concomitant MTX and PSL, and Bio/JAK switched number) with a Cox proportional hazards model and evaluated at 18 months. [Results] Discontinuation rate due to lack of effectiveness was BAR 15.5% vs. TOF 22.0% vs. SAR 15.7% (Cox P=0.77), due to toxic adverse events was BAR 12.3% vs. TOF 12.3% vs. SAR 15.7% (Cox P=0.35). Overall retention rates (%) excluding non-toxic reasons and remission was BAR 72.5% vs. TOF 66.8% vs. SAR 68.8% (Cox P=0.53). [Conclusions] After adjustment by potent confounders, BAR, TOF, and SAR showed similar discontinuation rate due to lack of effectiveness and toxic adverse events in short-term follow-up.

W26-4

The Efficacy and Safety of Janus Kinase (JAK) inhibitors in Rheumatoid Arthritis-associated Interstitial Lung Disease

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) is a common extraarticular manifestation of RA and can have significant morbidity and mortality. There are only few reports about JAK inhibitor's (JAKi) effect on RA-ILD. We aimed to assess the efficacy and safety of JAKi in RA-ILD. [Methods] Single-center, retrospective study of 14 RA patients with ILD treated with JAKi. The CT score (fibrosis and GGO score) and the KL-6 level were evaluated. And we checked if there was any episode of acute exacerbation of ILD. [Results] At baseline, the age; 68 years, the duration of RA-ILD from diagnosis; 17 years, DAS28-CRP; 3.95. Both the fibrosis

(before: 3.0 and 12 months after: 2.8) and the GGO score (before: 5.0 and 12 months after: 3.0) were improved after JAKi initiation, but not statistically different (p= 0.375 and 0.109, respectively). There was also no significant difference of the KL-6 level between before and after the JAKi initiation (p = 0.750). One event of organizing pneumonia, but no acute exacerbation of ILD was observed. (The data presented as median value) [Conclusions] JAKi appears to be an acceptable therapeutic choice for RA patients with ILD. In addition, ILD was improved after treatment of JAKi in some cases. To clarify the efficacy, further extensive studies are needed.

W26-5

Comparison according to the age group of the change of eGFRcys of 54 RA patients treated for 3 years with tofacitinib in our hospital

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Keiyu Orthopedic Hospital

Conflict of interest: None

[Purpose] There is the report of the ascent of reversible serum creatinine by TOF. As we examined influence on renal function of TOF for Japanese and elderly patients with the long-term dosage for 3 years this time, we report it. [Method] We weighed a change of eGFRcys for 3 years about 54 RA patients treated for 3 years with TOF according to the age groups in our hospital. In the background of the case mentioned above, 42 of 54 patients were treated with biologics (following BIO). Average of the disease duration is 13.2 years. during three men, woman 51, average age 66.5 years old, mean contraction of a disease period, as for the number of the use of in front of TOF dosage BIO, an average of 1.9 drugs, the disease activity at the time of the TOF dosage start are DAS28ESR: 4.3, DAS-28CRP: It was 4.0. I divided it into a 64 years or younger example (1 group), examples (2 group) less than 65~74 age, a 75 years or older example (3 group) and weighed a change of eGFRcys for 3 years. [result] The change of mean eGFRcys in three years- It was 69.6 (96.9%). [consideration and conclusion] In this examination, the renal function drop with the TOF dosage for 3 years was not seen.

W26-6

Comparison of the change of the eGFRcys for 3 years according to the renal function and age for 550 RA patients in our hospital

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Keiyu Orthopedic Hospital

Conflict of interest: None

[Purpose] As we weighed a change of eGFRcys of 3 years according to the age group and renal function, we report 550 cases that we were able to observe eGFRcys for RA patients in our hospital this time for three years. [Method] The patient setting is average age 65.9 years old. The age structure at the time of the observation start a 64 years or younger example (A group) /65~74 age example (B group) /75 years or older example (C group): 220/213/117. I divided A, B, C3 group into (eGFRcys> 100, 90, 80, 70, 60, 50, 40 according to the renal function, 40>) more and weighed a change of eGFRcys for 3 years. [Result] eGFR at the time of the observation start was low as an elderly patient, and a drop ratio of eGFR of 3 years was high. eGFR at the time of the observation start was equal to a younger patient, and the elderly patient had a big drop ratio of eGFR of 3 years. [Consideration and Conclusion] However, even the elderly patient considered that there was not decline of the renal function had the case that drop speed of the renal function had a big in comparison with a younger patient, and it was revealed that the observation that after all was careful was necessary.

W27-1

Periarticular osteophyte formation is a predictor of reduced perioperative blood loss in total knee arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Periarticular osteophyte formation, an anabolic bone change, is observed during the repair of damaged joints in rheumatoid arthritis (RA). This study aimed to determine the impact of periarticular osteophyte formation on perioperative blood loss in total knee arthroplasty (TKA) in RA patients. [Methods] This retrospective study reviewed 221 primary TKAs in 182 RA patients. Intraoperative blood loss and total blood loss, which were calculated from preoperative and postoperative hematocrit values, were compared according to the presence or absence of osteophytes on plain anteroposterior radiographs [osteophyte (+/-)]. Predictors of perioperative blood loss were assessed by multiple regression analysis. [Results] The osteophyte (+) group (n=169) had significantly lower intraoperative blood loss (100±116 vs. 142±153 ml, P=0.035) and total blood loss (1,487±579 vs. 1,761±832 ml, P=0.008) compared to the osteophyte (-) group (n=52). The multivariate analysis revealed that osteophyte formation on plain radiography was an independent predictor of reduced intraoperative (B=-46.14, 95% CI=-84.23, -8.04) and total blood loss (B=-237.71, 95% CI=-443.05, -32.38). [Conclusions] Osteophyte formation is an independent predictor of reduced perioperative blood loss in TKA.

W27-2

Clinical outcome and perioperative complications of total knee arthroplasty in patients with rheumatoid arthritis -Valgus deformity versus varus deformity-

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Conflict of interest: Yes

[Objective] To investigate whether preoperative alignment of the lower extremities affect the clinical outcomes and perioperative complications of TKA in patients with RA. [Methods] The study included 62 knees in 46 patients with RA who underwent primary TKA between June 2010 and July 2017 with a minimum of 2-year follow-up. Patients included 4 men and 42 women, with a mean age of 67.4 years, with an average follow-up of 50.4 months. They were classified into two groups (valgus, neutral + varus) by preoperative femoro-tibial angle (FTA). At final follow-up, ROM, KSS, KOOS, and FTA were compared between the groups. In addition, operative time, blood transfusion, and perioperative complications were compared between the groups. [Results] Valgus deformity was observed in 22.6%. Both group of patients achieved similar functional ROM and reported similar clinical outcomes. There were no significant differences in ROM, KSS, KOOS, FTA, operative time, and blood transfusion. The incidence of perioperative complications of valgus groups was higher than another groups (21.4% vs 4.2%, p=0.07). [Conclusions] Both group of patients achieved similar functional ROM and reported similar clinical outcomes. But, the incidence of perioperative complications of valgus groups was higher than another groups.

W27-3

Comparison of preoperative diagnosis and histological diagnosis in patients with rheumatoid arthritis or knee osteoarthritis who underwent total knee arthroplasty

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Conflict of interest: None

[Objective] In patients who underwent total knee osteoarthritis (TKA) due to rheumatoid arthritis (RA) or knee osteoarthritis (OA), to clarify whether preoperative diagnosis is associated with histological findings, RA treatment, CRP level, complications. [Methods] The subjects were 212 cases who underwent TKA at our hospital from 2014 to 2019. We investigated the relationship with preoperative diagnosis (RA or OA) and diagnosis based on knee synovial tissue findings, CRP value (preoperative and 3 days after surgery), medication (biologics, glucocorticoid (PSL) and methotrexate), BMI, complications (heart disease, diabetes, respiratory diseas-

es and history of malignant tumors). [Results] The cases in which the histological diagnosis was RA were 72% (80/111) in RA patients and 2% (2/101) in the preoperative diagnosis of OA. The CRP values 3 days after surgery were 11.07 ± 4.47 mg/dl in RA group and 10.11 ± 4.48 mg/dl in OA group (n.p.). There was no postoperative infection. In RA patients who treated without PSL, the group receiving biologics had fewer cases of tissue RA findings (38% vs 80%). [Conclusions] In TKA patients, the preoperative RA diagnosis and the synovial tissue findings did not always match. Of the OA patients, 2% were diagnosed with RA by histological findings.

W27-4

Changes in perioperative C reactive protein with total knee arthroplasty -Verification of factors affecting postoperative CRP-

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Orthopedic Surgery, Nagoya University Graduate School of Medicine

Conflict of interest: None

[Objective] This study aimed to compare changes in perioperative serum CRP levels in total knee arthroplasty (TKA) with and without early surgical site infection (SSI), and to investigate the factors that affect postoperative CRP without complications. [Methods] We compared changes of CRP in normal groups (649 knees) and SSI groups (11 knees) underwent primary TKA at our institute between 2005 and 2019. Data on serum CRP levels before and 1, 2-3, 7, and 14 days after TKA were also retrospectively collected. In the normal group, factors affecting postoperative CRP were identified by multiple regression analysis using age, gender, BMI, disease [RA vs. OA], operation time, and intraoperative bleeding as explanatory variables. [Results] The SSI group was significantly higher compared to the normal group 2-3 days, 7 days and 14 days after surgery. In the normal group, BMI≧25 and operation time≧120 minutes 2-3 days after surgery, and RA 2 weeks after surgery was a factor that independently affected perioperative CRP. [Conclusions] The possibility of SSI should be considered in cases where high CRP levels persist 2-3 days after TKA. It should also be noted that obesity and RA disease activity affect postoperative CRP.

W27-5

Is BCS-TKA useful for RA patients?

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Conflict of interest: None

[Objective] In recent years, the introduction of BCS (Bi-Cruciate-Stabilized)-TKA, which is an implant to supplement the function of the ligaments, has been increasing in Japan as well. We investigated whether BCS-TKA is useful for patients with rheumatoid arthritis. [Methods] The BCS group consisted of five knees. The preoperative FTA, knee flexion angle and JOA scores were 177.8°, 105.0° and 43.4 points. PS TKA cases (six knees) performed in the two years prior, were used as a control group (PS group). The preoperative FTA, knee flexion angle and JOA scores for the PS group were 180.0°, 113.3° and 42.8 points. We assessed knee range of motion, postoperative FTA, JOA score/stair elevation items, RA disease activity, and complications. [Results] Post-operative flexion angle in the BCS/PS group improved to 131.6/114.2°, FTA to 173.2/174.5°, and JOA score to 89.4/82.2 points. Postoperative ROM was significantly improved in the BCS group. At the stair-climbing item, there were 3 cases in BCS group and 1 case in PS group where only handrails were used. There were no complications such as fractures, infections or loosening in both groups, and there were no cases that led to revision. [Conclusions] BCS-TKA may be more useful in RA patients for whom PS types have been heavily used in the past.

W27-6

Examination of peri-cup fractures caused by Cementless total hip arthroplasty

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Conflict of interest: None

[Background] Intra-operative peri-cup fracture is a rarely reported complication of primary total hip arthroplasty (THA). It may potentially be associated with cup instability and may lead to clinical symptoms such as postoperative pain. [Objective] Postoperative CT should be used to evaluate fractures around the cup that are unclear during surgery, and to investigate the location of the fracture and risk factors. [Methods] The subject was 108 hips, which was using a cementless cup at the primary THA performed in our department from June 2010 to March 2020, and CT was taken within first 30 post-operative days. Average age is 68.8 ± 10.5 years, gender is 30 males, 78 females, BMI is 24.3 ± 3.95, implants used are Pinnacle 56 hips, plasmacup 23 hips, Dynasty 9 hips, Trident HA 8 hips, Continum 7 hips, Trinity 5 hips. Cup is classified into two types: hemispherical type and Peripheral Self Locking (PSL). We reconstructed CT images of axial, sagittal, and coronal sections. Fractures lines were evaluated in at least two planes. Fractures were evaluated at 5 sites: inner wall, anterior wall, posterior wall, superior laterality, and extra-articular. [Results] In 13 hips, Peri-cup fractures were confirmed using postoperative CT whereas they had not been identified postoperative standard X-ray.

W28-1

Effects of corrective ankle surgery on whole lower limb alignment

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Conflict of interest: None

[Objective] Hip and knee surgeries for the patients with rheumatoid arthritis (RA) or osteoarthritis (OA) have been reported to correct the alignment of whole lower limbs including ankle joint, subsequently contribute to pain relief. The purpose of this study is to assess the effect of ankle surgery on whole lower limb alignment including upstream region. [Methods] A retrospective study included 16 cases (10 RA and 6 OA patients) of corrective ankle surgery. Radiographic evaluation was investigated using hip to calcaneal views of the entire length of legs in the upright position preoperatively and 2 months postoperatively. [Results] The femoral head-calcaneal distance increased (from 828.3±51.7 mm to 838.2±48.9 mm; p=0.004) and the FTA (reference value 176°) changed from 174.1± 5.4° to 175.9±3.0° (p=0.049). In the valgus foot group (preoperative tibio calcaneal angle >valgus 3°; including 8 cases), the position of the load axis passing at the talus joint changed from 92.2±9.5% to 64.8±14.3% from the medial margin of the canopy (p<0.001). The angle between the vertical line and the tibial axis decreased from 5.3±1.7° to 3.0±1.2° in the valgus foot group (p=0.006). [Conclusions] Corrective ankle surgery has a potential to change whole lower limb alignment including upstream region.

W28-2

Comparison of the difference in incidence rates of metatarsal deviation at the osteotomy sites after hallux valgus surgery in patients with rheumatoid arthritis

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Conflict of interest: None

Objective Proximal rotational closing-wedge osteotomies of the first metatarsal have been performed for rheumatoid arthritis (RA)-induced hallux valgus deformities at our institute. Patients were allowed to start heel gait a day after surgery, but some cases suffered from metatarsal deviations at the osteotomy site. To prevent this complication, we revised the start time of heel gait to 10 days after surgery. The aim of this study was to

compare the incidence rates of metatarsal deviation with regard to the difference of the heel gait start times. **Methods** We evaluated 77 RA patients (80 feet) who underwent this procedure between 2018 and 2019. The subjects were divided into two groups: started heel gait a day after surgery (40 feet) and started heel gait 10 days after surgery (22 feet). The incidence rates of metatarsal deviation in each group were evaluated. **Results** The incidence rate of metatarsal deviation in the group who started heel gait 10 days after surgery (3 feet, 13.6%) was significantly lower than those who started heel gait a day after surgery (21 feet, 52.5%) ($P<0.01$). **Conclusions** We found that the incidence rate of metatarsal deviation at the osteotomy sites 10 days after rheumatoid hallux valgus surgeries was significantly lower than that conducted a day after surgery.

W28-3

Comparison of the changes of post-operative hallux valgus angle (HVA) between distal lineal metatarsal osteotomy (DLMO) and modified Scarf osteotomy (Scarf) in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] No consensus has been obtained for the selection of joint preservation surgery for hallux valgus deformity in patients with RA. We compared radiographic changes of DLMO and Scarf. [Methods] 66 feet in 43 cases who underwent the joint preservation surgery for forefoot deformity of RA with minimum follow-up period of 1 year after surgery were included (DLMO; 36 feet in 25 cases, Scarf; 30 feet in 18 cases). The HVA, sesamoid displacement by Hardy's classification and postoperative complications (infection, non-union and recurrence of the painful callus) were analyzed and compared between two groups. [Results] The HVA (mean±SE) for DLMO and Scarf was 43.9°±1.5 and 48.2°±1.8 preoperatively (n.s.), -7.2°±0.8 and 14.7°±1.3 immediately after surgery, and 3.4°± 2.2 and 21.9°±2.3 at 1 year after surgery. The HVA was significantly improved at immediately after surgery and was maintained to 1 year in both groups. The HVA and Hardy's classification showed significant improvement in DLMO than in Scarf. The incidence rates of postoperative complications showed no difference between two groups. [Conclusions] Although, both groups showed good post-operative HVA and maintenance of improvement of HVA, the better improvement of HVA and sesamoid displacement are observed in DLMO group.

W28-4

Examination of the factors affecting to the re-operation after RA forefoot arthroplasty

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Conflict of interest: None

[Objective] Forefoot arthroplasty is effective for the severe forefoot deformities in RA patients. But in some cases, recurrence of the deformity causes the need of re-operation. We have examined the factors that caused the recurrence. [Methods] 5 re-operation cases were investigated retrospectively from January 2013 to August 2020 in our hospital. The transitions of blood test (CRP), clinical findings (recurrence of callosities et al.), X-ray analysis and JSSF scores are investigated throughout the two operations. [Results] No significant changes were observed in RA activities and hallux valgus deformity throughout the course. The recurrence of callosities in the second foot were the most frequent observed finding before two operations, and no recurrence of deformity was observed after the second operations. JSSF score improved from 48 (44-55) to 78 (68-87) in the second operation. [Conclusions] The amount of the bone resection and the balance of the length of the metatarsal bone in the first operation are the most essential factors affecting to the clinical result.

W28-5

Examination of Wound Complications in Forefoot Surgery for Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To examine the wound complications after forefoot surgery for rheumatoid arthritis (RA). [Methods] Forefoot surgery for RA was performed on 53 feet of 42 patients (38 females). The average age of the patients was 65.4 years, and the average disease duration was 18.6 years. Of the patients, 18 took steroids (average prednisolone dosage: 3.1 mg/day) and 36 took methotrexate (average dosage: 7.6 mg/week), and 32 used biologics or JAK inhibitors. Wound complications included not only infection and conditions (wound dehiscence and skin necrosis) that necessitated treatment, such as debridement and resuturing, but also delayed wound healing, for which wound treatment was continued after suture removal. [Results] Wound complications occurred in 13 feet (24.5%): wound infection in 2, skin necrosis in 5, wound dehiscence in 2, and delayed wound healing in 4. A comparison of the 13 feet with wound complications (group A) and the 40 feet without wound complications (group B) revealed that steroids and methotrexate were used by a higher number of patients in group A, and the biologics or JAK inhibitors were used by a higher number of patients in group B. [Conclusions] The use of biologics or JAK inhibitors was not a risk factor for wound complications in forefoot surgery for RA.

W28-6

Relationship between frailty status and joint surgery in patients with long-standing rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study is to explore the characteristics of frailty in longstanding RA by focusing on the history of surgery. [Methods] We conducted a multicenter study using a self-administered questionnaire survey of RA patients aged 40 to 80 years. The history of joint surgery and disease activity (DAS28-CRP) were recorded, and frailty evaluation using the basic checklist (KCL), physical function evaluation using HAQ-DI, and QOL evaluation using SF-36 were performed. [Results] The number of subjects analyzed was 375 (mean age 65 ± 9, 7 years, 84% of female, mean disease duration 16.4 ± 11.9 years), and frailty (KCL ≧8) was observed in 26.1%. Compared with the non-surgery group (253 patients), the frailty rate (41% vs 19%), disease duration (25.3 years vs 12.0 years), HAQ-DI (1.01 vs 0.28), DAS28 (2.35 vs 2.09) was significantly higher. In multiple logistic regression analysis, history of surgery was not a significant frailty-related factor after HAQ-DI adjustment. The SF-36 summary score was an independent frailty-related factor even after HAQ-DI adjustment. [Conclusions] The history of surgery was not a determinant of frailty in RA patients. In the future, we plan to examine the effects of long-standing RA surgery on flail, including psychosocial effects.

W29-1

Volume of the deltoid muscle affects postoperative shoulder elevation after reverse shoulder arthroplasty

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Conflict of interest: None

[Objective] To elucidate relationship between preoperative volume of the deltoid muscle and shoulder elevation after reverse shoulder arthroplasty (RSA). [Methods] We performed RSA on 39 patients (43 shoulders) with rheumatoid arthritis (RA) or cuff tear arthropathy (CTA) and followed them up for at least 6 months. We retrospectively examined active elevation, preoperative passive elevation and cross sectional area (CSA) of the deltoid muscle on preoperative MRI. Contracture was defined as passive elevation <100 degrees. To correct difference of body height, deltoid CSA was divided by square of the body height, named as deltoid index. [Results] Postoperative elevation was significantly correlated with deltoid index in contracture-positive patients whereas no correlation was observed in contracture-negative patients. There was a tendency that patients with RA have contracture more frequently than those with CTA. Deltoid index was significantly lower in patients with RA. Among these factors, deltoid index was extracted as the only significant factor that affects postoperative elevation by multiple regression analysis, [Conclusions] Volume of the deltoid muscle is important for elevation after RSA in contracted shoulders which are often observed in patients with RA.

W29-2

A study of the correlation between carpal axial alignment and change of ROM by DARTS total wrist arthroplasty

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Conflict of interest: None

[Objective] Although the DARTS total wrist arthroplasty (TWA) has be used, the relationship between the postoperative carpal alignment and the range of motion is still unknown. The objective of this study was to clarify the carpal axial alignment and the wrist range of motion after TWA. [Methods] The subjects were 18 patients who underwent TWA at our hospital from 2010 to 2020. The carpal axial alignment (vcR-CH), the implant rotation angle (vcR-PI and vcR-DI), and the wrist range of motion were measured before and 6 months after TWA. JMP Pro 14.0.0 was used for statistical analysis, and $p < 0.05$ was considered to be statistically significant. [Results] DARTS compornents were inserted at about 10° supination (vcR-PI: 12.8° and vcR-DI: 14.1°), and vcR-CH was also significantly increased from 73.0° to 83.3° after TWA. There was a significant positive correlation (0.58) between postoperative vcR-CH and wrist extention, and a significant negative correlation (-0.56) between postoperative vcR-CH and wrist flexion. [Conclusions] The extention-flextion axis of the implant was about 10° supination after TWA. The supination of the carpal axial alignment may increase writs extension and decrease wrist flexion.

W29-3

Outcome of the Sauvé-Kapandji procedure for the patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the clinical and radiological results of the SK procedure in RA wrists. [Methods] Studied were the 43 joints subjected to a follow-up for one year or more after operation in the author's department. The average age of the patients was 62.0 years old at surgery, and the average disease duration was 15 years. Biologics were used in 36 joints at surgery. The cases of complications of extensor tendon ruptures were 18 joints. The evaluation item was the excursion of the wrist and the forearm at surgery and at the time of the study. Radiographic evaluation was carpal height ratio (CHR) and carpal translation index (CTI). [Results] A significant difference was observed in pronation, but no significant difference was observed in supination and wrist excursion. No significant difference was observed in CHR and CTI. In the lateral views, remodeling was observed for 21 joints (48.8%) at the time of the study. It increased significantly. [Conclusions] The S-K procedure maintained excursion, and no carpal collapse or progression of ulnar deviation was observed. Due to the progress of pharmacotherapy, the effectiveness of the SK procedure was suggested in cases of progressed bone destruction.

W29-4

Association of Implant Fracture and Postoprative DASH score in Patients with rheumatoid arthritis after Silicone MCP Joint arthroplasty

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Conflict of interest: None

[Objective] AVANTA and Swanson are mainly used for MCP Joint arthroplasty in performed for finger deformity for patients with rheumatoid arthritis (RA). The 7.5-year survival rate is low with fracture as the endpoint. It is not long life compared to artificial implant of other joint. We evaluated the PROMs using the DASH score in the fracture group and the survival group. [Methods] We were recruited to the patients with RA undergone MCP joint arthroplasty between January 2000 and June 2019. DASH score was evaluated before and 6 months after the operation. [Results] We collected 124 hands including 22 hands were fracture, and except for 1 case was fracture 6 months after the operation (16.9%). The mean pre and post-operative DASH scores were 29.5 and 29.6 in the fracture group and 36.4 and 31.8 in the survival group. There was no significant improvement in the fracture group. There was no significant difference in preoperative DASH score between the two groups. [Conclusions] We found that the fracture group did not have a significant improvement in postoperative DASH score before damaging implant. Since the DASH score involves not only the functions of the hands but also the functions of the wrist and elbow joints, it is necessary to further examine the relationship with damage.

W29-5

Correction of rheumatoid swan-neck deformity of the fingers using modified Thompson-Littler method

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Conflict of interest: None

[Objective] Swan-neck deformity of the fingers is caused by persistent synovitis and palmo-ulnar subluxation at the MP joint followed by tight intrinsic muscles. The PIP joint extends with dorsally displaced lateral bands and the DIP joint is flexed. The objective of this study is to clarify the effect of modified Thompson-Littler (m-TL) method on rheumatoid swan-neck deformity. [Methods] Twenty-seven fingers in 10 patients with rheumatoid arthritis (RA) including one man and 9 women, underwent m-TL method. The average age at the time of surgery was 60.3 years, the average duration of RA was 19.3 years, and the average postoperative follow-up period was 2.4 years. Preoperative Nalebuff type (i.e. severity of deformity) was 5 fingers in type II, 13 fingers in type III, and 9 fingers in type IV. Release of extension contracture at the PIP joint was performed combined with m-TL method in type III and IV. [Results] Deformity was corrected in all cases, making it easier to pinch. However, gain in flexion range was small in type IV. [Conclusions] m-TL method provides favorable effect on swan-neck deformity of the fingers with Nalebuff type III or less.

W29-6

Effects of Upper Limb Joint Surgery on Physical Function Improvement in Depression and Quality of Life in Patients with Long-Term Rheumatoid Arthritis-From a Multicenter Prospective Cohort Study-

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Conflict of interest: None

[Objective] The purpose of this study is to examine the effect of upper limb joint surgery in RA patients using patient-reported outcome (PRO). [Methods] Evaluation of joint surgery for RA patients includes patient subjective evaluation (PRO) [patient general evaluation (PGA; VAS), physical function evaluation (HAQ, DASH), quality of life (EQ-5D), degree of depression (BDI-II))] was collected before and after surgery (half a year, one year). The relationship between each parameter before surgery and the relationship between changes in each parameter before and after surgery were examined by multiple regression analysis. [Results] Of the upper limb joint surgeries registered from 10 institutions, 205 cases were analyzed. The patient background was 88.3% female, average age 62.7 years. HAQ, DASH, BDI-II and EQ-5D were significantly improved by surgery ($p < 0.01$). In the change before and after surgery, HAQ is EQ-5D ($p = 0.03$), DASH is EQ-5D ($p < 0.01$), BDI-11 ($p < 0.01$). It was an independent factor of improving of EQ-5D. The cut-offs for HAQ and DASH improvements to achieve MCID for EQ-5D were 0.19 and 24.0. [Conclusions] Improvements in physical function by upper limb joint surgery were associated with depression and improved quality of life.

W30-1

Efficacy and Safety of Ixekizumab (IXE) for Patients with Non-Radiographic Axial Spondyloarthritis (nr-axSpA) According to the Japanese Diagnostic Guidance (J-Guidance): Subgroup Analysis from a Phase-3 Randomized, Placebo-Controlled Study (COAST-X)

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Conflict of interest: Yes

[Objective] To evaluate the efficacy/safety (E/S) of IXE in a subgroup of pts from the COAST-X and who met the J-guidance for nr-axSpA. [Methods] Out of the pts in COAST-X classified as nr-axSpA (met ASAS classification but not mNY criteria), we conducted a post-hoc analysis in a subgroup of pts who met the 2020 Jul J-guidance (in addition to ASAS classification, having inflammatory back pain and not having other relative diseases including psoriasis with MRI sacroiliitis [imaging criteria] or HLA-B27+ and elevated CRP [clinical criteria]). Pts were given PBO, or 80 mg IXE every 4wks (Q4W) or Q2W. [Results] Out of 303pts, 263 met the J-guidance. Significantly higher proportion of pts achieved ASAS40 at Wk16: IXEQ2W (36%, p=0.006), IXEQ4W (38%, p=0.003) vs PBO (18%), with efficacy sustained until Wk52. Pts on either IXE regimen showed greater improvements from baseline at Wks16/52 for disease activity assessed by ASDAS and sacroiliac joint SPARCC scores vs PBO. The frequency of SAEs and AEs that led to treatment discontinuation was low across arms. Similar trend of E/S was seen in pts of both imaging and clinical criteria populations. [Conclusions] Similar to the nr-axSpA overall population who met ASAS classification, IXE E/S were confirmed in the population who met the nr-axSpA J-guidance.

W30-2

Post-hoc analysis of MRI SIJ SPARCC score in a Phase-3 Randomized, Placebo-Controlled Study (COAST-X) in Patients with Non-Radiographic Axial Spondyloarthritis (nr-axSpA) Treated with Ixekizumab (IXE)

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Conflict of interest: Yes

[Objective] To evaluate the baseline (BL) characteristics and clinical outcomes based on stratification according to MRI responses (high or low responder) in nr-axSpA pts treated with IXE (COAST-X). [Methods] Pts were given PBO, or IXE 80 mg every 4 wks (Q4W) or 2 wks (Q2W). Probability plots of MRI SPARCC SIJ score (MRI score) were included in post-hoc analysis. BL characteristics and clinical outcomes were assessed by MRI high-responder (BL MRI score $\geqq 2.5$ and its decrease from baseline [DFB] at Wk16 $\geqq 2.5$) and low-responder (BL score $\geqq 2.5$ and DFB < 2.5). [Results] 267pts (PBO; 90, Q4W; 85, Q2W; 92) had MRI score at BL and Wk16; 72% had SIJ inflammation at BL. IXE-treated pts showed MRI score improvement at Wk16/52 regardless of its BL score. Compared to MRI low-responders (Q4W; 15, Q2W; 15), high-responders (Q4W; 22, Q2W; 32) were of younger age, lower female ratio, and shorter duration of symptoms since onset at BL, and no consistent tendency in ASAS40 and BASFI outcomes between MRI high- and low-responders was observed. [Conclusion] IXE-treated pts showed MRI score improvement regardless of its BL score. MRI high-responders had shorter duration of symptoms since onset at BL, and there was no consistent tendency in disease activity/physical function outcomes between MRI high- and low-responders.

W30-3

Efficacy and Safety of Upadacitinib Versus Placebo and Adalimumab in Patients With Active Psoriatic Arthritis and Inadequate Response to Non-Biologic Disease-Modifying Anti-Rheumatic Drugs (SELECT-PsA-1): a Double-Blind, Randomized Controlled Phase 3 Trial with Japanese subject sub-analysis

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Conflict of interest: Yes

Purpose: To assess the efficacy and safety of Upadacitinib (UPA) vs placebo (PBO) and adalimumab (ADA) in patients (pts) with psoriatic arthritis (PsA) and prior IR or intolerance to $\geqq 1$ non-biologic DMARD. **Methods:** Pts with active PsA were randomized 1:1:1:1 to once daily UPA 15 mg (UPA15), UPA 30 mg (UPA30), ADA 40 mg every other week, or PBO. The primary endpoint was the proportion of pts achieving ACR20 for UPA vs PBO at Wk 12. **Results:** 1704 pts including 15 Japanese received study drug and 90.8% of pts completed Wk 24. At Wk 12, ACR20 rates were 70.6% with UPA15, 78.5% with UPA30 vs 36.2% with PBO ($p < .001$ for UPA15/30 vs PBO) and 65.0% with ADA (non-inferiority, $p < .001$ for UPA15/30 vs ADA; superiority, $p < .001$ for UPA30 vs ADA). UPA improved musculoskeletal and skin manifestations, physical function, QoL and other PROs and inhibited radiographic progression. The rates of treatment emergent AEs and serious AEs were similar in PBO, UPA15 and ADA and higher with UPA30. Herpes zoster rate was similar for PBO and UPA15/30. One death occurred on PBO. Efficacy and safety

were generally consistent in Japanese pts. **Conclusion:** UPA was effective in treating the manifestations of PsA including structural joint damage. Safety findings were consistent with the safety profile observed in RA.

W30-4

Efficacy and Safety of Upadacitinib in Patients With Active Psoriatic Arthritis and Inadequate Response to Biologic Disease-Modifying Anti-Rheumatic Drugs (SELECT-PsA-2): a Double-Blind, Randomized Controlled Phase 3 Trial with Japanese subject sub-analysis

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Conflict of interest: Yes

Purpose: To assess the efficacy and safety of Upadacitinib (UPA) versus placebo (PBO) in patients (pts) with psoriatic arthritis (PsA) and prior inadequate response or intolerance to ≧1 biologic DMARD (bDMARD). **Methods:** Pts were randomized 1:1:1 to once daily UPA 15 mg (UPA15), UPA 30 mg (UPA30), or PBO. The primary endpoint was the proportion of pts achieving ACR20 at Wk 12. **Results:** 641 pts including 39 Japanese were randomized and 84.6% of pts completed Wk 24 study drug. At Wk 12, a significantly greater proportion of pts receiving UPA15 and UPA30 vs PBO achieved ACR20 (56.9% and 63.8% vs 24.1%; p<.001 for both comparisons). UPA improved musculoskeletal and skin manifestations, physical function, and QoL and other PROs. The rate of treatment emergent AEs were similar in PBO and UPA15 and higher with UPA30. Numerically higher rates of serious AEs were reported in the UPA arms. Herpes zoster was more frequent with UPA30. One non-fatal myocardial infarction and one pulmonary embolism were reported with UPA15. One death occurred on PBO. Efficacy and safety were generally consistent in Japanese pts. **Conclusion:** In this bDMARD-IR PsA population, UPA demonstrated improvements across PsA domains vs PBO. Safety findings were consistent with the safety profile observed in RA.

W30-5

Safety Profile of Upadacitinib in Psoriatic Arthritis (PsA): Findings in the Global Population and Japanese Subgroup From a Pooled Analysis of 2 Phase 3 Clinical Trials

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Conflict of interest: Yes

Objective/Methods: Phase 3 SELECT-PsA1 and SELECT-PsA2 clinical trials evaluated PBO, upadacitinib 15 mg once daily (QD; UPA15), upadacitinib 30 mg QD (UPA30) and also adalimumab 40 mg every other week (ADA) (only in SELECT-PsA1). Here we present the integrated safety data with treatment-emergent adverse events (TEAEs) from the trials through Week24, analyzed in total population and Japanese (Jpn) subgroup. **Results:** The number of patients (pts) in the total population and Jpn subgroup were N=635; 15 for PBO, N=640; 17 for UPA15, N=641; 18 for UPA30, and N=429; 4 for ADA respectively. The observed TEAE rates were generally consistent in total population and Jpn subgroup. In both populations, more serious AEs were observed in UPA30 vs PBO, UPA15 and ADA groups; similar results were seen for AEs leading to discontinuation. In Jpn pts, serious infections were observed only in UPA30, which also had a higher rate compared to the other arms in the total population. In Jpn pts, the number of pts with Herpes Zoster was 0/15 for PBO, 1/17 for UPA15, 1/18 for UPA30 and 0/4 for ADA; the number of pts with malignancies other than NMSC were 0/15 for PBO, 0/17 for UPA15, 1/18 for UPA30 and 1/4 for ADA. **Conclusions:** No new safety signals were identified with UPA in Jpn pts compared to total population.

W30-6

Efficacy and Safety of Upadacitinib (UPA) in Patients With Active Ankylosing Spondylitis (AS): 1-Year Results From a Randomized, Double-Blind, Placebo (PBO)-Controlled Study With Open-Label Extension (OLE)

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Conflict of interest: Yes

Purpose: Upadacitinib (UPA) is a Janus kinase (JAK) inhibitor. The interim analysis of the phase 2/3 SELECT-AXIS 1 was reported efficacy and safety of UPA through 1 year. Methods: SELECT-AXIS 1 (NCT 03178487) included a randomized, placebo-controlled, 14-W followed by 90W OLE; reported here are up to 64W. Results: Of 187 pts, 178 pts (each n=89) completed 14W and entered OLE; 160 pts completed 64W. Efficacy was maintained or continued to improve throughout the study in the UPA group: 85% (95% CI, 77%-93%) of pts achieved ASAS40 at 64W (AO) and 72% (63%-81% (NRI)). Pts who switched from PBO to UPA at 14W showed a similar speed of onset and magnitude of response compared with pts initially randomized to UPA: 81% (95% CI, 72%-89%) of pts (AO) and 70% (61%-80%) of pts (NRI) achieved ASAS40 at 64W. Among 182 pts of UPA (237.6 PY), 618 AEs (260.1/100 PY) were reported. AEs leading to discontinuation (15 events [6.3/100 PY]) and serious AEs (14 events [5.9/100 PY]) were low. No SI, active TB, VTE, gastrointestinal perforation, MACE, renal dysfunction, or deaths were reported. Conclusion: UPA 15 mg QD showed consistent efficacy over 1 year. No new safety findings were observed compared with UPA clinical development data in other indications.

W31-1

Risk factors for progression of spinal lesions in psoriatic arthritis

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Conflict of interest: None

[Objective] Axial lesions of PsA may cause a decrease in the range of motion due to the progression of the lesion, resulting in dysfunction. To evaluate the risk factors for progression of spinal lesions in PsA. [Meth-

ods] For PsA patients who were able to evaluate bone Xp during the first evaluation (BL, baseline) and after the course, it was divided into a progression group and a progression-free group with or without extension of syndesmophyte. We evaluated about background, clinical symptoms at BL and imaging. [Results] The participants were 42 patients (age 61.5y, 52% male, PsA history 4.5y). In both groups, there was no difference in age, gender, the symptoms of peripheral joints, enthesitis, and dactylitis. The history of PsA, CRP, and the rate of DM were high in the progression group, but there was no significant difference. In the progression group, ASDASCRP (2.2 vs. 1.5, p=0.046), BASMI (2 vs. 1, p=0.005), mSASSSS (11 vs. 2, p=0.01), BMI (30.5 vs.22.9, p=0.03) and the rate of complication of HT (100% vs. 43.2%, p=0.05) were significantly higher. [Conclusions] Although it was an analysis of a small number of cases, the progressive factors of spinal lesions of PsA were not only disease activity and high mSASSS at BL, but also high BMI and complications of hypertension.

W31-2

The rate and distribution of the spinal lesions in the Spondyloarthritis and Pustulotic arthro-osteitis

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Conflict of interest: None

[Objective] We organize the virtual unique outpatient care for SpA patients with collaboration of Rheumatology, Dermatology, and Orthopaedics. We investigate the rate and distribution of spinal lesions. [Methods] Thirty-five patients participated in this research; 22 PsA, 8 PAO, and 5 AS patients. We checked their X-ray images of spine, and acquired score from the lateral view of them in reference to mSASSS score. At each inter-vertebral space, we consider it as a spinal lesion, when either upper or lower vertebra had score 2 or more. [Results] Of 35 patients, 20 were males and 15 were females. Mean age was 55.1 (27-74) years, and mean duration of treatment was 7.3 (0-24) years. The rate of patients with the spinal lesions was PsA 77%, PAO 75%, and AS 20%. In PsA patients, they were frequently observed at the lower cervical spine and thoracic-lumbar junction. PAO patients exhibited similar tendency. In the AS, they were observed at the lower cervical spine. [Conclusions] In the PsA and PAO, the rate of patients with the spinal lesions was relatively high, and the lesion were observed frequently at the lower cervical spine and thoracic-lumbar junction. It may be important to check X-ray regularly, and to observe the progression of the spinal lesions in conjunction with disease activity.

W31-3

Usefulness of quantified bone scintigraphy in assessing osteoarthritis in SAPHO syndrome / PAO

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Conflict of interest: None

[Background] Bone scintigraphy is used to evaluate the activity of osteoarthritis in SAPHO syndrome / PAO, but it is a qualitative test and it is difficult to judge whether it is physiological or pathological accumulation. In recent years, quantified bone scintigraphy has become available. [Purpose] We investigated the usefulness of quantified bone scintigraphy in the evaluation of bone lesions in SAPHO syndrome / PAO and the evaluation of therapeutic effects. [Method] 12 patients with SAPHO syndrome / PAO being treated at our hospital were evaluated for accumulation in the thoracic-costal joint by taking quantified bone scintigraphy before treatment. Two of them were evaluated after treatment. Quantified bone scintigraphy was taken 3 hours after injection of 99mTc-HMDP using a GE SPECT-CT device. [Results] The average value of SUVmax was 9.38, which was higher than the average value of SUV max of 4.3 for normal bone. SUVmax also decreased in patients who had a therapeutic effect. No association was found between the presence or absence of osteosclerosis on CT and the SUVmax value. [Discussion] Quantitative bone scintigraphy is considered to be useful as a screening test for osteoarthritis of SAPHO syndrome / PAO and as an evaluation method for determining the therapeutic effect.

W31-4

Synovitis in wrist and finger joints is associated with joint destruction in patients with psoriatic arthritis

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Conflict of interest: None

[Objective] The enthesitis and synovitis assessed by ultrasound (US) were not associated with joint destruction by cross-sectional analysis in patients with psoriatic arthritis (PsA). We investigated the relationships longitudinally. [Methods] Forty-seven patients with PsA underwent US and clinical examination of wrist and finger joints and 14 entheses (the bilateral humeral medial epicondyles and insertions of the triceps, distal quadriceps, proximal/distal patella, Achilles tendons, and plantar fascia). GS and PD score of the joints and number of entheses presenting inflammation and tenderness were calculated. The relationships between the change in radiographic damage (ΔmTSS) at baseline and follow-up and US or clinical findings were investigated. [Results] ΔmTSS was significantly correlated with age (r=0.44, p=0.01), RF (r=0.38, p=0.03), MTX dose (r=0.38, p=0.03), joint GS score (r=0.44, p=0.01), and joint PD score (r=0.38, p=0.03). The number of enthesitis, disease activity showed no associations with ΔmTSS. The joint PD score, adjusted by age, was significant factor for ΔmTSS (β=0.50, p<0.001). [Conclusions] US synovitis, not enthesitis, was significant factor for ΔmTSS. It is important to assess joint as well as entheses both by US and tenderness.

W31-5

Comparison of clinical features between the patients with axial and peripheral spondyloarthritis

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Conflict of interest: None

[Objective] The ASAS classification criteria have distinguished between axial Spondyloarthritis (axSpA) and peripheral SpA (pSpA). We compared the clinical features between axSpA and pSpA. [Methods] We assessed patient's background, disease activity index, comorbidities, in 6 patients with axSpA and 22 with pSpA. [Results] The two groups were similar with respect to age, sex and disease duration. Smoking history, hypertension and hyperuricemia were more common in axSpA than pSpA. Hyperlipidemia was found in half of both groups. Psoriasis was found in one patient with axSpA and in all of pSpA. BMI was statistically higher (22.4±2.4/26.8±5.8, P=0.03) and more patients were obese in pSpA (17% vs. 55%). The groups did not differ significantly with respect to disease activity index such as DAPSA, MASES, spinal VAS and mSASSS. Spinal lesions were detected by imaging in 83% of ax SpA and 86% of pSpA. HLA-B27 was positive in 3 patients with axSpA, but not in pSpA. Biologics users (66.7%/40.9%) were more common in axSpA. [Conclusions] The prevalence of obese and psoriasis were more in pSpA than axSpA. The two groups were similar with respect to spinal lesions. Early detection of spinal lesions may provide an opportunity for therapeutic intervention in pSpA as well as axSpA.

W31-6

3 cases of SpA mimicked multiple bone metastasis

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Conflict of interest: None

[Objective] Recognition of difficulties of DDx of multiple bone metastasis and SpA spinal lesions. [Methods] We reported 3 cases of SpA mimicked multiple bone metastasis. [Case 1] A 60 y.o. male with multiple compression fractures suggestive of bone metastasis. Hypertrophy of costovertebral joints and sacroiliitis leads to the correct diagnosis of AS. [Case 2] A 70 y.o. female with osteolytic lesions of Th 5, 9. Biopsies showed neither metastatic malignancy nor anti-fast bacilli. Patients reported palmar pustulotic lesion. [Case 3] A 70 y.o. female with Th 8 osteosclerotic lesion with Th4/5, 7/8 irregular disc findings. Negative FDG-PET study suggested Dx of SpA. [Conclusions] Simple Spinal lesions without other SpA features sometimes make correct diagnosis difficult. We should pay more attention to other clinical findings of SpA.

W32-1

In HR-pQCT Study, examination of bone mineral density, geometry, and bone microstructure in patients with steroid-induced osteoporosis

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Conflict of interest: None

[Objective] The bone structure of patients taking glucocorticoid (GC) were examined using HR-pQCT. [Methods] The subjects were 39 female patients aged 55 years or younger who had been taking prednisolone 5 mg / day or more for 2 years or more. 21 patients (Tx-group) treated with bisphosphonate or other drugs and 18 patients (nTx-group) who had not been treated for osteoporosis because of good bone mineral density (BMD) in DXA. 41 female aged 55 years or younger who had no underlying disease were control group (C-group). [Method] HR-pQCT was used to measure the bilateral distal radius. [Results] In Tx-group, total vBMD, trabecular vBMD, cortical bone area (Ct. Ar), cortical bone thickness, trabecular number (Tb. N) and trabecular thickness (Tb. Th) were significantly lower than C-group, there was no significant difference in cortical bone porosity. In nTx-group, only the Tb. N was significantly lower than that in the C-group. In Tx-group and the nTx-group, trabecular vBMD and Tb. Th were significantly lower, and Ct. Ar tended to be lower in Tx-group. [Conclusions] In nTx group, which had good BMD with DXA despite oral administration of GC, the geometry of cortical bone and trabecular vBMD were maintained as compared with Tx-group.

W32-2

The characteristics and risk factors of non-traumatic vertebral fractures in rheumatoid arthritis complicated with glucocorticoid induced osteoporosis: post-hoc analysis of RISOTTO study

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Conflict of interest: Yes

[Objective] RISOTTO study had shown that Sodium Risedronate (RIS) increased lumbar spine bone mineral density in rheumatoid arthritis (RA) patients with glucocorticoid-induced osteoporosis (GIO). This post-hoc analysis of RISOTTO study is conducted in order to clarify the characteristics and risk factors of non-traumatic vertebral fractures (VF) in RA patients with GIO. [Methods] Radiographs of the whole spine were taken at baseline, then at 6 months after treatment. VF was evaluated by two readers using grading by semiquantitative assessment. Bone mineral density (BMD) and disease activity score in RA were measured three times at baseline, after 3 and 6 months. The risk factors were identified by multivariate logistic regression analysis. [Results] VF was evaluated in 97 patients and 44 patients (45.3%) had existing VF at the baseline, which includes 20 (20.1%) multiple VF. Age at the baseline was identified as a risk factor of multiple VF (odds ratio 1.1 95%CI 1.0-1.1). The new-onset VF was evaluated in 90 patients and identified in 10 patients (12.1%) at 6 months. In RIS treatment group, the change of F-LMD at 3 months in patients with VF was lower than those without VF ($p<0.03$). [Conclusions] This study clarified a high incidence of VF regardless of RIS in RA patients with GIO.

W32-3

Risk factors associated with lack of treatment of glucocorticoid-induced osteoporosis in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Glucocorticoid-induced osteoporosis (GIOP) is one of the side effects associated with GC therapy. In 2014, Japanese Society for Bone and Mineral Research (JSBMR) provided new guidelines for the management and treatment of GIOP. We aimed to clarify the prevalence and treatment status of GIOP and to identify risk factors associated with lack of treatment of GIOP in patients with RA. [Methods] Patients who met the treatment criteria of the 2014 guidelines for GIOP by the JSBMR were enrolled. Patient information between 2 groups (treated and untreated groups) was collected. We also investigated risk factors associated with lack of treatment of GIOP. [Results] Among 2,234 patients with RA, 683 (30.6%) met the treatment criteria of the guidelines, and 480 (70.3%) had been treated for GIOP. The untreated group included a larger number of males, young patients, and patients treated in clinic ($p < 0.001$, $p = 0.015$, and $p < 0.001$, respectively). Multivariate analyses found male sex, younger age, and clinic visits were significant risk factors associated with lack of treatment for GIOP in patients with RA ($p < 0.001$, $p = 0.013$, and $p < 0.001$, respectively). [Conclusion] Male sex, younger age, and clinic visits were identified as risk factors associated with lack of treatment for GIOP.

W32-4

Disease Activity in Rheumatoid Arthritis is associated with vertebral fractures

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Conflict of interest: None

[Objective] To clarify the factors associated with prevalent vertebral body fracture (VF) in rheumatoid arthritis (RA) patients. [Methods] 107 RA patients who had femoral neck bone mineral density (BMD) by DEXA and plain X-rays of the thoracolumbar spine were targeted for VF. The prevalence and the number of VF were investigated. Divided into 2 groups

according to the presence of VF (N group: no fracture, F group: with fracture), we statistically examined the relationship between the prevalence and the number of VF and each factor. [Results] The average age was 67.9 years, the average DAS28 was 2.8, and the prevalence of VF was 31%. DAS28 was significantly higher, BMD was significantly lower, and glucocorticoid (GC) use history ≧ 3 months was significantly higher in group F than in group N. A logistic regression analysis was performed with the dependent variable as the presence of VF, DAS28 and BMD were independently VF-related factors. Furthermore, when multiple regression analysis was performed using the dependent variable as the number of VF, DAS28 was an independent factor related to the number of VF. [Conclusion] The prevalence of VF in RA patients was associated not only with BMD but also with disease activity. The number of VF was higher as the disease activity was higher.

W32-5

Effect of treatment of biologic agents for 10 years on bone mineral density in rheumatoid arthritis patients: from the viewpoint of 10-year-follow up study

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Conflict of interest: None

[Objective] The purpose of this study is to clarify the effect of biologic agents on bone mineral density (BMD) in patients with rheumatoid arthritis (RA), based on the 10-year-follow up study. [Methods] The subjects were 123 patients whose BMD has been measured for 10 years. Among them, 74 patients received biologics continuously for 10 years, and 49 did not receive any biologics. We divided these patients into two groups, in which BMD increased by more than 10% or not, and analyzed various clinical factors by univariate analysis and multiple logistic regression analysis. [Results] In lumbar spine, MTX dose and the administration period of osteoporosis drugs turned out to be significant factors that increased the lumbar BMD. As to the femoral neck, a similar analysis revealed that the continuous administration of biologics and the duration of osteoporosis treatment were significant factors that increased BMD in femoral neck. [Conclusion] Administration of biologics for 10 years might increase BMD in the femoral neck in RA patients. Furthermore, administration of osteoporosis drugs independently increased BMD in both lumbar spine and femoral neck, indicating its importance for the management of RA-associated osteoporosis.

W32-6

Effect of Tocilizumab or Abatacept on bone metabolism in postmenopausal female patients with Rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify the early effect of Tocilizumab (TCZ) or Abatacept (ABT) on bone metabolism in postmenopausal female patients with rheumatoid arthritis (RA) [Methods] 40 postmenopausal female patients with active RA were started on treatment with TCZ (n=23) or ABT (n=17). Circulating levels of NTx, osteocalcin (OC), soluble RANKL (sRANKL), osteoprotegerin (OPG), and dickkopf-1 (DKK-1) were examined at baseline and after 4 weeks. [Results] In TCZ group, average of NTx, sRANKL, sRANKL/OPG, and DKK-1 levels at 4 weeks decreased significantly from the baseline (25.9 vs 23.6 nmol BCE/L: p=0.0079, 0.23 vs 0.19 pmol/L: p=0.0147, 5.18 vs 4.11%: p=0.0166, 2619 vs 2131 pg/mL: p<0.0001). Average of OC levels at 4 weeks increased significantly from the baseline (9.4 vs 11.0 ng/mL: p=0.0323). In ABT group, average of NTx, OC, sRANKL, and sRANKL/OPG levels at 4 weeks were not change from the baseline. Meanwhile, average of DKK-1 levels at 4 weeks decreased significantly from the baseline (2278 vs 1990 pg/mL: p=0.025). [Conclusions] These results indicate that TCZ rapidly improves bone metabolism in postmenopausal female patients with RA via the control of RANKL/OPG and DKK-1. In promoting bone formation, TCZ may be a useful treatment strategy in postmenopausal female patients with RA.

W33-1

Risk factors for denosumab non-responder are glucocorticoid use and bisphosphonate pretreatment, not rheumatoid arthritis

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Conflict of interest: None

[Objective] To identify risk factors for no-responders (NR) to denosumab (DMAb). [Methods] The subjects were 173 women (age 72.7 years, 64 with RA, 74 with pre-treatment) treated with DMAb for 3 years. Cases without exceeding LSC (least significant change) were defined as NR. [Results] Glucocorticoid (GC) was used in 23 (13.3%), pre-treatment with bisphosphonate (BP) in 40 and teriparatide in 34. Overall, lumbar bone mineral density (LBMD) increased significantly by 11.9% and total hip BMD (TBMD) increased by 5.6% over 3 years ($p < 0.01$). Using LBMD and TBMD as indicators, NR was 8 cases (4.6%) and 33 cases (19.1%), respectively. As to LBMD, only GC use (HR 2.01, 95% CI 120-3.37, $p < 0.01$) was a risk factor for NR. Cox proportional hazard analysis revealed that pre-treatment by BP (HR 1.77, 95% CI 1.13-2.78, $p < 0.01$) and TBMD values at baseline (HR 0.03, 95% CI 0.01-0.22, $p < 0.001$) were identified as risk factors for NR in TBMD. BMI (body mass index) was a boundary risk factor (HR 2.66, 95% CI 0.99-6.92, $p = 0.06$). RA was not a risk factor for NR in either analysis. [Conclusion] BP pre-treatment and GC use are likely to decrease the effect of DMAb. Low TBMD values are less likely to cause NR is thought to indicate a phenomenon in which the lower the BMD, the higher the effect.

W33-2

Examination of switching drug from Denosumab

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Conflict of interest: None

[Objective] We investigated whether overshoot could be prevented by using lysedronate (BP), zoledronic acid, and romosozumab as switching agents from denosumab. [Methods] Bone metabolism markers for patients with 100% compliance rate after switching from 6 months after the final injection of denosumab to cases in which denosumab administration increased to 70% or more in both lumbar spine and femur DXEA after 3 years or more., Measure lumbar and femoral bone mineral density. [Results] TRACP-5b could not be suppressed by switching to any drug, and the rate of change showed similar changes. On the other hand, in P1NP, BP increased from 6 months after administration, whereas romosozumab showed a marked increase from an early stage. In addition, maintenance of lumbar and femoral bone mineral density, which could not be maintained by BP, was observed. [Conclusions] When switching, it is considered that a bone formation promoter is better than a bone resorption inhibitor. Since the PTH preparation increases the bone resorption effect as well as the bone resorption effect, the bone density temporarily decreases, but romosozumab is considered to be suitable as a switching drug because it has a bone resorption effect without an increase in bone resorption.

W33-3

Results of three-year denosumab treatment in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] The use of denosumab (DMB) in patients with osteoporosis has been proven to be effective. We examined the continuation status and therapeutic effect of the cases more than 3 years after the start of this administration. [Subjects and methods] The subjects were 64 cases (3 males/61 females, average age 74.9 years). Pre-administration treatment was untreated in 17 cases. The continuation of treatment was investigated for these cases, and bone mineral density (lumbar spine, proximal femur, femur neck, radius) and bone metabolism markers (TRACP-5b, BAP) were measured at the start of administration and every 6 months. Then, the change of over time for 3 years was examined. [Results] The continuation status was 61 cases (95.3%) for 1 year and 50 cases (78.1%) for 3 years. In 44 patients whose bone mineral density could be measured for 3 years, the lumbar % YAM (mean) at the start and 36 months was 83.0, 90.2, and proximal femur% YAM was 71.3, 74.5, femoral neck% YAM was 73.2, 76.9, radius% YAM was 60.9, 63.5, showing significant increases in all sites. On the other hand, regarding bone metabolism markers, TRACP-5b (mU/dl) at the start, 6/12 and 24 months was 477.0, 285.3, 289.5, 324.8, and BAP (μg/L) was 17.5, 10.7, 10.2, 10.0, and significant decrease was maintained.

W33-4

Examination of bone mineral density, geometry, and bone microstructure for 12 months after the start of administration of the anti-sclerostin antibody Romosozumab in HR-pQCT study

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Conflict of interest: None

[Objective] HR-pQCT was used to examine bone changes 12 months after the start of Romosozumab (ROMO) administration. [Methods] Bone volumetric mineral density (vBMD), geometry, and bone microstructure before, 3, 6, 9, and 12 months after ROMO administration in 61 patients with severe osteoporosis (73 ± 9 years) were measured by HR-pQCT. [Results] Total vBMD and cortical (Ct.) vBMD decreased significantly over time up to 12 months. Trabecular (Tb.) vBMD and inner Tb. vBMD decreased significantly up to 6 months, but increased significantly at 9 and 12 months compared to before administration. Geometry showed a significant decrease in Ct. bone area and Ct. thickness after 3 months, and a significant increase in Tb. bone area up to 6 months. Ct. porosity increased significantly after 12 months, and Tb. number decreased significantly after 6 months. [Conclusions] In a study using HR-pQCT, Ct. vBMD decreased with increased Ct. porosity after ROMO administration, but in Tb. bone, a significant increase in vBMD was observed after the decrease at the early stage of administration. Furthermore, the decrease in Ct. thickness and Ct. bone area and the increase in Tb. bone area suggested bone resorption on the endosteal side.

W33-5

Effects of the treatment of Romosozumab in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We investigated whether the effects of ROMO treatment could be obtained in the RA group in the same manner as in the non-RA group. [Methods] Propensity score matching was performed, and clinical results were examined for the rate of increase in bone mineral density (BMD) for 6 months and 1 year. We used Statistical methods by repeated measures ANOVA. [Results] In the matched 33 RA patients, 13 patients used biologics, disease duration was 21 years, and DAS28-CRP was 1.94. 33 cases were extracted from the non-RA group, and the average age for RA / non-RA was 73/80 years ($p<0.01$), and the BMI was 21/20 ($p=0.13$), lumbar spine (LS) BMD was 0.81 / 0.79 ($p=0.51$), femoral neck (FN) BMD was 0.46/0.43 ($p=0.06$). Prior to treating by ROMO, patients were non-treated in 16/12 cases ($p=0.46$), treated with bisphosphonate in 10/7 cases ($p=0.37$), Denosumab in 7/2 cases ($p=0.43$), PTH in 3/8 cases ($p=0.16$). There was no significant difference in background factors other than age. The rate of change in LS-BMD for 6 months/year was 7.3/9.7% in RA and 8.5/10.7% in non-RA and FN-BMD was 1.5/3.4% in RA and -0.1/1.9% in non-RA. There was no significant time or interaction. [Conclusions] We showed that the effect of ROMO treatment in the RA group was equivalent to that in the non-RA group.

W33-6

Prevalence and Treatment Rate of Osteoporosis in Patients with Rheumatoid Arthritis at First Appearance to Specialty Section (Second Report)

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Conflict of interest: Yes

[Objective] Rheumatoid arthritis (RA) often occurs concomitantly with osteoporosis (OP). This retrospective study investigated the prevalence and treatment rate of OP in patients first presenting with RA. [Methods] In the Toyohashi RA Database, 180 patients were diagnosed with RA from January 2017 to August 2020. Bone mineral density (BMD) was measured in the lumbar spine (LS), total hip (TH), and femoral neck (FN). Patients were categorized as N-RA (initially diagnosed with RA at this visit) and A-RA (previously diagnosed with RA elsewhere). The prevalence of OP was evaluated using only BMD < 70% young adult mean (YAM), and the prevalence of OP treatment was measured. [Results] The prevalence (%) of OP in LS, TH, and FN were as follows: female N-RA: 12.7, 18.3, and 31.0, respectively; male N-RA: 3.1, 6.3, and 9.4, respectively; female: A-RA 1.7, 21.7, and 28.3, respectively; and male A-RA: 5.9, 0.0, and 11.8, respectively. The prevalence of treatment for OP in N-RA was 7.8% at our initial visit and 52.4% after our evaluation. The prevalence of treatment for OP in A-RA was 36.4% at our initial visit and 71.4% after our evaluation. [Conclusions] N-RA and A-RA frequently had concomitant OP requiring treatment. OP in the FN was more common among RA patients than elsewhere.

W34-1

Relationship of falls, fractures, and osteosarcopenia in rheumatoid arthritis patients analyzed by four years data of longitudinal study

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Conflict of interest: None

[Objective] Osteosarcopenia was defined as combined with osteoporosis and sarcopenia. Relationship of falls, fractures, and osteosarcopenia in rheumatoid arthritis (RA) was investigated by longitudinal study (CHIKARA study). [Methods] The patients are divided four groups as SP-OP-, SP+OP-, SP-OP+, and SP+OP+ at baseline status. SP was diagnosed by criteria of AWGS 2014. OP was defined as patients treated with osteopo-

rosis. Survival rate (SR) and cox hazard ratio (HR) were analyzed by using falls and fractures as endpoint. [Results] 100 RA patients (female rate: 78%, mean age: 66.1 years) were divided SP-OP- (n=45), SP+OP- (n=17), SP-OP+ (n=27), and SP+OP+ (n=11). There were 35 falls and 19 fractures. The SR of falls in SP+OP+ (36.4%) was significantly lower than other groups (SP-OP-: 75.6%, SP+OP-: 64.7%, SP-OP+: 51.9%, P=0.021). The SR of fractures in SP+OP+ (54.5%) was relatively lower than other groups (SP-OP-: 86.7%, SP+OP-: 82.4%, SP-OP+: 81.5%, P=0.121). The HR of falls and fractures in SP+OP+ significantly increased 3.32-hold (95%CI: 1.01-10.9) and 2.73-hold (95%CI: 0.61-12.2) compared that in SP-OP-. [Conclusions] The survival rate as endpoint of falls and fractures in osteosarcopenia was lower during 4 years. Osteosarcopenia is an independent risk factor of falls in RA patients.

W34-2

Prevalence of and factors associated with frailty in Japanese patients with rheumatoid arthritis; results from the IORRA cohort study

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Conflict of interest: None

Objective: The aim of this study was to evaluate the prevalence and associated factors of frailly in Japanese patients with rheumatoid arthritis (RA) enrolled in the IORRA cohort study. **Methods:** For the current study, we analyzed the database for the 39th IORRA survey conducted in 2019. In this survey, patients were invited to complete 5 questionnaires as reported previously (J Am Med Dir Assoc, 2015). Patients who had ≧3 points of frailty score were defined as having frailty. Logistic regression analysis were used to evaluate association of frailty with gender, age, disease duration, body mass index, Japanese Health Assessment Questionnaire Disability Index (JHAQ-DI), DAS28, and medication uses. **Results:** Among 3,290 Japanese patients with RA included in this analysis, 549 (16.7%) complicated frailty. In multivariate models, JHAQ-DI [Odds Ratio (OR) 2.1, 95% confidence interval (CI) 1.8-2.6)], DAS28 (OR 1.4, 95% CI 1.2-1.6), NSAIDs use (OR 1.8, 95% CI 1.4-2.4), amd methotrexate (MTX) use (OR 0.67, 95% CI 0.50-0.89) were siginificantly (P<0.01) associated with frailty. **Conclusion:** Many Japanese patients with RA complained with frailty. Disability, disease activity of RA, NSAIDs use, and MTX disuse appears to be associated with frailty in japanese patients with RA.

W34-3

Characteristics of osteopenia and osteoporosis in psoriatic arthritis

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Conflict of interest: Yes

[Objective] This study examines the factors associated with osteopenia and osteoporosis in PsA. [Methods] This study is a cohort study. The subjects were osteopenia (PsA16, RA5) and osteoporosis (PsA14, RA11). PsA was divided into two subtypes, axPsA (n=11) and peripheral PsA (n=19). The PsA group had an average age (55.2 ± 9.8) and the RA group (72.4 ± 7.7). Bone density was measured by the DXA method. Serum bone metabolism markers (P1NP, TRACP-5b) and bone remodeling effector molecules (Dkk1, sclerostin, 25 (OH) D), and serum IL-17 were compared and examined. We also compared the frequency of fragility fractures and the evaluation of nutritional status (CONUT). [Results] Proximal femur T-score was PsA -1.4±0.7, RA-2.1±0.8, axPsA -1.7±0.9, and periPsA -1.3 ±0.5. P1NP (PsA 50.0±21.7, RA40.5±25.7), TRACP-5b (PsA 314.2±133.2, RA456.9±200.9), Dkk1 (PsA 3642±1237, RA3114±1606) and sclerostin (PsA 145.0±96.5, RA86) and IL-17 (PsA 3.0±6.2, RA1.2±1.2) were calculated. The frequency of fragile fractures was PsA50% (axPsA80%, periPsA 33.3%) and RA27.3%, and axPsA had many fragile fractures. CONUT score were PsA 0.9±0.9, RA1.8±2.1, axPsA1.3±1.5, and periPsA 0.7±0.7. [Conclusions] axPsA has lower bone mass, malnutrition, and a higher rate of fragile fractures (80%) than periPsA.

W34-4

The therapeutic effect for osteoporosis on femoral neck bone mineral density is diminished under the COVID-19 pandemic

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Conflict of interest: None

[Objective] To test the effect of lack of exercise due to COVID-19 pandemic on the treatment of osteoporosis (OP). [Method] Patients (n=364) who received BMD (bone mineral density) measure from June to September 2020 were enrolled. Patients (n=167) with 5 consecutive data every 6 months were analyzed. [Result] The total treatment period was 75.2 ± 114.8 months. Denosumab was the most commonly used medicine, followed by bisphosphonates. Eldecalcitol was the most common as a concomitant vitamin D. Lumber BMD increased stably with the rate of 1.62, 1.24, 1.29, 1.70%. However, increasing rate of femoral neck BMD (NBMD) fluctuated to -0.14, 2.14, 1.44, and 0.45%, and the rate of increase in the last 6 months was low. A logistic regression analysis adjusted for age and gender was performed to predict risk factor for negative rate of increase in past 6 months (n=79). The body weight and the rate of increase during previous 6 months were extracted as significant risk factors. There was no effect of the duration of treatment or the type of medicines. [Conclusion] Decreased activity under COVID-19 pandemic might diminish the therapeutic effect of medicine for OP on NBMD, and more attention should be paid to underweight patients and those with good therapeutic effect before self-restraint.

W34-5

Macrophage migration inhibitory factor and fibronectin released from degenerated cartilage by mechanical loading may cause synovial pathologies and pain in OA knee joints

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Conflict of interest: None

[Objective] To investigate whether macrophage migration inhibitory factor (MIF) and fibronectin (FN) released from degenerated cartilage by mechanical loading can cause synovial changes in OA. [Methods] Cartilages were obtained from 7 OA knees at both macroscopically preserved areas (P) and degenerated areas (D). Control cartilages (C) were obtained from 9 non-OA knees at dissection. A cartilage tissue was placed in PBS and 1MPs of load was given repeatedly. After 60 times of loading, PBS was recovered, and the concentrations of MIF and FN were determined. The effects of rhMIF and 29kDa FN fragments (FN-F) on primary cultured OA synovial fibroblasts was evaluated by gene expression analysis. [Results] MIF and FN were released in greater amounts from D cartilages than C or P cartilages. In the cultured fibroblasts, the treatment with rhMIF increased the expression of IL-1β, TNF-α, IL-8, MMP-1, NGF, and COX-2 significantly, and a similar trend was observed with FN-F. When the cells were treated with rhMIF and FN-F, the expression of IL-1β and MMP-1 was more enhanced than in the cells treated with either protein alone. [Conclusion] MIF and FN may be released from degenerated cartilage by loading and may induce the expression of inflammatory cytokines and NGF in OA synovial fibroblasts.

W34-6

Analysis of synovial fluid samples collected from OA knees that underwent synovial flare

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Conflict of interest: None

[Objective] In order to obtain clues to dissect synovial pathology in OA, an analysis was performed on synovial fluid (SF) samples collected from OA knees that underwent synovial flare. [Methods] Synovial flare was determined by acute aggravation of pain and the presence of tenderness on synovium. SF samples were obtained twice in each knee in the middle of flare (F) and after the resolution of flare symptoms (AF). Using Luminex, concentrations of several proteins that could be involved in OA pathology were compared between each pair of samples. Plasmin activity of the SF samples was determined by an activity assay kit. [Results] A total of 22 pairs of samples (44 in total) were used for the analysis. The all SF samples contained substantial amounts of MMPs-1, 2, 3, and their concentrations were higher in F than in AF in 16-21 sample pairs out of 22. Unexpectedly, the concentration of uPA was also higher in F than in AF in all sample pairs but one. The result of the activity assay indicated that 10 out of the 22 F samples had detectable levels of plasmin activity. [Conclusions] Our analysis has shown that the SF of the knees undergoing synovial flare may have enhanced proteolytic activity. This may account for rapid OA progression often observed in flare cases.

W35-1

Social participation in old rheumatoid arthritis patients does not affect cognitive impairment but reduces depressive symptoms

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Conflict of interest: None

[Objective] This study aims to clarify the assosiations between social participations and cognitive impairments or depresseive symptoms in old rheumatoid arthritis patients (oRA). [Methods] We colletced clinical, social, and cognitive/depressive information of oRA patients through self questionnaire method in X prefecure in Japan in 2019. We compare this data with a dataset on Japan Gerontological Evaluation Study performed in 2016. [Results] oRA patients did not show high incidence of subjective cognitive impairement, but showed significantly higher score of depressive symptoms compared with general residents in the same area. The odds ratio for depressive symptoms in non-social participation oRA patients was 1.46 (1.1-2.0) compared with oRA enjoying social participations. [Conclusions] Social participation in old rheumatoid arthritis patients does not affect cognitive impairment but reduces depressive symptoms.

W35-2

Senior Rheumatoid Arthritis Patients' Walking Habits and Features

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Conflict of interest: None

[Objective] This research aims to reveal the walking habits of senior rheumatoid arthritis (RA) patients and the respective features. [Methods] Targets are RA patients over the age of 65. The walking experiment group (experiment group) was asked to walk twice a week (20 mins or above for each time) for a year. Gender, height, weight, BMI, incidence period, medication status (MTX, PSL, biological formulation), blood samples (anti-CCP antigen, creatinine, cystatin C, Sarcopenia Index (SI), CRP, ESR, MMP-3, eGFR), diseases activity, thigh bone density (T-score), and dysfunction index. Statically, subjects are divided into two groups with or without walking habit for the χ^2 inspection of the independence of their gender and medication status. As for other items, the two groups were compared using Mann-Whitney U test and two-sample t test were taken as background factors. [Results] The number of target was 87 (average age 71.0±10.7). The experiment group contained 44 subjects (50.6%). There are significant differences in the SI inter-group comparison (experiment/control group 0.78±0.13/0.65±0.12) and T-score (-1.5±1.1/-2.0±0.9). The experiment group achieved better scores. [Conclusions] When compared with the control group, it is proved that the walking group has better bone mass and density.

W35-3

Coexistence of Locomotive syndrome and assessment of Locomo25 in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] Rheumatoid arthritis (RA) causes systemic functional disability with multiple joint involvement and is recently considered as a causal disease of locomotive syndrome. However, it is still unknown how RA is associated with locomotive syndrome. [Methods] We conducted a cross-sectional study in KURAMA cohort in 2019. We recruited a consecutive 470 patients and collected demographic data and functional assessment such as mHAQ, Locomo25, muscle mass, and others. [Results] DAS 28-ESR was 2.90 in average. The ratios of users of bDMARD+tsDMARDs, MTX, and PSL were 44.9%, 62.3%, and 21.9%, respectively. Multivariate analyses showed that PtVAS, the dose of PSL, the duration of the disease, and BMD independently contributed to mHAQ, while PtVAS, the dose of PSL, BMI, and BMD did to Locomo25. Moreover, the duration of the disease, the dose of MTX, BMI, and BMD contributed to the muscle mass, but the dose of PSL did not. [Conclusions] mHAQ seems to reflect a disease-specific factor, while Locomo25 does a global functional disability. Furthermore, PSL may contribute to functional disability without influence of muscle mass.

W35-4

Incidence and risk factors for falling in patients with rheumatoid arthritis: a comparison after introduction of treat-to-target strategy

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Conflict of interest: None

[Objective] The incidence of falls in rheumatoid arthritis (RA) patients due to muscle weakness and painful joints has increased over the past decade compared with older adults, although RA disease activity may currently be well controlled with a treat-to target strategy. This study assessed the incidence and risk factors of falls in RA patients compared with previous incidence data. [Methods] Participants were 228 patients with RA (age 20-92 years [mean 67.6 years], 82.5% women) who responded to a questionnaire on falling and history of falling during the previous 1 year.

These data were compared to results of a 2007 retrospective study. [Results] The current fall incidence was 25.9%, was no difference in the 2007 study, nevertheless mean age was higher. Univariate analysis showed characteristics of patients who reported any falls were higher Steinblocker class/stage, visual analog scale score, health assessment questionnaire score, and number of drugs; disability walking up/downstairs without handrail use and on 1-km walking; wearing socks while standing; squeezing a wet cloth; and a strong fear of falling, which aligned with the 2007 study results. [Conclusions] Well controlled disease activity may decrease fall incidence under treat to target strategy.

W35-5

A study of self-efficacy in patients with rheumatoid arthritis-Factors affecting the relationship between patients' self-efficacy and quality of life in general-

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Conflict of interest: None

[Introduction] The self-efficacy of RA patients is affected by their disease, and low self-efficacy is a factor in the decline in physical activity and quality of life. In this study, we examined the characteristics of outpatients with RA based on the relationship between self-efficacy and RA symptoms. [Methods] Seventy-one female RA patients (65.9±14.0 years old) who were able to maintain good disease activity were included in the study. Patient demographics, HAQ, locomotive25 and EQ-5D were Z-scored and classified using hierarchical cluster analysis for multiple comparisons. The assessment items were PDAS, PCS, HADS, PSEQ, TSK and GSS. [Results] Based on the dendrogram, the number of clusters was determined to be 3. Differences in PDAS, PCS, PSEQ, TSK, and GES were found between clusters, and patients with low self-efficacy tended to have negative thoughts, modulated pain perception, and were inactive and had a lower quality of life. [Discussion] Patients were classified into three clusters based on their self-efficacy status. In order to improve the quality of life in RA, it is important to increase patients' self-efficacy and to establish a new type of rehabilitation medicine that focuses on the promotion of physical activity.

W35-6

Investigation of catastrophizing and splint fixation in CRP remission patients with chronic pain

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Conflict of interest: None

[Objective] Catastrophizing in chronic pain was investigated. We examined the effect of splint fixation. [Methods] Thirty-five patients with hand or hand joint pain for more than 3 months and CRP remission for more than 6 months before and after ultrasound examination were included in the study. The survey was conducted as follows: catastrophizing, ultrasound assessment, and MMP-3. Statistics were examined for catastrophizing and MMP-3 by chi-square tests, dividing the inflamed and uninflamed groups by ultrasound. Splint fixation was prescribed for those who couldn't rest. [Results] Inflammation was observed in 24 cases (68%). catastrophizing was observed in 8 patients (33%) in the inflammation group and 5 patients (45%) in the no inflammation group, which was not significantly different. There was a significant difference in MMP-3 in the inflammation group (50% vs. 18%). Splint fixation was prescribed for six patients in the inflammatory group, and pain and inflammation were reduced after three months. [Conclusions] In those CRP remission, 68% of patients present with inflammatory findings. Intensified treatment is needed. In patients with a PCS score of 30 or higher, 61% (8 of 13) had inflammation. There is a need for treatment for inflammation.

W36-1

Clinical implications of early LLDAS achievement in remission induction therapy for active systemic lupus erythematosus

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Conflict of interest: None

[Objective] To find the clinical implications of achieving lupus low disease activity state (LLDAS) within 12 months after induction therapy in systemic lupus erythematosus (SLE). [Methods] We prospectively enrolled patients with active SLE received induction therapy since 2015. Inclusion criteria were the patients with BILAG A≧1 or B≧2 or severe SLENA-SLEDAI Flare Index (SFI) and who were followed for at least 12 months after using prednisolone (PSL)≧0.4 mg/kg/day. LLDAS achievement within X months of initiation (LLDAS≦XM) was investigated every 3 months until X=18, along with clinical measures. [Results] Seventy-nine patients were enrolled. The mean observation period was 39.7 months, and 71 (89.9%) patients experienced LLDAS with 28 flares based on SFI and 17 having severe flares. Compared to non-achievement, LLDAS≦XM achievement was associated with significantly fewer overall flares during the period, X=9, 12 (p=0.016, p=0.009), and only X=12 (p=0.008) with significantly fewer severe flares. The group LLDAS≦12M had fewer severe flares during and after achieving LLDAS and had lower SLEDAI and PSL at last observation, but no difference in change in SLICC damage index. [Conclusions] Achievement of LLDAS within 12 months after induction therapy may lead to a reduced risk of flare.

W36-2

Close relationship between Lupus Low Disease Activity State (LLDAS) and DORIS (Definitions Of Remission In SLE) remission, usefulness, and clinical characteristics of unremitted patients

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Conflict of interest: None

[Objective] To clarify relation between LLDAS and DORIS remission, usefulness, and clinical characteristics of unremitted patients. [Methods] Eighty-tree SLE were divided into LLDAS, not LLDAS and 4 stages of DORIS remission. [Results] Seventy-eight % of 51 LLDAS and 98% of 49 cumulative LLDAS≧50 had remission. Nineteen clinical ROT and 21 complete ROT had LLDAS. LLDAS and DORIS remission were, thus, tightly overlapped. When following up SLE, it was useful to use LLDAS with PSL≦7.5 mg/day and no subdivision, combined with DORIS remission with maintenance of PSL≦5 mg/day and four stages of remission. Fourteen patients never had remission: 5 without LLDAS and remission, and 9 with LLDAS and without remission. Eight had nephropathy: 2 thrombocytopenia, 1 thrombocytopenia + pulmonary hypertension, 1 leukocytopenia + discoid erythema, 1 LLDAS and 1 flaring LLDAS. Fourteen unremitted patients had significantly higher minimal and maximum SLEDAI-2k with tendency to have higher PSL maintenance, more nephropathy and SDI than those of 69 remitted patients. [Conclusions] LLDAS and DORIS remission were tightly overlapped, and combined use of LLDAS and DORIS remission was useful to follow up SLE. Renal damage and thrombocytopenia frequently prevented to achieve LLDAS and DORIS remission.

W36-3

Predictors for early achievement of low disease activity or remission in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] This study aimed to reveal predictors of achieving low disease activity or remission in patients with systemic lupus erythematosus (SLE). [Methods] The subjects of this study were 26 SLE patients (age 37.1 ± 16.5 years, 25 females) who received induction treatment from September 2015 to August 2019. We assessed the cumulative rate of Lupus Low Disease Activity State (LLDAS), clinical remission on treatment (ROT), and complete ROT. We evaluated the association between clinical characteristics and outcomes. [Results] Sixteen patients had nephritis, 9 had neurological involvement, 8 had cardiopulmonary involvement, and SLE disease activity index (SLEDAI) score was 15.8 ± 8.7. The achievement rates of LLDAS, clinical ROT, and complete ROT at 2 years were 90%, 64%, and 27%, respectively. Cox proportional hazards model identified that use of mycophenolate mofetil (MMF) for maintenance treatment was associated with earlier achievement of LLDAS. [Conclusions] Achieving LLDAS and clinical ROT is a realistic therapeutic goal, and a maintenance regimen including MMF may be effective in SLE patients.

W36-4

Factors involved in the time to achieve treatment goals for serositis associated with systemic lupus erythematosus

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Conflict of interest: None

[Objective] Several risk factors for the development of serositis associated with systemic lupus erythematosus (SLE) have been reported, but none have been implicated in the time to treatment goal achievement (TGA) for serositis. We attempted to clarify these predictors. [Methods] The time to TGA was assessed on a weekly basis in SLE serositis (n=28). TGA was defined as reaching resolution of serositis on imaging, resolution of symptoms, and Hugh-Jones classification 1 degree. [Results] The median age was 44 years, and 75% were female. The most common time to achieve TGA was between 1 and 2 weeks (36%). Cases less than 2 weeks were classified as the early group (n=10) and the rest were as the late group (n=18). There were significantly more cases of pericarditis (p=0.01), renal impairment (p=0.006), high steroid doses (p=0.0497), positive anti-dsDNA antibodies (p=0.02), and decreased C3 (p=0.04) in the late group than in the early. There was no significant difference in CRP and erythrocyte sedimentation rate at the start of treatment. A multivariate analysis showed a significant difference in pericarditis (OR=39.6, p=0.048). [Conclusions] Pericarditis, renal failure, positive anti-dsDNA antibodies, and low complement may prolong the time to achieve treatment goals in SLE serositis.

W36-5

Comparisons of Different Models of SF-36 Summary Scores in Patients with Systemic Lupus Erythematosus: US vs. 2/3-Component Japanese Models

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Conflict of interest: None

[Objective] We aimed to compare the different computing models of SF-36 physical and mental component summary (PCS and MCS) scores in patients with SLE. [Methods] The data of Japanese SLE patients were retrieved from the APLC prospective cohort. PCS and MCS scores were computed using the US 2-component model, and the Japanese 2 and 3-component models. Their association with SLEDAI-2K and SDI were analyzed. [Results] A total of 114 patients and 258 visits were eligible. The PCS scores were significantly different between the US 2-component and the Japanese 2 or 3-component models ($p < 0.01$), whereas they were not significantly different between the Japanese 2 and 3-component models. The MCS scores were not significantly different between the 3 models. By the multiple linear regression analyses with the SLEDAI-2K and SDI scores as the dependent variables, the PCS scores computed by all the 3 models were significantly associated with the SDI scores ($p < 0.01$). The MCS scores computed by any of the 3 models were not significantly associated with the SDI or SLEDAI-2K scores. [Conclusions] Among Japanese SLE patients, the different computing models derive distinctive PCS scores. Although this may not cause huge difference, it should be kept in mind while interpreting the summary scores.

W36-6

The rate of achieving LDA with additional belimumab and its underlying background

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Conflict of interest: None

[Objective] We have studied the rate of achieving low disease activity (LDA) with additional belimumab (BEL) and its predictors. [Methods] We retrospectively investigated 21 patients, who visited our hospital from February 2018 to September 2020, with systemic lupus erythematosus (SLE) that lasted for more than 6 months after starting BEL. We defined LDA as having SLEDAI of 4 or less and taking 5 mg/day or less prednisolone (PSL). [Results] Of the patients, 19 were females. In average, the age of patients was 44.5 years, their duration of illness 17.2 years, and SLEDAI 5.8. Seventeen of them had taken concomitant PSL, with the dose of 11.2 mg/day. Average observation period was 14.2 months and the rate of BEL continuation was 90.5%. At the final observation, SLEDAI was decreased to 2.4 (p<0.01), PSL decreased to 5.9 mg/day (p<0.01), and LDA achievement rate significantly increased to 57.1% (p = 0.02). More patients in LDA-achieved group had taken concomitant immunosuppresant than those in non-achieved group (10 vs 3, p=0.03). Univariate analysis revealed that concomitant immunosuppresant was an independent factor associated with LDA achievement (OR 10.0, 95%CI 1.28-78.12, p=0.03). [Conclusions] These results suggest that concomitant immunosuppressants enhance the efficacy of BEL.

W37-1

Glucocorticoid discontinuation associated with disease duration and chronic damage in systemic lupus erythematosus: a cross-sectional study from LUNA registry

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Conflict of interest: Yes

[Objective] A recent randomized controlled trial reported that discontinuation of glucocorticoid (GC) increases relapse in patients with systemic lupus erythematosus (SLE). However, 73% of patients without GC maintained remission in that study. Thus, some patients could discontinue GC without relapse. Here, we evaluated whether GC discontinuation related to disease duration and chronic damage. [Methods] Using data form lupus registry of nationwide institutions, disease duration and SDI (SLICC-damage index) were compared between patients with and without GC at baseline. Relapse was evaluated in patients without GC during the observational period. [Results] Of enrolled 1019 patients, 101 (9.9%) patients did not receive GC. Patients without GC were more frequent in ≦5 or ≧20 years of disease durations (≦5: 32/254 [12.6%], 5 to 20: 35/480 [7.3%], and ≧20: 29/260 [11.1%], respectively, p = 0.043). Particularly, patients with lower SDI received GC less frequently in patients with ≧20 years of disease duration (SDI≦1: 119/141 [84.4%] and SDI≧2: 112/119 [94.1%], respectively, p=0.01). Only five patients developed relapses in 67 patients during a 2-year observation. [Conclusion] The patients with longer disease duration without severe damage might maintain remission without GC.

W37-2

Predictive factors for complete withdrawn of glucocorticoid in systemic lupus erythematosus

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Conflict of interest: None

[Objective] To elucidate predictive factors for complete withdrawn of glucocorticoid (GC) in patients with systemic lupus erythematosus (SLE). [Methods] We examined SLE patients who achieved clinical remission on treatment in our hospital from Jan 2019 to Oct 2020. Patients were divided into 2 groups according to complete withdrawn of GC. Baseline clinical characteristics and immunophenotype of peripheral blood mononuclear cells (PBMCs) were compared. [Results] Twenty patients were selected. There were 18 (90.0%) patients who could discontinue GC and 2 patients experienced flare. Baseline GC dose was not differed between patients who could discontinue GC and those who could not (3.1 ±1.8 vs 4.0 ± 1.4 mg/day). There was no difference in baseline clinical characteristics, including disease duration, immunosuppressant use, and serological activities between them. PBMCs findings showed a significant lower count of lymphocyte, CD3+T cell, and basophil in patients who flared than those who could discontinue GC (p=0.008, p=0.026, and p=0.003, respectively). [Conclusions] We found 90.0% of SLE patients who achieved clinical remission on treatment successfully discontinued GC without flare. A low number of peripheral lymphocytes, CD3+T cells, and basophils may predict flare in discontinuing GC.

W37-3

Effects of immunosuppressive drugs on successful steroid dose reduction in patients with SLE during maintenance phase: from the LUNA registry

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Conflict of interest: None

[Objective] To investigate whether the concomitant use of immunosuppressants (IS) contributes to achieving glucocorticoid reduction in patients with SLE taking PSL ≦10 mg/day. [Methods] A retrospective cohort study was conducted using data from the LUNA registry. Patients with SLE who took PSL ≦10 mg/day at the 2018 survey (baseline) and were subsequently followed up were enrolled. The main exposure was the concomitant use of IS, and the main outcome was successful PSL reduction, defined as achieving PSL dose reduction without relapse of SLE or death. [Results] Of the 461 patients analyzed, the mean age was 46.1 years, and the average dose of PSL was 5.8 mg/day. Comparing between 310 patients who received IS at baseline and 151 patients who did not, the proportions who tried PSL reduction were 62% vs 47%, respectively, and the relapse-free survival rates 1-year after reduction were 93% vs 89%, respectively. Multiple logistic regression analysis adjusted for SLEDAI, SDI score, HCQ, etc. showed that concomitant use of IS was independently associated with successful PSL reduction (adjusted odds ratio, 1.59; 95% confidence interval, 1.03-2.44). [Conclusions] In patients with SLE during maintenance phase, the concomitant use of IS may contribute to achieving glucocorticoid reduction.

W37-4

Association between glucocorticoid doses and emotional health in patients with systemic lupus erythematosus: a longitudinal analysis of a LUpus registry of NAtionwide institutions (LUNA)

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Conflict of interest: None

[Objective] We previously reported that daily glucocorticoid (GC) doses were negatively associated with emotional health (EH) among SLE patients. This study investigated whether GC tapering was associated with EH improvement. [Methods] Patients registered in LUNA were eligible if following criteria met: the history of oral glucocorticoid use; multiple follow-up visits within 5 years from 2016. The outcome was the change in EH domain score of LupusPRO. The exposure was contemporaneous differences in GC doses. The association was analyzed using both the fixed- and random-effects linear regression after multiple imputation of missing

values. [Results] Overall, 611 patients with a median of 3 visits (IQR 2-4) were included: 85% were female and the median age was 45 (IQR 35.9-57.2) years. Median SLEDAI was 4 (IQR 2-8), daily GC dose was 5.0 (prednisolone, IQR 4-9) mg and EH score was 67.2 (IQR 48.6-86.0). β coefficient was -0.76 ($p<0.01$) and -0.88 ($p<0.001$) for daily GC dose and EH score using the fixed- and random-effects, respectively. Multivariate analysis showed that β coefficient was -0.56 ($p<0.01$) and -0.71 ($p<0.001$), respectively. [Conclusions] The results suggested that GC dose reduction was associated with improvement in emotional health such as anxiety or depression in SLE.

W37-5

Efficacy of Steroid-tapering in patients of Pregnancy with Systemic Lupus Erythematosus

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) appears most commonly in young women, so it is not rare to experience pregnancy. The aim is to analyze the effects of disease activity and treatment in the course of pregnancy. [Methods] We analyzed 26 pregnancies of 20 patients in SLE from April 2011 to September 2020. [Results] Average onset of SLE was 22.1 years old, and pregnancy was 30.4. At the beginning of pregnancy, prednisolone was taken in 25 cases (average 5.7 mg), immunosuppressive (IS) drugs in 12, HCQ in 7, low dose aspirin in 5. The average SLEDAI was 1.25, anti ds-DNA antibody (Ab) was 9.6 U/mL and CH50 was 45.6 U/mL. Antiphospholipid Ab was detected in 5 patients. SLE relapsed in 5 cases during pregnancy. A case had preeclampsia with antiphospholipid antibody syndrome. There were no spontaneous abortion, 7 preterm births and 14 low birth weight infants. Prednisolone dose at pregnancy was significantly higher in preterm birth than in full term birth (5.0±3 mg vs 8.5±3.5 mg), but the use of IS drugs was not significantly different. There was no significant difference between relapse and steroid dose, SLEDAI, CH50, any antibody titers and use of IS drugs. [Conclusions] To prevent preterm birth, it was considered to taper steroid dose with IS drugs during pregnancy.

W37-6

Examination of treatment and steroid weight loss for systemic lupus erythematosus with belimumab

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Conflict of interest: Yes

[Purpose] Belimumab (BEL) is a new drug that has recently become available for SLE, but its experience is not yet sufficient. So we examined the clinical course of SLE patients who had BEL introduced in our classroom. [Method] We analyzed the patient background, PSL weight loss effect 12 weeks after the introduction, SLEDAI-2K, and LLDAS achievement rate for 15 SLE patients. Results: At baseline; average age 48.5 years, disease duration 13.4 years, and the female was 72.7%. The average SLEDAI-2K before the introduction of BEL was 6.2, the LLDAS achievement rate was 14.2%, and the average prednisolone (PSL) was 13.3 mg/day. Twelve weeks after the BEL, the PSL could be reduced by 18.2%. In terms of disease activity, SLEDAI-2K improved to 4.1, and LLDAS was achieved in 2 to 5 cases. In some cases with severe pathological conditions, there were cases in which remission was maintained and immunosuppressive drugs were added. The administration was discontinued in 5 cases, infection in 1 case, relapse of lupus enteritis in 2 cases, injection reaction in 1 case, and insufficient effect in 1 case. [Conclusion] BEL improved SLE disease activity, suggesting a PSL weight loss effect. It may also be effective in maintaining remission for severe conditions such as lupus nephritis.

W38-1

Late-onset nephritis identified as a risk factor for severe and refractory lupus nephritis

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Conflict of interest: None

[Objective] We searched for risk factors contributing to severe and refractory lupus nephritis. [Methods] We recruited patients with renal biopsy-proven lupus nephritis from the SLE database of Kyoto University Hospital. We analyzed risk factors associated with renal organ damage defined by the SDI scores, eGFR<50, and refractory nephrotic syndrome. Using multivariate analysis, including disease duration, type of nephritis, use of immunosuppressants, and late-onset nephritis. We defined late-onset nephritis as cases with renal biopsy more than 12 months after diagnosis. [Results] Among the 105 patients recruited, 36 patients (34%) had eGFR<50, and 36 (34%) had a refractory nephrotic syndrome. By single regression analysis, patients with eGFR<50 and refractory nephrotic syndrome showed a significant negative correlation with late-onset nephritis (P=0.0155, 0.0488). By multivariate analysis, including other risk factors, the same negative correlation was shown (P=0.0060, 0.0318). Notably, 77% of late-onset nephritis patients were having steroid therapy. [Conclusions] We showed that late-onset nephritis is an independent risk factor that causes renal damage. Many of these patients were having steroid therapy, which may be why they were relatively resistant to other treatments.

W38-2

Long-term outcome of lupus nephritis evaluated by revised ISN/RPS classification

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Conflict of interest: None

[Objective] Revision of ISN/RPS (International Society of Nephrology/ Renal Pathology Society) classification was suggested and modified NIH (National Institutes of Health) activity and chronicity scoring system was recommended to evaluate active and chronic lesions of lupus nephritis. 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 among Japanese subjects with biopsy proven lupus nephritis from 1977 and 2018. Pathologic lesions were evaluated according to the ISN/RPS 2003 classification and modified NIH scoring system. Patients were divided into three groups stratified by activity index and chronicity index. The primary endpoint for this study was composite of death and end-stage kidney disease (ESKD). [Results] A total of 55 subjects with a median age of 31 years were included. During the mean follow-up period of 16.1 years, 13 patients reached the primary outcome. High chronicity index increased the risk of composite events with a multivariable-adjusted hazard ratio of 15.83 (P = 0.010), adjusted by age and serum creatinine. [Conclusions] High chronicity index was associated with increased risk for composite event of ESKD and death in lupus nephritis patients.

W38-3

Clinicopathological analysis of late-onset lupus nephritis

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Conflict of interest: None

[Objective] To clarify the characteristics of late-onset lupus nephritis (l-LN). [Methods] We included LN patients subjected to renal biopsy at 12 hospitals from 2000 to 2019, and compared retrospectively between l-LN patients (>50 years at the onset of LN) and non l-LN ones. Renal pathology was evaluated by revised ISN/RPS classification 2018. [Results] Among 123 LN patients (median 39 years), l-LN included 37 (30%, median 63 years), and had higher frequencies of hypertension and diabetes, lower eGFR (61 vs 91 mL/min/1.73 m^2), and similar serum immune abnormalities. L-LN had higher rates of chronic lesions (global and segmental glomerular sclerosis, interstitial fibrosis and tubular atrophy), while ones of active lesions were similar. There were no differences in the medication for LN and total observation period (66 vs 71 months). L-LN had lower eGFR at the last visit (55 vs 82 mL/min/1.73 m^2) and a significant increase in the cumulative rates of CKD and/or death by Kaplan-Meier method. Cox regression analysis showed age as one of the independent risk factors of both CKD and death. The most frequent cause of death was infections. [Conclusions] L-LN showed a distinctive renal pathology affected by aging and comorbidities, and poorer renal and life prognoses.

W38-4

The long-term efficacy of mycophenolate mofetil in Japanese patients with lupus nephritis

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Conflict of interest: None

[Objectives] Since mycophenolate mofetil (MMF) has recently been approved for lupus nephritis (LN) in Japan, there are few reports evaluating the effects of MMF in Japanese patients. We therefore conducted a retrospective clinical study to assess the long-term efficacy of MMF in Japanese patients with active LN. [Methods] Sixteen patients (mean age 40.0±12.5 years, 14 females) who received MMF as induction therapy for LN and continued as maintenance therapy for more than 2 years were included in this study. We assessed the therapeutic effects of MMF every 3 months until 36 months after starting treatment. We collected eleven patients who received intravenous cyclophosphamide (IVCY) as induction therapy and took tacrolimus as maintenance therapy to compare the efficacy of MMF. [Results] Median urine protein levels decreased from 1.8 g/gCr to 0.2 g/gCr in the MMF group. Median serum levels of anti-double stranded DNA antibody titer decreased from 71 IU/mL to ≦12 IU/mL, median SLE Disease Activity Index decreased from 13 to 0, median daily prednisolone dosage decreased from 40 mg to 5 mg. There was no significant difference in the therapeutic effect between the MMF group and the IVCY group. [Conclusion] We have shown the long-term efficacy of MMF in Japanese patients with active LN.

W38-5

Characteristics and pathological analysis of patients with 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 SLE. [Methods] Thirty patients who underwent cardiac surgery among inpatients diagnosed with SLE from 2012 to 2018 at our hospital were included. Paraffin sections were prepared for patients who had undergone left atrial appendage resection during surgery, and consent was obtained, and immunohistochemical staining was performed using anti-human IgG antibodies, compared with histology of non-collagenous disease group investigated. [Results] Antiphospholipid antibodies were positive in 12 cases, SS-A antibodies were positive in 12 cases, and RNP antibodies were positive in 8 cases, suggesting that these autoantibodies are associated with heart disease. The left atrial appendage is stained in the myocardial tissue, and in the pathological tissue, the SLE is more dominant in the group with SLE than in the control group, and the immune complex deposition in the muscle tissue is related to the onset mechanism. We also validate another mechanism which are related to NET formation in dramatic onset. [Conclusions] The possibility of the onset of immune complex deposition in muscle tissue may be the cause of heart disease in SLE patients.

W38-6

Evaluation of joint cartilage damage by ultrasonography in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] Previously we have confirmed the usefulness of the direct imaging of finger joint cartilage by ultrasound (US) in patients with rheumatoid arthritis. In this study, we aimed to examine cartilage thickness in patients with SLE by US. [Methods] We enrolled 44 SLE patients with an episode of joint symptoms and 42 healthy subjects. The cartilage thickness of bilateral metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints were visualized from a dorsal view with joints in approximately 90 degrees flexion and measured at the middle portion. One US examiner performed the semiquantitative scoring (0-2) of the recorded cartilage images in a blinded manner. [Results] The total cartilage thickness of 16 joints tended to be decreased in SLE patients as compared with healthy control (the median 7.0 versus 7.5, p=0.057; and 4.1 versus 4.4 in MCP joints and 2.9 versus 3.0 in PIP joints, respectively). The total semi-quantitative score of 16 joints was comparable between patients with SLE and healthy subjects (the median 4.0 versus 4.0, p=0.395; and 2.0 versus 2.0 in MCP joints and 2.0 versus 2.0 in PIP joints, respectively). [Conclusions] The evaluation of finger joint cartilage damage by US is valid and the cartilage damage is limited in most of the patients with SLE.

W39-1

The efficacy and safety of anifrolumab in Japanese patients with systemic lupus erythematosus (SLE) (TULIP-2 subanalysis)

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Conflict of interest: Yes

[Objective] Evaluate anifrolumab's efficacy and safety in Japanese patients with SLE from TULIP-2 (*N Engl J Med*. 2020;382:211-21). [Methods] The phase 3 randomized placebo-controlled TULIP-2 trial (N=362) evaluated efficacy and safety of anifrolumab (300 mg IV) vs placebo at Week 52 after treatment every 4 weeks in patients with moderate to severe SLE despite standard-of-care treatment. We performed an analysis of the Japanese subpopulation of TULIP-2. [Results] In the Japanese subpopulation (anifrolumab, n=24; placebo, n=19), 40/43 (93%) had a high type I interferon gene expression signature. The proportion of pa-

tients who achieved a BILAG-based Composite Lupus Assessment (BICLA) response at Week 52 (primary endpoint) was numerically greater in the anifrolumab group vs placebo (50.0% [12/24] vs 15.8% [3/19]; treatment difference: 34.2%, 95% CI 6.9, 61.5; nominal *P*=0.014). Improvement in skin activity and flare rates (major secondary endpoints) were favorable for anifrolumab vs placebo. Consistent with the overall population, anifrolumab had an acceptable safety profile and was well tolerated. [Conclusions] The efficacy and safety of anifrolumab 300 mg in Japanese patients with SLE was consistent with the demonstrated clinical benefit of anifrolumab for the overall TULIP-2 population.

W39-2

An Open-Label Extension Study of the Safety and Efficacy of Belimumab (BEL) for up to 7 years in Japanese Patients (pts) With Systemic Lupus Erythematosus (SLE)

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Conflict of interest: Yes

[Objective] Evaluate long-term safety and efficacy of BEL in Japanese pts with SLE. [Methods] This subpopulation analysis of Phase 3 study (NCT01597622) evaluated BEL 10 mg/kg IV plus standard therapy in eligible completers (either BEL or placebo) of BEL113750 or BEL112341. Primary endpoint: safety. Secondary endpoints: SLE Responder Index 4 (SRI4); change from baseline (BL) in SELENA-SLEDAI (SS) and PGA; prednisone-equivalent dose reduction. Descriptive analyses (*post hoc*) were based on observed data and summarized relative to first BEL dose in parent/current study. [Results] Of 71 Japanese pts enrolled, 49 (69.0%) completed study, 21 (29.6%) withdrew, and 1 (1.4%) died. At any time post BL, 70 (98.6%) pts had ≧1 adverse event (AE), 42 (59.2%) had ≧1 treatment-related AE, 23 (32.4%) had serious AEs, and 11 (15.5%) had severe AEs. Proportion of SRI4 responders increased numerically from 40.9% (27/66) at Year 1, Week 24, to 84.6% (11/13) at Year 7, Week 48. Mean SS and PGA change from BL decreased numerically over time. Median (IQR) prednisone-equivalent dose decreased from 9.0 (6.7, 12.0) mg/day at BL to 5.0 (3.5, 5.0) mg/day at Year 7, Week 48. [Conclusions] A favorable safety profile and treatment response to BEL in Japanese pts with SLE were maintained for ≧7 years.

W39-3

Efficacy and safety of patients with systemic lupus erythematosus treated with belimumab for maintenance therapy

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Conflict of interest: None

[Objective] To investigate the efficacy and safety of belimumab (BEL) for systemic lupus erythematosus (SLE) [Method] Among 63 SLE patients who had passed 52 weeks after the administration of BEL at our hospital and Yodogawa Christian Hospital, patient background, persistency rate, treatment course after 12, 26, 38, and 52 weeks and adverse events were examined retrospectively. [Results] Age was 44.2 ± 14.0 years, 57 women and disease duration was 12.5 ± 10.1 years. 29 patients had a history of lupus nephritis. Before administration, C3 73 mg / dl (65-89), anti-ds-DNA antibody titer 10 IU / ml (2.4-14.2), SELENA-SLEDAI 4 (2-6), 12 cases achieved LLDAS, and PSL level was 10 mg / day (7-16). The persistency rate was 88.9%, and 7 cases were discontinued. Significantly increased from 12 weeks after BEL add on, serum C3 level increased, anti-ds-DNA antibody titer decreased, SELENA-SLEDAI improved, PSL could be reduced, and these effects persisted even at 52 weeks. The LLDAS achievement rate increased significantly from week 26 to 48% at 52 week. 3 Refractory cases and 5 relapse cases. Infectious disease occurred in 5 cases, but all improved. [Conclusion] Disease activity improves after BEL introduction and steroid dose could be reduced, but we should pay attention to infectious diseases.

W39-4

Clinical features of SLE with belimumab

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of belimumab (BLM) in systemic lupus erythematosus (SLE). [Methods] We conducted a retrospective analysis of the patient background, steroid dosage, anti-DNA antibody titers (A-DNA), and adverse events in patients with SLE treated with BLM at Shinonoi General Hospital and Kitasato University Medical Center by October 2020. [Results] There were 4 males and 25 females. The mean age was 37.6±11.8 years, the mean duration of the disease was 14.1±11.3 years. Organ lesions included nephropathy in 21 patients, skin lesions in 17, arthritis in 13, and neurological lesions in 5. At the time of BLM induction, 28 patients were treated with HCQ 15 with tacrolimus, and 10 with MMF. The steroid dosage was 12.3 ± 6.9 mg/day. A-DNA was 32.7±31.8 U/ml. Three patients temporarily suspended or discontinued BLM treatment; one patient discontinued BLM due to herpes zoster. One patient had been given an increased dose of steroids due to SLE flare. The anti-DNA antibody titers tended to decrease (p=0.056) and the steroid dosage was significantly lower (p<0.001) than at the beginning of BLM. [Conclusions] The disease was mostly well-controlled and the steroid dosage could be significantly reduced, but attention should be paid to the possibility of infection.

W39-5

Therapeutic effect of belimumab in SLE with impaired renal function

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Conflict of interest: None

[Objective] To investigate the nephroprotective effect of belimumab (Beli) in SLE with mildly impaired renal function and proteinuria. [Method] We studied 28 patients in the maintenance phase of SLE who was treated with Beli for more than 6 months. The patients were divided into those with reduced eGFR less than 60 ml/min/1.73 m2 (n=5; R group) and those with normal renal function (n=23; N group), and the effects of Beli were compared 6 months after treatment. In addition, the effect of Beli on lupus nephritis was investigated in patients with urinary protein of 0.2 g/gCr or more. [Result] After Beli treatment, urinary protein decreased in both groups, 0.48 to 0.22 g/gCr in N group and 0.32 to 0.17 g/gCr in R group. The eGFR changed from 88.9 to 89.1 and from 50.3 to 57.1, while dsDNA ab (IU/mL) decreased from 57.3 to 30.6 and from 19.5 to 9.7, respectively. The doses of prednisolone decreased in both groups. The IgG level decreased from 1377 to 1204 (mg/dL) in N group and from 1009 to 865 in R group. In 18 patients with urinary protein of 0.2 g/gCr or more, proteinuria significantly decreased from 0.54 to 0.20 to 0.23 and dsDNA antibody improved from 67 to 34 to 35.1 at 3 and 6 months after Beli. [Conclusion] Beli may be effective in treating patients with impaired renal function.

W39-6

The efficacy of Belimumab (BEL) as a sparing corticosteroid agency in patients with systemic lupus erythematosus (SLE)

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Conflict of interest: None

[Objective] The aim of this study is to evaluate the efficacy and the safety of BEL as co-treatment in the standard therapy of SLE. <second report> [Methods] Fourteen patients were enrolled. Dose of PSL, titer of anti-DNA antibody, WBC count, serum complement and SLEDAI were examined retrospectively at baseline and 24 months after administration of BEL. [Results] At the baseline, the mean age of patients was 48 years old, 11 patients were female, and the mean disease duration was 8.6 years. The mean dose of PSL was significantly reduced (mean±S. E) (baseline: 6.1±1.1 mg/day, 24 months after administration of BEL: 1.2±0.4 mg/day, *p=0.001*). Furthermore, 6 patients could withdraw PSL without the flare of SLE. There were also statistical significance about SLEDAI (2.1±0.6 vs 0.6±0.3, *p=0.03*) and the titer of anti-DNA antibody (6.8±2.2 vs 1.3±0.9 IU/ml, *p=0.03*). There were no statistical significant in WBC count and serum complement. As for adverse event, bacterial pneumonia and pulmonary cryptococcosis were revealed. [Conclusions] Our study is suggested that co-treatment with BEL on standard SLE therapy may prevent the flare of SLE and reduce the dose of PSL among the patients under the maintenance treatment of SLE. In almost half of the cases, patients could withdraw PSL without the flare.

W40-1

Risk factors for idiopathic femoral head necrosis in systemic lupus erythematosus

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Conflict of interest: None

[Objective] To clarify the factors related to idiopathic osteonecrosis of the femoral head (ION) in patients with SLE. [Methods] One hundred and twenty-seven patients with SLE were selected on the basis of having been newly diagnosed and requiring high-dose prednisolone, including pulse therapy, as the initial treatment. All the patients initially underwent MRI at 3 months after the start of treatment to detect any early changes in the femoral head. These examinations were then performed again 3 months later. Laboratory parameters were evaluated at the start of treatment and at 1 month thereafter. [Results] By 3 months after the start of treatment, ION was diagnosed by MRI in 33 patients (25.9%). Ten patients were unilateral. The occurrence of ION was not related to SLEDAI except for proteinuria (p=0.04). However, the total cholesterol level at 4 weeks after the start of steroid treatment tended to be higher in patients with ION. Patients with a higher triglyceride (TG) level showed a significantly higher frequency of ION both before (p<0.001) and 4 weeks after (p<0.001) steroid initiation. In a bilateral and unilateral comparison of ION, CH50 was lower in bilateral (p =0.01). [Conclusions] A high TG level and proteinuria are risk factors for ION in patients with SLE.

W40-2

The flare and damage of patient with systemic lupus erythematosus in long term maintenance therapy (The second report)

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Conflict of interest: Yes

[Objective] Results of long term conventional maintenance therapy in patients with SLE are not clear. [Methods] The flare and damage of 33 patients with SLE who had history of maintenance treatment more than 20 years were examind retrospectively. [Results] The onset of SLE was an average of 26.2 years old and a duration of treatment period was 20- 46 years, an average of 25.8 years. At the time of onset strong activity including lupus nepheritis, alveolar hemorrhage and CNS lupus was seen. Large dose steroid treatment, steroid pulse therapy and cyclophosphamid IV therapy were carried in more than 80 percent. Less than 5 mg of steroid was done in the majority an average of 25 years later. At the onset of SLE, the DNA antibody was positive and became negative by 80 percent, and positiveness of a ANF and anti SS-A antibody continued. Flare was observed in a case of 3/4, and there was serious flare in a case of 1/4, and significant correlation was observed in accumulation of damage and the number of times of flare. 3 patients of more than 7 damage score were dead by cardiovascular disease. [Conclusions] For the more improving of vital prognosis and QOL, the restrain accumulation of damage by prevention of flare should be need in long treatment of a SLE patient.

W40-3

Risk factors of in-hospital mortality in patients with systemic lupus erythematosus using Japanese health insurance database

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Conflict of interest: None

Objective: To investigate risk factors of in-hospital mortality in Japanese patients with systemic lupus erythematosus (SLE). **Method:** Using claims data, we defined individuals as SLE cases if they had at least one ICD10 code of SLE, had at least one medication for SLE between April 2008 and January 2018, and were >=18 years old (n=20,991). Patients were followed from the first month in which cases met the above criteria until the month of loss of follow-up or June 2018. In-hospital mortality was defined using the summary of discharge. We calculated adjusted hazard ratio (adjHR) of covariates for in-hospital mortality using the Cox proportional hazard model. **Results:** The median age was 54 years, 81.0% were female. 10,832 cases had been admitted to the hospital, and 902 cases died. Covariates with significant adjHRs for in-hospital mortality were as follows: age by decade, 1.7 [1.6-1.8]; male, 1.5 [1.2-1.7]; hypertension, 1.2 [1.0-1.4]; renal failure, 1.5 [1.3-1.8]; depression, 1.5 [1.0-2.2]; pulmonary disease, 1.3 [1.1-1.6]; malignancy, 2.6 [1.9-3.5]; the calendar year of the observation start 2013-2018 (vs. 2008-2012), 0.5 [0.4-0.5]; and admission to intensive care unit, 2.6 [2.1-3.2]. **Conclusions:** In-hospital mortality and its risk factors were identified in patients with SLE.

W40-4

Differences in the impact of Juvenile-Onset and Adult-Onset SLE patients on SDI: a cross-sectional study using the LUNA registry

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Conflict of interest: None

[Objective] It has been reported that juvenile-onset SLE is more likely to be high disease activity, and accumulate SDI. We evaluated the impact of onset age on the current accumulation of SDI in SLE patients by adjusting for onset era. [Methods] A cross-sectional study was conducted using 2019 data from the LUNA registry. We included patients with SLE onset since 1990 who were diagnosed on younger than 18 years of age (juvenile-onset) and between 18 and 50 years of age (adult-onset), and compared SDI at 2019 considering onset era (past-era; 1990-1999, middle-era; 2000-2009, recent-era; 2010-2019). [Results] Of the 687 patients analyzed, 103 juvenile-onset and 584 adult-onset SLE were included. (the mean age was 14 and 31 years at onset, and 30 and 44 years in 2019, respectively). The mean SDI scores were 1.0 (interquartile range 0-2.0) in both groups. Linear regression adjusted for onset era, steroid dose, age, and gender showed that, juvenile-onset SLE was significantly associated with an elevated SDI (β-coefficient: 0.48, 95% confidence interval: 0.09-0.87). [Conclusions] We found that SLE patients with juvenile-onset are more likely to have an elevated SDI than those with adult-onset.

W40-5

Clinical features of 26 cases with late-onset systemic lupus erythematosus

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Conflict of interest: None

Objective: Late-onset systemic lupus erythematosus (SLE) has been considered to have the features of atypical manifestations compared with early-onset SLE. The aim of this study is to assess the features of late-onset SLE by age. Methods: Medical records of 26 patients who was diagnosed with SLE and over 50 years old at onset were reviewed. Results: There were the 50s (n=17), 60s (n=7), 70s (n=1) and 80s (n=1). We compared the 50s group and over 60s group including the 70s and 80s on the clinical features at onset. Skin rash was more frequent in the over 60s group as compared to the 50s group. There was no significant difference in the male to female ratio (0. 1 vs 0.3, p=0.302), arthritis (76.5% vs 55.6%, p=0.382), lupus nephritis (41.2% vs 33.3%, p=0.061) and pleuritis (0% vs 22.2%, p=0.111). The usage rates of immunosuppressants were lower in the over 60s group (22.2%) than the 50s group (58.8%), although there was no significant difference (p=0.110). Conclusion: In our study, there were not many differences in the comparison of the 50s and over 60s. The usage rates of immunosuppressants tends to be lower in over 60s group. As the risk of complications is high in the treatment of late-onset SLE, it is necessary to set therapeutic strategy and goal for late-onset SLE.

W40-6

Clinical features of late-onset systemic lupus erythematosus in comparison to early-onset patients

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Conflict of interest: None

Objectives: To assess the clinical features of patients with late-onset systemic lupus erythematosus (SLE) in our hospital. Methods: We retrospectively compared the features late-onset and early-onset SLE in patients admitted to our hospital between 2009 and 2019. Patients who developed SLE at an age ≧ 50 years were classified as having late-onset SLE. Results: Out of the 90 patients with SLE, 25 were late-onset cases. Fever (28.0% vs 36.9%) and rash (28.0% vs 47.7%) were less frequently observed in late-onset SLE, but the difference was not statistically significant. Arthritis, pleuritis, and renal and neuropsychiatric involvements were similar between the two groups. Regarding laboratory findings, anti-Smith antibodies (16.0% vs 58.5%, p=0.0003) were significantly less common in late-onset SLE, but the other parameters were similar between the two groups. The percentage of patients with fragility fracture receiving steroid therapy was significantly higher in the late-onset group (28.0% vs. 0%, p=0.0003). Conclusion: In contrast to previous reports, most of the clinical and laboratory characteristics of patients with late-onset SLE were not significantly different from those with early-onset SLE. However, there was a higher risk of fracture during treatment in late-onset SLE.

W41-1

Association between peripheral blood immune cell trends and clinical outcomes in remission induction therapy for systemic lupus erythematosus

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Conflict of interest: Yes

[Objective] To find the relation between peripheral immune cells and clinical outcome in induction therapy (IT) for systemic lupus erythematosus (SLE). [Methods] We prospectively enrolled patients with active SLE since 2015. Peripheral immune cells were analyzed before and after 3 months (3M) of treatment and compared with and without achieving lupus low disease activity state within 12 months (LLDAS≦12M). [Results] Forty (49.4%) of 81 patients achieved LLDAS≦12M. The percentage of LLDAS≦12M was significantly higher in the group with high plasmablast (PB) at baseline and decrease after 3M. In the IVCY group, naïve T cells and general B cells decreased after 3M, and in the MMF group, activated T cells, PB, plasma cells, and dendritic cells (DCs) were reduced. The percentage of LLDAS≦12M was significantly higher in the IVCY group with higher activated Th1/17 at baseline, and decreased activated Th1/17, NK, and DCs after 3M, and the MMF group with activated Th2 at baseline, elevated naïve B cells after 3M, and decreased activated Th2, Th1/17, Tfh1, Tfh1/17. [Conclusions] Trends of PB during IT for SLE was associated with LLDAS achievement. Different peripheral immune cells fluctuated after treatment depending on the therapy, and the cells associated with the outcome were also different.

W41-2

Outcomes in Serologically Active Clinically Quiescent Patients with Systemic Lupus Erythematosus: A Large Multicenter Cohort Study

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Conflict of interest: None

[Objective] We aimed to investigate the outcomes in serologically active clinically quiescent (SACQ) patients with systemic lupus erythematosus (SLE) focusing on the corticosteroid dosages. [Methods] SACQ was defined as the state with serological activity (increased anti-dsDNA or hypocomplementemia) and without clinical activity (clinical SLEDAI-2K≦0). SACQ SLE patients treated with 10 mg/day or less prednisolone at enrolment having at least 2-year observational periods were included from the APLC prospective cohort. Primary and secondary endpoints were time to the first flare and increase in SDI. Data were analyzed by the time-dependent Cox-model. [Results] A total of 2363 cases were included. Less subsequent flare was observed in patients treated with 0 mg/day of prednisolone than in those treated with 7.5< and ≦10 mg/day of prednisolone (HR 0.60, p = 0.01). No other corticosteroid dosage-related association was observed with flare. Corticosteroid dosage-related association was not observed with increase in SDI, either. [Conclusions] Among SACQ SLE patients, lower dosage of corticosteroids were not significantly associated with subsequent flare. In a span of just 2 years, no significant corticosteroid dosage-related association was not observed with subsequent accrual of damage.

W41-3

Hypocomplementemia and elevated serum IgG levels during maintenance therapy as risk factors for lupus relapse

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Conflict of interest: None

[Objective] To investigate the risk factors for relapse in patients with systemic lupus erythematosus (SLE) during maintenance therapy. [Methods] We enrolled SLE patients with prednisolone (PSL) dose >10 mg/day. The visit when the dose was reduced to 10 mg/day was defined as the baseline. A relapse was defined as an event with one or more organ lesions that met British Isles Lupus Assessment Group Index category A or B and required additional treatment. Clinical information at the enrollment was collected, and Kaplan-Meier analysis and Cox regression analysis were performed. [Results] Of the 112 participants enrolled, forty-five patients (40.0%) experienced a relapse, with a 5-year relapse rate of 41.0% and a mean PSL dose of 7.1±2.6 mg/day at the time of relapse. At the time of relapse, dermatological and neurological lesions were the most common [13 patients (28.8%)], and 35 patients (77.8%) had symptoms in the same category of BILAG as those of diagnosis. Hypocomplementemia and elevated serum IgG levels were identified as independent risk factors in the multivariate analysis. [Conclusions] Hypocomplementemia and elevated serum IgG levels during maintenance therapy could be risk factors for relapse, which may give a hint for glucocorticoid tapering during the maintenance of remission.

W41-4

TIM-3/Galectin-9 pathway in systemic lupus erythematosus

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Conflict of interest: None

[Objective] As a negative checkpoint receptor, T cell immunoglobulin and mucin-domain containing molecule 3 (TIM-3) and its ligand galectin-9 (Gal-9) are thought to be involved with pathogenesis of various autoimmune disease. We investigated the associations between serum soluble TIM-3 (sTIM-3) and clinical parameters of SLE. [Methods] This study included 65 SLE patients. All patients underwent physical examination, laboratory test, and review of medical records. The serum levels of sTIM-3 and Gal-9 were measured using ELISA. [Results] sTIM-3 were significantly higher in SLE patients compared to healthy controls. sTIM-3 in SLE patients showed positive correlation with SLEDAI and negative correlation with C3 and C4. sTIM-3 were significantly higher in SLE patients with at least one organ damage (SDI≧1) than those of without organ damage (SDI=0). sTIM-3 were significantly higher in SLE patients with active renal involvement determined by BILAG score compared to those without renal involvement. sTIM-3 in SLE patients showed positive correlation with Gal-9. [Conclusions] Serum sTIM-3 can be an useful biomarker for SLE-mediated organ involvement and activity. Shedding of TIM-3 and following binding with Gal-9 can inhibit TIM-3/Gal-9 pathway, and finally exacerbate the SLE disease activity.

W41-5

High rates of anti-dsDNA antibodies positivity in hepatitis B antigen-positive cases

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Conflict of interest: None

[Objective] To determine the prevalence of anti-dsDNA antibodies, SLE prevalence, and clinical characteristics by the presence or absence of HBsAg [Methods] We examined the positive rate of anti-dsDNA antibodies, the prevalence according to the ACR 1997 revised SLE classification criteria, and clinical characteristics by HBsAg positivity in 3659 patients. [Results] Age was 55.3 years old, 67.6% was female and 1.4% was HBsAg positive. Although the rate of anti-dsDNA antibody positivity was significantly higher in hepatitis B carrier patients (23.1% vs. 13.0%, p= 0.03), there was no significant difference in the percentage of patients meeting SLE classification criteria by the presence or absence of HBsAg (7.7% vs. 8.2%, p=0.88). Hierarchical cluster analysis was performed, and SLE diagnosed cases were classified as cutaneous, non-renal, arthritic, and non-arthritic, whereas HBsAg-positive cases were classified into different clusters. Comparing SLE patients and HBsAg-positive cases, the percentage of patients who met both immunological abnormalities and positive antinuclear antibodies of SLE classification criteria was significantly lower in HBsAg-positive cases (81.4% and 8.3%, respectively) (p<0.001). [Conclusions] SLE diagnosis should be made with caution.

W41-6

Anti-dsDNA Antibody in non-nephritis Systemic Lupus Erythematosus: comparison Farr assay with CLEIA, a single center, retrospective analysis

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Conflict of interest: None

[Objective] The Farr radioimmunoassay (RIA) and chemiluminescent enzyme immunoassay (CLEIA) are well established assays. There few reports compare to RIA assay with CLEIA assay inpatients without nephritis. The objective of this study is to compare the RIA assay with the CLEIA assay, especially in SLE patient without lupus nephritis. [Methods] We performed a retrospective analysis of 144 SLE patients who received moderate dose steroid therapy (>0.4 mg/kg/d). Control patients are 9 polymyositis, 16 dermatomyositis, 24 vasculitis, 31 others collagen diseases, 2 IBD, 8 hematologic disorder patients. All SLE patients had met 1997 ACR classification criteria for SLE. [Results] RIA assay was superior in both all SLE (AUS: 0.868 vs 0.847), and in non-nephritis SLE patient (AUC: 0.817 vs 0.793). RIA assay has significantly correlation with SLEDAI in all SLE patients (p <0.0001), but not in non-nephritis patients (P = 0.28). We found that RIA assay has mild correlation with CLEIA assay (p < 0.001), while only RIA assay has correlation with C3 levels in non-nephritis patients (Figure2), but CLEIA assay had not. [Conclusions] In our experience, RIA assay was superior to CLEIA assay in all SLE patients and non-nephritis patient in respect to diagnostic potential.

W42-1

The effect of hydroxychloroquine on glucocorticoid tapering in systemic lupus erythematosus: a longitudinal observational study of the LUNA registry

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Conflict of interest: None

[Objective] To examine the effect of hydroxychloroquine (HCQ) on glucocorticoid tapering in systemic lupus erythematosus (SLE) in the Japanese cohort. [Methods] The patients who were registered in the multicenter SLE registry "LUNA" and taking less than 15 mg/day of prednisolone (PSL) were included. Those who used and did not use HCQ both at baseline and one year belonged to the HCQ and non-HCQ groups, respectively. [Results] Seventy-seven and 302 belonged to the HCQ and non-HCQ groups, respectively. At baseline, the HCQ group showed significantly higher rates of alopecia (13.0% vs 5.6%, p = 0.025), anti-DNA antibody seropositivity (48.1% vs 29.1%, p = 0.002), hypocomplementemia (60.3% vs 45.2%, p = 0.021), hematuria (16.0% vs 7.27%, p = 0.019), and mycophenolate mofetil use (22.1% vs 10.9%, p = 0.010), and higher PSL dose (7.28±3.46 vs 6.27±3.14 mg/day, $p = 0.014$), as compared to the non-HCQ group. Although the PSL reduction in the 1-year observation period was significantly larger in the HCQ group than the non-HCQ group (1.85 ± 2.15 vs 1.25 ± 2.08 mg/day, $p = 0.02$), we could not identify HCQ as a factor for PSL reduction by multivariate analysis. [Conclusions] We could not identify HCQ as a contribution factor for glucocorticoid tapering in the maintenance therapy of SLE.

W42-2

Effects of additional hydroxychloroquine administration on cytokine expression in systemic lupus erythematosus

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Conflict of interest: None

[Objective] In addition to immunosuppressive drugs, HCQs are the first choice for the treatment of SLE, however, the effect of HCQ alone on cytokine expression has not been fully elucidated. To clarify the effect of additional HCQ therapy on cytokine expression in maintenance phase SLE. [Methods] Patients with maintenance-phase SLE who received additional HCQs at our institution since January 2016 were studied. The effects of IFN-α, TNF-α, IL-2, IL-6, IL-8, VEGF-A, MCP-1, MIP-1α, IL-1β, IL-1ra, and G-CSF on cytokine expression were assessed at the start of treatment and at 3 months after treatment using ELISA and multiplexing. [Results] Forty-two patients (4 males and 38 females, mean age 41.4±13.3 years) had lupus nephritis at the start of HCQ. Changes in IFN-α did not show a consistent trend in the 9 cases in which it was detected. The effect of HCQs was large. [Conclusions] Additional HCQ administration to patients with maintenance SLE significantly reduced the expression of inflammatory cytokines and contributed to the onset of effect.

W42-3

Effects of hydroxychloroquine on peripheral blood cytokine expression associated with atherosclerosis in systemic lupus erythematosus

Risa Wakiya, Kiyo Ueeda, Hiromi Shimada, Shusaku Nakashima, Mikiya Kato, Yusuke Ushio, Koichi Sugihara, Rina Senba, Tomohiro Kameda, Hiroaki Dobashi
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Conflict of interest: None

[Objective] To determine the effect of HCQ treatment on serum cytokines associated with atherosclerosis in SLE. [Methods] SLE patients who received additional HCQ and maintained low disease activity from January 2016 were included in this study. Disease activity was assessed by SLEDAI, CLASI and LLDAS, and serum complement titers, anti-ds-DNA antibodies, serum insulin and serum cytokines (adiponectin, resistin and leptin) were analyzed before and after HCQ treatment. [Results] Fifty-four patients (3 males, 51 females, mean age 41.1±12.6 years) were included. Thirty-three patients achieved LLDAS at baseline. Serum adiponectin and insulin levels were significantly increased after 3 months of HCQ treatment compared to baseline, and serum resistin levels were significantly lower ($p < 0.0001$). Patients with a history of renal disease had greater degree of changes in adiponectin and resistin. among SLE patients who did not achieve LLDAS, those who still did not achieve LLDAS after 3 months had significantly lower serum leptin levels before HCQ treatment than those who achieved it after 3 months. [Conclusions] Additional HCQ treatment in SLE patients improves lipid abnormalities. HCQ may improve prognosis by controlling disease activity in SLE and reducing risk factors for atherosclerosis.

W42-4

QTc interval prolongation induced by hydroxychloroquine in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] To reveal the effect of Hydroxychloroquine (HCQ) treatment on QTc interval in patients with systemic lupus erythematosus (SLE) and to investigate factors which affect the QTc prolongation during HCQ treatment. [Methods] We recruited SLE patients who had ECGs more than twice between 2015 and 2020 and assigned to a HCQ treatment group and a control group. We measured the change of QTc before and after the administration of HCQ in the HCQ group, and compared it with the control group. We also divided the patients treated with HCQ into two groups with or without QTc prolongation, and compared the characteristics between two groups. [Results] A total of 126 SLE patients was recruited and 42 were treated with HCQ. In the HCQ treatment group, the mean (±SD) QTc significantly increased from 425.2 (±20.6) msec to 436.9 (±22.0) ms ($p < 0.001$), while there was no significant difference of that in the control group. Moreover, in the HCQ treatment group with QTc prolongation, the proportion of hypertension was significantly larger and the SLE duration were significantly longer than in the group without QTc prolongation. [Conclusions] HCQ increases the risk of QTc prolongation in SLE patients. SLE patients with hypertension or long disease duration might have more risk of QTc prolongation.

W42-5

Hydroxychloroquine Retinopathy Support Program (H-SUPPORT)

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Conflict of interest: None

[Objective] Information about Hydroxychloroquine (HCQ) retinopathy is lacking in Japan. We launched HCQ Retinopathy Support Program (H-SUPPORT) for patients and doctors. [Methods] The HCQ retinopathy evaluation committee consisted of ophthalmologists (Shinoda (Saitama Medical University), Kondo (Mie University), Fujinami (National Hospital Organization Tokyo Medical Center), Ohno (Tokyo Metropolitan Tama Medical Center)), rheumatologist who used HCQ in both Japan and USA (adult: Yokokawa, pediatric: Akamine) The international advisory board commissioned HCQ retinopathy experts Browning (USA) and Ahn (Korea). Inquiries from patients or doctors are made from the website. The HCQ retinopathy evaluation committee with support from the international advisory board perform consultation from doctors using the anonymized data. Patient's second opinion will be provided through the HCQ retinopathy clinic (telemedicine, available) [Results] Three cases were consulted (2020/10). Two cases were diagnosed with mild HCQ retinopathy and one with moderate HCQ retinopathy. Two cases were the Pericentral type, which is common among Asians, and one was the classic parafoveal type. [Conclusions] In 2020, we launched HCQ Retinopathy Support Program.

A nationwide registry of HCQ retinopathy is in preparation.

W42-6

A study for establishing blood level threshold for hydroxychloroquine retinopathy

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Conflict of interest: None

[Objective] As a risk of hydroxychloroquine (HCQ) retinopathy, doses such as 6.5 mg / IBW kg and 5 mg /ABW kg have been emphasized, but in 2019 Petri et al. Increased the drug blood concentration (> 1733 ng / ml). He reported that he could be at risk for retinopathy. [Methods] Whole blood is stored within 48 hours of the last dosing in patients diagnosed with HCQ retinopathy, and the concentration of HCQ and its metabolites is measured at a later date. The concentration of metabolites, namely, desethylhydroxychloroquine (DHCQ), desethylchloroquine (DCQ), and bisdesethylchloroquine (BDCQ), were measured. The blood concentration of HCQ and metabolites is measured by validatedLC-MS/MS or HPLC. [Results] As of October 2020, the blood levels of HCQ and metabolites were measured by LC-MS / MS in one case. A 69-year-old SLE with chronic kidney disease (eGFR 32-54) who took 300 mg (6.4 mg/ IBW kg) daily for 50 months (a cumulative dosage of 452 g) discontinued HCQ due to retinopathy. The HCQ level measured 27 hours after the last dose was 2240 ng/ml. The DHCQ, DCQ, and BDCQ levels were 1310 ng/ml, 230 ng/ml, 280 ng/ml, respectively. Currently, we are collecting samples nationwide. [Conclusions] HCQ retinopathy may become preventable by therapeutic drug monitoring.

W43-1

Analysis of gut microbiome in patients with new onset systemic lupus erythematosus

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Conflict of interest: Yes

[Objective] Recently, the altered gut microbiota has been reported to be linked to the development of various diseases. On the other hand, there have been no reports on the gut microbiota in Japanese patients with systemic lupus erythematosus (SLE). We aimed to analyze the involvement of the gut microbiota in the pathogenesis of Japanese patients with SLE. [Methods] Stool samples were collected from 22 new onset SLE patients (noSLE) aged 16 years and older, 30 SLE patients in remission with SLEDAI ≦4 (rSLE), and 25 healthy individuals (HC). The V3-V4 regions of 16S rRNA gene were PCR-amplified from genomic DNA of the stool for Illumina MiSeq sequencing. The 16S database (Greengenes) was used for the analysis of homology and phylogenetic analysis. [Results] Compared to HC, the noSLE showed lower values of the Chao1, Shannon index, indicating the reduced diversity, which was also observed in rSLE. There was no difference at either phylum or family level between the SLE and HC. The seven species significantly increased and 42 species decreased in the noSLE compared to the HC. Of the seven species increased, the three were reduced in the rSLE. [Conclusions] The gut microbiota in noSLE showed reduced diversity accompanied by significant change in the abundance of several bacterial species.

W43-2

Interferons Type I and III Promote Generation of PD-1hi CXCR5- Tph Cells in vitro

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Conflict of interest: Yes

[Objective] IL-21-producing PD-1^{hi}CXCR5^{-} T peripheral helper (Tph) cells are thought to play an important role in various autoimmune diseases. However, the process of Tph cell differentiation remains unclear. Since frequency of Tph cells in the blood was positively correlated with serum levels of interferon (IFN)-α and -λ1 in patients with systemic lupus erythematosus (SLE), we investigate the effects of IFNs on the generation of PD-1^{+}CXCR5^{-} cells from naïve CD4 T cells. [Methods] Human naïve CD4 T cells were stimulated with anti-CD3/anti-CD28 mAbs and cultured with IL-12 and TGF-β in the presence of IFN-α, or -λ1 for 5 days. After the culture, the levels of cytokines or mRNA were measured. The 5 day-cultured CD4 T cells were co-cultured with allogeneic B cells and IgG concentrations in the culture supernatants were measured. [Results] We found that IFN-α or -λ1 can promote the generation of PD-1^{+}CXCR5^{-} cells, the production of IL-21 and IFN-γ, the expression of Tph-related genes and the B cell helper function under IL-12 plus TGF-β condition. Intracellular cytokine staining revealed that IFN-α effectively induces IL-21^{+}IFN-γ^{+}CXCR5^{-}CD4^{+} T cells. [Conclusions] It is strongly suggested that IFNs type I and type III promote Tph cell generation and contribute to the pathogenesis in SLE.

W43-3

Relationship between PD-1hi CXCR5- Tph cells and interferons Type I and III in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] PD-1^{hi}CXCR5^{-}CD4^{+} T peripheral helper (Tph) cells, a new subset CD4 T cells, produce IL-21 and promote B cell response. We investigated relationship between frequency of Tph cells and the blood levels of interferon (IFN) s type I and III in SLE patients. Moreover, we also examined a relation between Tph cells and CD11c^{hi} B cells in SLE patients. [Methods] Seventy patients with SLE (primary: 14, flare: 22, inactive: 34), 63 patients with rheumatoid arthritis (RA) and 11 healthy volunteers (HC) were included. The population of Tph cells in memory CD4^{+} T cells and CD11c^{hi} B cells in B cells were determined by FACS. The blood levels of IFNs and IL-21 were measured by ECL. [Results] The population of Tph cells in memory CD4^{+} T cells and the blood levels of IFN-α2a and IFN-λ1 were significantly higher in active SLE as compared to inactive SLE, RA or HC. Tph cells was positively correlated with SLEDAI (r=0.47), anti-dsDNA antibody (r=0.31), IFN-α2a (r=0.42), IFN-λ1 (r=0.59) in SLE patient. In addition, we revealed that Tph cells was also positively correlated with CD11c^{hi} B cells (r=0.43). [Conclusions] Our results suggest that higher levels of IFN-α2a and IFN-λ1 are closely related to the expansion of Tph cells in SLE and that Tph cells contribute to activation of CD11c^{hi} B cells.

W43-4

Stratification of SLE based on the BLyS biological activities

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) is an autoimmune disease clinically heterogeneous, and the pathophysiology is also heterogeneous. Many clinical trials for SLE have failed due to the heterogeneity of SLE, and stratification is crucial for selecting the optimal treatments for each patient. [Methods] IFN-I is the most important humoral factor. So, we recently established a cell-based assay system for monitoring IFN-I bioactivity in serum and identified SLE patients with elevated IFN-I. However, despite their high disease activity, some SLE patients showed low IFN-I bioactivity, suggesting the involvement of other factors. B-lymphocyte stimulator (BLyS) is known to facilitate the survival of B cells and involved in the pathogenesis of SLE. Although a monoclonal antibody specific for BLyS (Belimumab) was recently approved for SLE, the profiles of the Belimumab-effective patients are yet to be elucidated. In order to monitor BLyS bioactivity in serum, we generated NFkB-reporter cells with stable expression of BLyS receptors. [Results] We found that serum BLyS bioactivity in SLE was higher than that in healthy donors. [Conclusions] The measurement of BLyS bioactivity may be useful for stratification of SLE patients and selection of the optimal treatment for SLE.

W43-6

Pathogenic effect of physiopsychological stress-induced interleukin-12p40 on neuropsychiatric system in murine lupus model

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Conflict of interest: Yes

Objectives: To investigate an impact of physiopsychological stress on the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE) via analyzing lupus mouse model. **Methods:** We placed sleep disturbance stress (SD) for 2 weeks on 6-8-week-aged female MRL/lpr lupus mice using SD cage. Elevated plus maze (EPM) test was used to assess anxiety-like behavior. We performed immunohistochemistry to evaluate neuronal and microglial activation, and Golgi-Cox staining to assess dendrites. Gene expression was comprehensively analyzed using RNAseq, followed by interested protein level measurement using ELISA. **Results:** SD+lpr exhibited less anxiety-like behavior than their counterparts in EPM, while control mice showed more anxiety when stressed. In the medial prefrontal cortex (mPFC), SD+lpr showed the significantly highest numbers of phospho-cFos positive neuronal cells. RNAseq of mPFC revealed that *Il12b* was differentially expressed in SD+lpr. SD+lpr had the highest numbers of activated microglia with CD68 aggregation, and the increment of dendric spines in mPFC. The CSF level of IL-12p40 was the highest in SD+lpr, also elevated in NPSLE patients compared with healthy controls and non-NP SLE patients. **Conclusions:** IL-12p40 would be a potential therapeutic target for NPSLE.

W44-1

An impact of the revision of classification criteria for systemic autoimmune rheumatic diseases (SARDs) on the survival data of the patients

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Conflict of interest: None

[Purpose] To compare the survival data between patients classified by previous and revised criteria for SARDs including their overlap syndrome. [Methods] A total of 952 patients with SARDs are included in this study. The following criteria were used: 1997 revised ACR criteria and 2019 ACR/EULAR criteria for SLE, 1980 ACR criteria and 2013 ACR/EULAR criteria for SSc, the criteria by Bohan and Peter (definite or probable) and 2017 EULAR/ACR criteria for PM/DM. [Results] A total of 103 and 106 patients fulfilled old and new SLE criteria, respectively. Similarly, 35 (old) and 47 (new) patients met SSc criteria, and 12 (PM) /7 (DM) and 11 (PM) /12 (DM) patients met old and new criteria. Seven (old; 5 SLE-SSc and 2 SLE-PM) and 6 (new; 5 SLE-SSc and 1 SLE-PM) patients were identified as overlap syndrome by the old and the new criteria sets. Ten-year survival rate of patients with overlap syndrome defined by clinical diagnosis, old and new criteria was 100%, 100% and 100%, respectively. Similarly, that of SLE patients was all 100%, SSc patients 96%, 96% and 97%, and PM/DM 85%, 79% and 85%. [Conclusions] Survival rates were unaffected by the revision of classification criteria for SARDs.

W44-2

Characteristics of Male Systemic Sclerosis (SSc) in Japanese

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Conflict of interest: None

[Objective] SSc is a rheumatic disease characterized by fibrosis and peripheral circulatory failure. SSc is more common in females. The Canadian group reported that male patients with SSc have a higher rate of diffuse type, pulmonary arterial hypertension (PAH) and interstitial pneumonia (IP), and exhibits lower 5-years survival rate than female patients. Few studies focusing on gender have been reported in Japanese. This study aimed to characterize the clinical and laboratory findings of male SSc patients. [Results] The male to female ratio was 1:14. Males showed significantly less frequency of nail epithelial bleeding (NFB) ($P<0.01$) peripheral bone resorption ($P<0.05$) and skin calcification ($P<0.05$) than women. Males had significantly fewer cases of anti-centromere antibodies ($P<0.05$) and significantly more cases of anti-RNP polymerase III antibodies ($P<0.05$) positivity. There were no significant differences in pathotype or modified Rodnan total skin score (mTSS) by gender. [Conclusions] Our finding is different from previous reports. Therefore, we speculate that clinical and laboratory characteristic influenced by gender is different between races.

W44-3

Clinical study of Usability and Safety under the use of disposable warmer on each site for the patients with upper limb circulation disorder. Second report, Relationship with capillaroscopic stages

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Conflict of interest: Yes

[Objective] Raynaud's phenomenon (RP) is a circulation disorder occurs in systemic sclerosis. We conducted a "clinical trial to verify the Raynaud's symptom-relieving effect of disposable body warmers worn on parts other than fingers (UMIN000035332)" and found that the RP severity was alleviated by warming the neck or elbows. Here, we report whether the capillaroscopy (CS) stages affected the results of this study. [Methods] The 14 subjects in the above study, excluding one missing, were classified into normal, early, active, and late CS findings according to the Cutolo's criteria (Rheumatology 2004;43:719-26.). We investigated the influence of the CS stage on the changes in severity of RP, expressed with visual analog scale (ΔVAS), before and after the warming at neck, elbows, and wrists. [Results] There were 2 early, 6 active, and 5 late cases. At the neck warming, the improvement of ΔVAS tended to be large in the early and active cases, and at the elbows warming, it tended to be large in the late cases. None of the subjects classified into late were worsened ΔVAS at the elbow warming. [Conclusions] As a group of subjects, RP was alleviated by neck or elbows warming, but their mechanisms may be different. Elbow warming was expected to be effective even in relatively advanced cases.

W44-4

Incidence and prevalence of systemic Sclerosis (SSc) and SSc with interstitial lung disease (SSc-ILD) in Japan using Japanese claim database

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Conflict of interest: Yes

[Objective] To estimate the incidence and prevalence of SSc and SSc-ILD based on Japan claims data. [Methods] In this non-interventional retrospective cohort study, patients with SSc or SSc-ILD were identified based on administrative diagnosis of SSc (ICD10 M34) or SSc-ILD (ICD10 M34 and any of J84.1, J84.8, J84.9, J99.0, J99.1 or J98.4), in the JMDC claims database from 1 Sep 2016 to 31 Aug 2019. Incidence was calculated as cases with first SSc/SSc-ILD code in the study period divided by the sum of the follow-up time at risk in person-years (PY) for all eligible study participants. Prevalence was calculated as existing cases divided by the eligible study participants at risk. All analyses were descriptive. [Results] Among 6882535 eligible patients, 933 and 261 patients were newly identified as having SSc and SSc-ILD, crude incidence were 4.44 and 1.24 per 100000 PY, respectively. For prevalence, 2548 and 957 existing cases were identified, the crude prevalence were 37.02 and 13.90 per 100000 persons, respectively. [Conclusions] The incidence and prevalence of SSc and SSc-ILD in Japan estimated using a large-scale claim data are useful for government policies and planning clinical trials. The ratio of SSc-ILD to SSc was similar to that of published data in the world (22-67%).

W44-5

Survey on Dysphagia Using Simple Questionnaire EAT-10 in Patient with Systemic Sclerosis. -2nd report-

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Conflict of interest: None

[Objectives] Our aim was to investigate the actual condition of dysphasia in patient with SSc. [Methods] SSc patients who visited outpatient clinic in Fujita Health University between 2016 and 2020 were involved and those with PM/DM were selected as a control group. Simple questionnaire for swallowing functional evaluation (EAT-10) were examined. Demographic and clinical characteristics were retrospectively collected by medical chart. [Results] Thirty-two SSc and 22 PM/DM were included. No difference were observed with liquids or solids between SSc and PM/DM. However, swallowing difficulty of tablets was found in 12 SSc (40%) and 3 PM/DM (13.6%) (p=0.037). When SSc patients were stratified by the EAT-10 score, there were no difference in baseline characteristics. Eight patients with SSc were assessed by VF. Five patients had pooling of contrast agent in the valleculae show lower FSSG (p=0.004) and %FVC (p=0.004), and higher prevelance of ILD (p=0.09). [Discussion and Conclusion] These results suggested that the characteristics of swallowing difficulty in SSc is different from PM/DM, and swallowing difficulty might be independent organ involvement in SSc.

W44-6

Clinical outcomes after dose-reduction or discontinuation of tocilizumab in patients with diffuse cutaneous systemic sclerosis

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Conflict of interest: None

[Objective] To elucidate the clinical outcomes after dose-reduction or discontinuation of tocilizumab (TCZ) in patients with diffuse cutaneous systemic sclerosis (dcSSc). [Methods] We retrospectively surveyed the clinical course of 15 consecutive patients with dcSSc who were treated with TCZ after 2014. [Result] At the time of TCZ introduction, the median disease duration was 21.5 months with a modified Rodnan's total skin thickness score (mRSS) of 17.5. Prednisolone and MMF were concomitantly used in 86% and 14%, respectively. The median treatment duration of TCZ was 61.5 months. TCZ was reduced in dosage in 10 patients, and TCZ was discontinued in 4 of them, due to improvement of skin thickening. Two discontinued patients (50%) and one additional patient under dose-reduction experienced a recurrence of rapid progression of skin thickness and inflammatory complications, including edematous induration of the skin, polyarthritis, and pericarditis, with increased inflammatory markers. These manifestations were promptly improved by resumption or dose escalation of TCZ in all patients. [Conclusion] In dcSSc patients who experienced improvement of skin thickness during treatment with TCZ, dose-reduction or discontinuation of TCZ may result in a relapse of the disease.

W45-1

Cytokine analysis of pulmonary capillaries in pulmonary hypertension with connective tissue disease

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Conflict of interest: None

(Background) Cytokines are known to be involved in pathogenesis in connective tissue disease (CTD) and pulmonary hypertension (PH). However, these associations in PH with CTD-PH are unclear. (Objectives) To clarify the changes of cytokine profile by the pathogenic factors in CTD-PH and immunosuppressive therapy. (Methods) The subjects were 34 suspected PH (12 SSc, 7 MCTD, 2 SLE, and 13 others). At the time of cardiac catheterization (RHC), sera in pulmonary pre and post-capillary were collected and TIMP-1, MCP-1, IL-17 and IL-21, IL-12p70 and IL-6 were analysed by ELISA. Furthermore, we investigated the relationship between cytokines and pathogenic factors of PH and immunosuppressive therapy. (Results) 28 cases were diagnosed with PH by RHC. There was a positive correlation between IL-6 and mean pulmonary arterial pressure. In addition, MCP-1, IL-6, and TIMP-1 tend to be high in SSc-PH cases. On the other hand, in Non-SSc-PH, IL-12p70 and IL-17 were high. In cases who pulmonary vascular hemodynamics improved by treatment, IL-17, IL-21, and TIMP-1 decreased. (Conclusions) Cytokine profiles in pulmonary capillaries may vary depending on the disease. Furthermore, it suggested that IL-17, IL-21 and TIMP-1 may be biomarkers of therapeutic effect.

W45-2

Analysis of right heart catheterization (RHC) data in 61 patients with pulmonary arterial hypertension (PAH) associated with connective tissue diseases (CTDs)

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Conflict of interest: None

[Objective] PAH is a serious condition in CTDs, but the utility of immunosuppressive treatment and pulmonary vasodilators, their response to treatment and prognosis have not been fully elucidated and should be clarified. [Methods] We retrospectively reviewed the clinical records of 61 CTD-PAH patients fullfilled mPAP ≧25 mmHg and PCWP ≦15 mmHg by RHC and excluded other factors between January 2006 and September 2020 at the Kyoto University Hospital. [Results] The primary disease included 30 cases of SSc, 10 cases of SLE, and 21 others. Immunosuppressive therapy was either started or strengthened in 6.7% and 70% of SSc and SLE patients, respectively. Pulmonary vasodilators were administered

to almost all patients. The mean mPAP change was -8.3±10.2 mmHg for SSc and -21.3±14.6 mmHg for SLE; and significantly more decreased in SLE (p = 0.007). Deaths were observed in 24 patients (14 SSc, 2 SLE, and 8 others), and the causes of deaths in the SSc patients consisted of pulmonary hypertension in 3 patients, and others in 11. [Conclusions] SLE cases were treated more frequently with immunosuppressive therapy than SSc cases, and mPAP was more decreased by the treatments. SSc cases showed a poorer prognosis than SLE cases, but the majority of deaths were other than PAH.

W45-3

Comparison of systemic scleroderma group and non-systemic scleroderma group in pulmonary hypertension associated with connective tissue disease

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Conflict of interest: None

[Objective] Inflammation is considered to be involved in the pathology of pulmonary hypertension (PH) accompanying connective tissue disease (CTD), and use of immunosuppressive therapy is recommended. However, the effectiveness at PH associated with systemic sclerosis (SSc) is low. The pathogenesis of PH with SSc may be different from that of other CTD. [Methods] We analyzed 24 patients with CTD who underwent right heart catheter and were diagnosed as pulmonary hypertension. Patients already receiving pulmonary vasodilator were excluded. Patients were divided into 2 groups by SSc group, non-SSc group. The average pulmonary artery pressure, pulmonary artery wedge pressure, systolic right ventricular pressure, cardiac output, cardiac index, pulmonary vascular resistance, diastolic pressure gradient of the right heart catheter were compared. [Results] 15 cases were SSc group and 9 cases were non-SSc group. Diastolic pressure gradient was significantly lower in the SSc group (10.8±1.2 vs 17.3±3.9, t=0.04). [Conclusions] The diastolic pressure gradient is said to be low when the element of posterior capillary dysfunction due to left heart function decline. This is thought to suggest the myocardial disorder of the left heart associated with SSc.

W45-4

Change in serum KL-6 level is not useful for prediction for progressive interstitial lung disease in patients with systemic sclerosis

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Conflict of interest: None

[Objective] To investigate predictive value of short-term change in serum KL-6 level for progressive interstitial lung disease (ILD) in patients with systemic sclerosis (SSc). [Methods] We enrolled 89 patients diagnosed as SSc (disease duration ≦7 years) between 2007 and 2018 and whose repeated pulmonary function test and serum KL-6 level were available for ≧2 years. We conducted linear regression analysis to identify factors associated with change in serum KL-6 level using coefficient of variation (CV). Further, we investigated whether change in KL-6 during the first 6 months (regression coefficient, last/initial ratio, and area under the curve) can predict ILD progression for up to 2 years. [Results] In SSc patients, presence of ILD was associated with change in KL-6. Among 78 patients with ILD, ILD extensive disease, disease extent on CT, and low %predicted diffusing capacity for carbon monoxide were factors associated with subsequent KL-6 changes. ILD progression defined by various definitions was observed in 10-44%. Change in short-term KL-6 levels did not predict ILD progression. [Conclusion] Although KL-6 levels changed widely in patients with extensive SSc-ILD, short-term measurement of repeated KL-6 level was not useful for prediction for the progression of SSc-ILD.

W45-5

Serum KL-6 as a potential biomarker of nintedanib treatment in patients with systemic sclerosis-associated interstitial lung disease

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Conflict of interest: Yes

[Objective] To clarify biomarkers of nintedanib treatment in patients with systemic sclerosis (SSc)-associated interstitial lung disease (ILD) (SSc-ILD). [Methods] Twenty patients with SSc-ILD, who visited our clinic from 2014 through August 2020 and satisfied ACR/EULAR classification, and who were treated with nintedanib, were retrospectively investigated. In 9 (45%) patients, nintedanib was added to previous treatment with mycophenolate mofetil (MMF). We evaluated serum biomarkers such as CRP, ESR1h, platelets, and KL-6 before [-6, -3, 0 (baseline) months] and after [0, 3, 6, 12 months] the treatment. [Results] Nine patients (45%) had dcSSc. Mean age (SD) and median SSc duration [IQR] were 60 (12) and 20 [8-45], respectively. Median % forced vital capacity was 88 [69-101] %. Nintedanib was discontinued after 4, and 6 months in 2 patients due to liver dysfunction. Stable dose of ninedanib was 300 mg in 11 patients, 200 mg in 6, and 100 mg in 1. A significant change in serum KL-6 was observed (P = 0.024 by Friedman test) while other serum biomarker did not. No significant change in serum biomarker was observed before and after MMF treatment (n = 9). [Conclusions] A declined in serum KL-6, which might reflect disease modification by nintedanib.

W45-6

IL-5 and ST2 / IL-33R in borderline pulmonary hypertension and pulmonary hypertension associated with systemic sclerosis

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Conflict of interest: None

[Objective] Systemic sclerosis (SSc) is a refractory autoimmune disease that causes skin sclerosis and blood flow disorders in various organs and affects life prognosis due to pulmonary hypertension (PH). Recently, it has been reported that anti-IL-5 antibody suppresses pulmonary artery thickening in model mice that cause pulmonary artery thickening that can lead to PH by administration of IL-33. Therefore, we decided to investigate IL-5 and ST2 which is a receptor for IL-33, in borderline PH and PH associated with SSc patients. [Methods] 64 SSc patients was diagnosed the 2013 ACR/EULAR classification criteria who visited our department from August 2014 to April 2017 were SSc without PH (47), SSc with borderline PH (6), SSc with PH (11) divided. We measured by ELISA. [Results] In each group of SSc without PH, SSc with borderline PH, and SSc with PH, IL-5 (pg / ml) was 1.2 ± 0.3, 1.8 ± 0.6 ±, 1.3 ± 0.4. ST2 (ng / ml) was 16.9 ± 6.7, 29.7 ± 11.8, 25.0 ± 13.2. In both cases, borderline PH was significantly higher than SSc without PH. [Conclusions] IL-5 and ST-5 are involved in the onset of PH because IL-5 and ST2 are elevated in the borderline PH stage, which is the pre-PH stage, in SSc patients as well as in mouse models that cause pulmonary artery thickening The possibility was suggested.

W46-1

Muscle strength recovery progress from baseline in inflammatory myopathy patients

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Conflict of interest: None

[Objective] Muscle strength recovery have been reported in inflammatory myopathy patients after the start of therapeutic intervention, but no studies compared the recovery from the baseline. We aimed to analyze the muscle strength changes from the baseline until the stage of treatment as outpatient. We also investigated the major specific antibodies. [Methods]

Forty-five inflammatory myopathy patients with muscle weakness and elevated serum muscle enzymes joined the study at the baseline before the therapeutic intervention start. Quadriceps strength was measured at 4 timeline points: baseline, within 1 week after the start of medication (<1w), at discharge and as outpatient. We measured the muscle strength using a hand held dynamometer and obtained the percentage compared to the age-matched data from previous studies in healthy individuals. [Results] The mean muscular strength (right %/left %) were 69/67 (baseline), 78/76 (<1w), 87 /86 (discharge), and significantly higher in outpatient point reaching 117% /116 ($p<0.05$). By specific antibody, recovery of anti-TIF-1 antibody and anti-ARS antibody syndrome was good. [Conclusions] The muscular strength showed considerable improvement throughout the medication. The Quadriceps strength was fully recovered based in healthy individuals data.

W46-2

Efficacy of very intensive induction therapy with tofacitinib, rituximab, and plasmapheresis in rapidly progressive interstitial lung disease associated with anti-MDA5 antibody positive dermatomyositis

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Conflict of interest: None

[Objective] Rapidly progressive interstitial pneumonia (RP-ILD) associated with anti-MDA5 antibody-positive dermatomyositis (anti-MDA5+DM) is still resistant to the triple therapy and plasma exchange (PE) or rituximab (RTX). Recently, we treat such patients with very intensive induction therapy including tofacitinib (TOF), and aimed to analyze their therapeutic effects. [Methods] Twenty-six patients with anti-MDA5+DM during 2014 to 2020 were retrospectively analyzed for the efficacy and adverse events of very intensive induction therapy. [Results] 18 cases existed before the introduction of TOF, and eight of 10 RP-ILD cases with a ferritin level (>400 ng/mL) died in 2.5 months. In seven deaths, RTX or PE were used. Very intensive induction therapy, which included triple therapy with very high dose of steroid, liposteroid, TOF, PE, and RTX was performed in five patients with poor prognostic factors. Early death was avoided in all cases, and one patient died by the exacerbation of RP-ILD at 8 months. Complications of viral and fungal infections were frequent, but they were controllable. [Conclusions] Very intensive induction therapy is an effective treatment for the anti-MDA5+RP-ILD with poor prognostic factors, avoiding short-term death and improving survival rate.

W46-3

Efficacy and anti-MDA5 antibody titer of early immunosuppressive combination therapy for interstitial lung disease associated with anti-MDA5 positive dermatomyositis

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Conflict of interest: None

[Objective] Interstitial lung disease accompanied by anti-MDA5 positive dermatomyositis is often rapidly progressive and associated with poor prognosis. We investigated the efficacy and anti-MDA5 antibody titer of early immunosuppressive combination therapy for interstitial lung disease associated with anti-MDA5 positive dermatomyositis. [Methods] We retrospectively evaluated 10 anti-MDA5 positive dermatomyositis patients with ILD from 2016 to 2020 regarding their clinical features. [Results] As an initial treatment, all patients were treated with steroid pulse therapy followed by high-dose glucocorticoids (GCs), tacrolimus (TAC), and intravenous cyclophosphamide (IVCY). After an average of 10 IVCY therapies, anti-MDA5 antibody titers became negative in 7 of 8 patients, excluding 2 patients undergoing treatment. The HRCT score improved in all cases, and no relapse of interstitial lung disease were observed. Adverse events such as CMV infection, fungal infection, mediastinal emphysema, and diabetes were observed, but no cases leading to discontinuation of treatment were observed. [Conclusions] Our data indicated that the prognosis can be improved as well as the anti-MDA5 antibody titer by the combination immunosuppressive therapy from the early stage of the disease.

W46-4

Usefulness of the formula to decide the starting dose of tacrolimus for attainment target trough concentration based on CYP3A5 genotype

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Conflict of interest: None

[Objective] Recently, 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 the usefulness of this formula. [Methods] We decided the starting dose of TAC by using the formula, for treatment of the patients with DM-ILD visiting our hospital between November 2019 and May 2020. Next, we assessed the association between predicted and observed trough concentration at the initial (from day 2 to day 4) and second (day 6 or day 7) measurement date, using linear regression analysis. [Results] The significant correlation between the predicted and observed trough concentration were shown in initial ($r^2=0.897$, $p=0.0041$) and second ($r^2=0.948$, $p=0.0050$) measurement date. [Conclusions] The formula which we made for attainment target trough concentration based on CYP3A5 genotype was useful for deciding the starting dose of TAC.

W46-5

Proposed criteria for introducing therapeutic apheresis based on previous reports of interstitial pneumonia with polymyositis and dermatomyositis (PM/DM-IP)

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Conflict of interest: None

[Objective] To look for the new criteria for introducing therapeutic apheresis depend on the previously reports. [Patients] Patients with IP who were diagnosed PM/DM and were able to confirm the details of apheresis and clinical course by searching in October 2020. [Methods] There were 46 reports and 137 cases. Statistics on patient background, types of immunosuppressive agents, details of apheresis, clinical indicators and outcomes based on medical records. [Results] The average age is 67.4 years, and the male-female ratio is 44:65. Of the 76 CADM cases, 41 were positive for anti-MDA5 antibody. 43 deaths / 64 survivals. In almost all cases, immunosuppressive drugs were combined. Apheresis therapy was a total of 32 cases of simple plasma exchange (PE) and 31 cases of PMX. The clinical indicators and statistical significance could not be pointed out as the clear critria. However, in surviving patients, respiratory status and KL-6 were improved. The only reference was the P / F ratio, with an average of 208.8 survivors and 166.7 deaths. [Discussion and Summary] If multiple immunosuppressive drugs show treatment resistance, it is desirable to consider the introduction of apheresis before the P / F ratio drops to 200 or less.

W46-6

The clinical significance of anti- PC4 and SFRS1 interacting protein 1 antibody in polymyositis and Dermatomyositis

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Conflict of interest: None

[Objective] Anti-PC4 and SFRS1 interacting protein 1 (PSIP1) antibody (Ab) is reported as a potentially important biomarker that can be clinically used to discriminate autoimmune rheumatic diseases (AARD) from non-AARD and have been detected in healthy individuals. However, its clinical significance in polymyositis and dermatomyositis (PM/DM) is still unclear. [Methods] We evaluated anti-PSIP1 Ab titer of samples from 86 PM/DM, 17 systemic lupus erythematosus (SLE) and 41 controls using ELISA. Detection of anti-MDA5, ARS TIF1-γ and SRP Ab were detected by immunoprecipitation using [35S] Methionine-labelled HeK cell. [Results] Anti PSIP1 Ab was significantly positive in PM/DM at 56% (46/86) compared to that of controls (2%: 1/41) and SLE (12%: 2/17). In a stratified comparison of autoantibodies known for PM / DM, the positive rate was significantly higher in anti-MDA5 Ab (75%: 30/40, P <0.05) compared to that of anti-ARS Ab (54%: 15/28), anti-TIF 1 γ Ab (30%: 3/10) and anti-SRP Ab (0%: 0/9). In addition, anti-PSIP1 Ab titers decreased under the cut-off level at the time of remission. [Conclusions] Anti-PSIP1 Ab was frequently detected in PM / DM, especially in anti-MDA5 Ab-positive cases, and its titer was suggested to correlate with the disease activity of anti-MDA5 Ab-positive DM.

W47-1

Pulmonary abnormalities in survivors of a-MDA5 positive rapidly progressive ILD

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Conflict of interest: None

Objective: To describe what pulmonary abnormalities exist in the survivors of a-MDA5 positive rapidly progressive ILD (RP-ILD) **Methods:** The subjects were a-MDA5+ ILD patients who survived for at least one year and had stable ILD. The extent of GGO and consolidation were scored (0-24 (max)). The extent of liner opacities was substituted by the number of linear shadows arising from the pleura. **Results:** In 27 patients of MDA5+ RP-ILD, survivors were 15. Pulmonary abnormalities were found in 14/15 (93%) of the survivors. GGO was detected in 6 (42%) with 1.7 (mean) in CT score. Consolidation was found in 2 (14%) with 0.6 in CT score. Linear opacities (100%) were found in all survivors with the abnormalities. Honeycombing was not detected. Patients with a large extent of linear opacities had large extents of GGO/consolidation and high KL-6 levels at the acute phase. **Conclusion:** Linear opacities, fibrosing lesions, were found in almost survivors of a-MDA5+ RP-ILD. The pulmonary abnormalities in the survivors resulted from damage by inflammation of RP-ILD in the acute phase.

W47-2

Serial measurement of the levels of serum IP-10 in 3 cases of anti-MDA-5 antibody-positive dermatomyositis and comparison with other markers of interstitial pneumonia

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Conflict of interest: None

[Background] We found that the serum level of IP-10 is substantially higher in patients with anti-MDA-5 antibody-positive dermatomyositis (DM) on admission than other DM patients. Thus, we quantified its levels over time. [Case 1] A 52-year-old man. “Combination therapy” with prednisolone, tacrolimus, and intravenous cyclophosphamide (IVCY) was initiated, but his interstitial pneumonia deteriorated. IVCY was changed to oral CY, JAK inhibitor was added, and plasma exchange (PE) was performed 5 times, but they were discontinued due to bacteremia. After resuming CY, serum ferritin levels decreased. IP-10 decreased from 46836 to 1201 pg/ml. [Case 2] A 53-year-old man. The combination therapy was started, but he developed aspiration pneumonia and his interstitial pneumonia was worsened. After 7 times of PE, his symptoms improved. IP-10 decreased from 15124 to 2469 pg/ml. [Case 3] A 76-year-old woman. Ferritin elevated after the combination therapy, but her respiratory status was stable. IP-10 decreased from 16087 to 4504 pg/ml. [Clinical significance] In all three cases, serum IP-10 levels decreased rapidly after the start of treatment and further decreased until discharge. IP-10 may be associated with the pathogenesis and disease activity of anti-MDA-5 antibody-positive DM.

W47-3

The factors affecting theprognosis of anti-MDA5 Autoantibody Positive Dermatomyositis Developing Rapidly Progressive Interstitial Lung Disease

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Conflict of interest: None

(Objective) To clarify the factors affecting the prognosis of anti-MDA5 antibody positive dermatomyositis (DM) and rapidly progressive interstitial lung disease (RP-ILD). (Method) 28 patients who were diagnosed anti-MDA5 antibody positive DM and RP-ILD at Tokai University Hospital between 2012 and 2018 were enrolled. We retrospectively examined age, sex, therapy regimen and chest CT findings, oxygen requirement, blood gas anlaysis, serum CPK, aldolase, KL-6, LDH, CRP, ferritin concentration at admission. (Result) We excluded 3 patients because of insufficient clinical information. Of 25 anti-MDA5 positive DM and RP-ILD, female was 20 and male was 5 and mean age was 55.32 years. All patients received multiple immunosuppressive combination therapy (high dose prednisolone with calcineurin inhibitor and intermittent intravenous cyclophosphamide). In comparison of survival with deceased group, We found significant differences in oxygen therapy at admission in addition to older age, high serum CPK, KL-6, ferritin, CRP level. (Conclusion) Oxygen therapy at admission was newly identified as poor prognostic factor in patients with anti-MDA5 antibody positive DM and RP-ILD.

W47-4

Serum B2-microglobulin level is a prognostic factor for anti-melanoma differentiation-associated gene 5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objective] Anti-melanoma differentiation-associated gene 5 antibody (MDA5)-positive dermatomyositis (DM) is known as a disease with a poor prognosis which often presents with rapidly progressive interstitial lung disease. We retrospectively analyzed anti-MDA5-positive DM treated at our hospital and examined the prognostic factors of the disease. [Methods] For anti-MDA5-positive DM admitted to Showa University Hospital and Showa University Toyosu Hospital from 2012 to 2019, age, sex, treatment, clinical findings at the start of treatment, and blood data were examined. Each factor was compared in the survive group and in the death groups one year after the start of treatment. [Results] There were 23 cases of anti-MDA5-positive DM and all patient presented interstitial lung disease. In all patient, combined immunosuppressive therapy, including glucocorticoids, calcineurin inhibitors and intravenous cyclophosphamide were performed. In some cases, plasma exchange therapy and Polimyxin B immobilized fiber column direct hemoperfusion therapy were used in combination. Serum β-2MG levels (4.5 ± 0.5 vs 3.3 ± 1.4 mg) / L, p =

0.03) were significantly higher in the death group than in the survive group. [Conclusions] Serum β-2MG is one of the prognostic factors of anti-MDA5-positive DM.

W47-5

A clinical study of prognostic factors for anti-MDA5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objective] To investigate the relationship between the data at admission and the prognosis of anti-MDA5 antibody-positive dermatomyositis with interstitial lung disease. [Methods] We retrospectively investigated the medical records of 20 patients (8 men and 12 women) treated at our institution from 2012 to 2019. [Results] When we compared the cases (7 deaths and 13 remissions), the deaths were older (65.0 vs 45.2 y/o, p=0.003), the CRP was higher (3.11 [1.29-3.95] vs 0.32 [0.17-0.67] mg/dL, p=0.019), and the P/F ratio was lower (317.1 vs 394.8 mmHg, p=0.038). There was no significant difference in ferritin levels between deaths and remissions (841 [592-963] vs 191 [115-872] ng/mL, p=0.161), and the same goes for KL-6, CK, A-aDO_2. When we separated the cases by the median age, defining younger and older group, the number of weeks from onset to hospitalization was greater in the younger group (12 [10-14] vs 3.5 [3-9] weeks, p=0.016), and the P/F ratio was lower in the older (427.7 vs 317.4 mmHg, p = 0.021). The mortality rate was 10% (younger) and 60% (older). [Conclusions] In the dead cases, the age and CRP were higher, and the P/F ratio was lower. In the older group, the course from onset to admission was shorter, and the P/F ratio was lower. The disease may progress more rapidly in older patients.

W47-6

Clinical features and prognosis of patients with anti-MDA5 positive DM in our academic medical center

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Conflict of interest: None

[Background] Anti-MDA5 positive dermatomyositis (DM) -associated interstitial lung disease (ILD) was thought to be poor prognosis in previous reports. The aggressive treatment such as high dose glucocorticoids, intravenous cyclophosphamide, and calcineurin inhibitor (triple therapy) for MDA5-positive DM has been suggested in Japan since approximately 2014. [Objectives] This descriptive study aims to evaluate clinical features and prognosis of MDA5-positive DM. [Methods] We retrospectively reviewed clinical presentations, laboratory data, imaging studies, treatment, and outcome of patients with MDA5-positive DM who were treated in our academic medical center between January 2015 to October 2020. [Results] 13 cases of MDA5-positive DM were identified. 11 of 13 patients were female. Mean age was 55.5±10.9. All patients had typical DM rash and 11 of 13 patients also had palmar papules while one patient had cutaneous ulcer. 6 patients had CK elevation. ILD was present in 11 of 13 patients. In patients with ILD, all patient received triple therapy. 10 patients (91%) had stable or improved ILD and are still alive; ILD worsened in one patient who died within three months of onset. [Conclusions] This case series confirmed excellent prognosis of MDA5-positive DM-associated ILD.

W48-1

Risk factors for relapse of anti-synthetase syndrome

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Conflict of interest: None

[Objective] To identify risk factors for the relapse of the anti-synthetase syndrome. [Methods] Subjects were consecutive ASS patients who received the first induction therapy in our department. Relapse was judged when physicians intensified the therapy for ASS. The clinical features and treatments were reviewed retrospectively by reviewing medical records. [Results] Subjects were 44 patients (PM/DM; 26/18, ILD: 44, myositis: 32). Anti-EJ, Jo-1, PL-12, and PL-7 Abs were detected in 11, 22, 6 and 5 patients, respectively. Relapse occurred in 21 cases (47.7%). Between patients with and without the relapse, no differences were found in gender, age of the onset, organ involvement, levels of CK, LDH, and KL-6, and treatment. The relapse frequently occurred in patients with anti-EJ and Jo1 Abs (EJ: 72%, Jo-1: 55%, PL-12: 16%, PL-7: 0%). The relapse occurred in 33% and 58% of patients with and without TAC/CsA, which did not show a significant difference. Multiple relapses occurred in 14 of the 20 cases and were positive for anti-EJ and Jo-1Abs. [Conclusions] The specificity of ARS Abs was associated with the relapse. TAC/CsA might have little effect on preventing relapse.

W48-2

Clinical features of anti-aminoacyl tRNA synthetase antibody syndrome with severe peripheral circulatory disorders

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Conflict of interest: None

[Objective] Anti-aminoacyl tRNA synthetase antibody syndrome (ASS) may present with severe peripheral circulatory disorders such as fingertip ulcer/necrosis. The purpose was to clarify the clinical features of ASS. [Methods] We analyzed patients with ASS who were treated in our department from January 2009 to June 2019, in addition to patients of ASS with severe peripheral circulatory disorder reported in the past. [Results] In 9 patients with ASS who had severe peripheral circulatory disorder (4 our cases, 5 previously reported cases), the average age was 58.4±21.4 years, the proportion of women was 88.9%, Raynaud's phenomenon was observed in 85.7%, myositis in 87.5%, interstitial pneumonia in 88.9%, mechanic's hands in 85.7%, Gottron's sign in 50%, and arthralgia in 50%. In patients with ASS (42 patients without peripheral circulatory disorder and 9 patients with severe peripheral circulatory disorder), Raynaud's phenomenon (Odds ratio 34.76, 95%CI 3.49-1019.72, p=0.0013) and myositis (Odds ratio 16.55, 95%CI 1.28-773.91, p=0.0291) was identified as a risk factor for severe peripheral circulatory disorders in multivariate analysis. [Conclusions] Raynaud's phenomenon and myositis in ASS are likely to cause severe peripheral circulatory disorder.

W48-3

Clinical trials of anti-aminoacyl-tRNA synthetase (anti-ARS antibody)

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Conflict of interest: None

[Objective] Anti-ARS antibodies have come to be measured, and tests have been conducted more widely than the conventional concept of dermatomyositis, polymyositis. We examined the current status of tests at our hospital and the symptoms of positive cases. [Methods] We examined the age, sex, clinical department of measurement, and symptoms of positive cases of anti-ARS antibody positive cases measured in our hospital from October 2016 to September 2020 for 4 years. [Results] There were 83 cases with INDEX 25 or higher, the average age of which was 62.5 ± 14.0, 30 males (3.2%) and 53 females (5.9%), and the positive rate was higher in females. Interstitial pneumonia was the most common lesion in 77 cases (93%), and was found in 36 cases (43%) with myopathies and 26 cases

(31%) with typical eruptions. The most common combination of symptoms was interstitial pneumonia alone in 36 cases, skin symptoms, muscle symptoms, and dermatomyositis with interstitial pneumonia in 18 cases, followed by muscle symptoms and interstitial pneumonia in 17 cases. The diseases were DM 22 cases, PM 17 cases, interstitial pneumonia 28 cases, and others (RA, SS, SLE, etc.). [Conclusion] Anti-ARS antibody-positive cases have a high prevalence of interstitial pneumonia.

W48-4

Histological characteristics of tertiary lymphoid structures (TLS) in tumor tissues of patients with cancer-associated myositis (CAM)

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Conflict of interest: None

[Objective] To investigate histological features of TLS in primary tumor tissues of CAM patients. [Methods] Three CAM patients (gastric cancer: 2, breast cancer: 1) were examined. As a control, we randomly selected 6 cancer patients without CAM matched for age, gender, and tumor type and stage from the tumor tissue repository. TLS was defined as ectopic lymphoid-like structures with DC-Lamp$^+$mature dendritic cells, CD23$^+$ follicular dendritic cells (FDC) and PNAd$^+$ high endothelial venules. The distribution of TLS was categorized into “invasive margin” (IM), “central tumor” (CT), and “peri-tumor” (PT). [Results] In gastric cancer, the density and distribution (CT: IM: PT) of TLS was 0.036/μm^2 and 20%:70%:10% in 2 CAM patients, and was 0.011/μm^2 and 9%:45%:45% in 4 non-CAM patients. In breast cancer, TLS was exclusively found in IM with density of 0.025/μm^2 in a CAM patient. CD4$^+$ T cells around the germinal center (GC) and FDC inside the GC were increased in CAM, although there was no difference in proportions of CD3$^+$, CD8$^+$, and CD20$^+$ cells. [Conclusions] In the primary tumor tissue of CAM patients, TLS was detected more abundantly inside and boundary of tumors, suggesting a potential relationship between pathogenic process of CAM and adaptive immune responses within tumors.

W48-5

Clinical characteristics and outcome of dermatomyositis associated with malignancy

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Conflict of interest: None

[Objective] To investigated clinical feature and outcome of patients with dermatomyositis (DM) associated with malignancy. [Methods] Data of 35 patients with polymyositis or DM, diagnosed at Itami City Hospital between January 2016 and April 2020, was retrospectively assessed. 5 out of 35 patients were diagnosed with cancer within 1 year before or after DM diagnosis. [Results] 4 out of 5 patients of DM associated with malignancy were men. The mean age of the patient at the time of diagnosed DM was 65 years. Sera from 4 of 5 patients were confirmed to be positive anti TIF-1 gamma antibody. All patients had myositis and severe skin changes, 4 of them had dysphagia and 3 of them had interstitial lung disease. One patient had a surgery for ovarian cancer without systemic glucocorticoid (GC) and IVIG. The others were initially started on oral prednisolone 48 mg/day, and 3 of them were treated with IVIG additionally. All patients showed excellent improvement in skin lesions and myositis. On the other hand, 3 of 5 patients died of their malignancy 3~12 months after their diagnosis. [Conclusions] Symptoms of DM associated with malignancy may be suggested to treated successfully with high dosage of systemic GC and/or IVIG. Cases complicated with refractory advanced cancer may have very poor prognosis.

W48-6

Comparison of clinical feature with and without malignancy in Idiopathic inflammatory myopathy (IIM)

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Conflict of interest: None

[Introduction] IIM, is accompany extramuscular involvements such as ILD, malignancies, includes Polymyositis (PM), Dermatomyosotos (DM), Amyopathic DM (ADM) and Inclusion body myositis. Immune-mediated necrotizing myopathy (IMNM) is included in IIM in a broad sense. [Method] To clarify the clinical features of IIM patients who visited our hospital divided into a malignancy group (MG) and a non-malignancy group (NMG) for comparison. [Results] 13 patients in a MG included 4 PM, 6 DM and 3 ADM, 2 cases had antibody of ARS, 5 cases had TIF1γ, 2 cases had MDA5. 26 patients in a NMG included 9 PM, 12 DM, 4 ADM and 1 IMNM, 11 cases had ARS, 6 cases had MDA5, 3 cases had Mi-2. The significant differences between a MG and a NMG were the prevalence of mechanics hands (20.0%, 50%, P=0.029), the combination rate of Tacrolimus (27.3%, 76.9%, P<0.001), the days until steroid tapering (40.3 days, 27.0 days, P=0.021). There was no significant difference between the two groups in the prevalence of skin symptoms, muscle weakness, ILD, the initial dose of steroid, laboratory data such as CK, myoglobin, ferritin and KL-6, and respiratory function test. [Conclusion] In MG, there are many cases that are difficult to treat, so treatment should be performed earlier and more intensely.

W49-1

Treatement of chronic phase of dermatomyositis/polymyositis-interstitial lung disease (DM/PM-ILD) and usefulness of KL-6 measurement

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Conflict of interest: None

[Objective] Regarding progression of DM/PM-ILD fibrosis, examine the usefulness of KL-6 in predicting changes in forced vital capacity (FVC). [Methods] Among our DM/PM-ILD cases observed from 10/2015 to 9/2020, we choose cases in which FVC and KL-6 could be measured in the early and late stage of the observation period. [Results] There are 46 fitted cases with 6 males. Treatment for these cases at 10/2015 and at 9/2020 consists of CS (average dose 8 mg, 7 mg), 57%, 52% tacrolimus, 22%, 24% cyclosporin, 22%, 28% azathioprine, 4%, 15% MMF respectively. According to changes in FVC, the cases devided into improved group (>5%), unchanged group (-5% to 5%), and aggraveted group (<-5%). Improved group, unchanged group, aggraveted group were consisted of 10, 8, 28 cases respectively, and the changes in KL-6 was -22%, -9%, +10% respectively. [Conclusions] In DM/PM-ILD, the change in KL-6 may be used as index to predict the decline in FVC.

W49-2

Prediction of surgical lung biopsy proven diffuse alveolar damage in rapidly progressive myositis-associated interstitial lung disease

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Conflict of interest: None

[Objective] Some patients with rapid progressive myositis-associated ILD had poor respiratory outcomes. Though pathological DAD was considered to indicate poor outcomes, it is too invasive to perform surgical lung biopsy. The aim is to evaluate whether we could predict pathological DAD from clinical and radiological findings. [Methods] We included consecutive treatment-naïve patients with rapidly progressive myositis-associated ILD who underwent surgical lung biopsy between March 2008 and September 2019. [Results] The median age was 57 years, eight were male and seven were anti-MDA-5 antibody positive. Pathological DAD was found in four. Patients with pathological DAD had worse ventilation-free

survival than those without (P <0.01). The prevalence of anti-MDA-5 antibody and subpleural crescent GGA in upper-middle lobe on HRCT was significantly higher in patients with pathological DAD than in those without. Both anti-MDA-5 antibody and subpleural crescent GGA were found in three patients and PPV and NPV for pathological DAD were 75% and 95%, respectively. [Conclusions] Pathological DAD was found in 17% of rapidly progressive myositis-associated ILD and had worse ventilation-free survival. Anti-MDA-5 antibody and subpleural crescent GGA in upper-middle lobe could predict pathological DAD.

W49-3

Clinical analysis of 23 cases of pneumomediastinum in myositis-associated interstitial lung disease

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Conflict of interest: None

[Objective] To identify clinical characteristics of myositis-associated interstitial lung disease (ILD) with pneumomediastinum and predicte prognosis factors. [Methods] We enrolled 164 of myositis-associated ILD patients who visit Tokai University Hospital 2011-2020. We retrospectively compared cases complicated by pneumomediastinum to the others. [Results] We collected 23 cases complicated by pneumomediastinum. The mean age was 59.6±9.1 years old, 12 were female.12 were positive of anti-MDA5 antibody and 8 were anti-ARS antibody. The initial dose of prednisone was 54.5±9.1 and 13 patients received high-dose methylprednisolone infusions. The time for the onset of the pneumomediastinum was 32.4±18.8 days.9 patients died. In univariate analysis, anti-MDA5 antibody positivity was predictive factor of pneumomediastinum (p=0.001). Serum biomarkers (CK, ferritin, CRP, KL-6) levels were not significantly associated. In our series, poor survival was associated with a pneumomediastinum (p=0.006). However, in analysis by logistic regression, only anti-MDA5 antibody positivity was significantly associated with mortality (p=0.01). [Conclusions] Pneumomediastinum is the factor with a poor prognosis in myositis-associated ILD. However, in multivariate analysis, pneumomediastinum is not associated with mortality.

W49-4

Elevation of SP-D levels during therapy is a poor prognostic factor in anti-MDA5Ab + RP- ILD, but not in anti-ARS Ab + ILD

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Conflict of interest: None

[Objective] To clarify change in KL-6 and SP-D levels during treatment for RP-ILD in PM/DM patients with anti-MDA5 Ab and ARS Ab and the relation of their change to prognosis. [Methods] A retrospective analysis was performed on 48 consecutive DM/PM patients with RP-ILD who were admitted to our department from 2009 to 2016. Serum KL6 and SP-D levels were regularly measured. [Results] Subjects were 48 RP-ILD patients including 25 patients positive for a-MDA5 ILD (MDA5-ILD) and 23 ones positive for a-ARS Ab (ARS-ILD). At the starting therapy, the SP-D levels were significantly lower in a-MDA5+ ILD than those in ARS+ ILD (MDA5 vs ARS: 57 (28-77) vs 146 (74-271), median (IQR)). Elevation of SP-D levels occurred in 13/25 of MDA5-ILD patients during therapy for ILD. Importantly, 11/13 (84%) of MDA5-ILD with SP-D elevation died from respiratory failure. In contrast, the elevation of SP-D levels was found in 17/23 of ARS-ILD and none of them died. Elevation of KL-6 level was found in all patients in both MDA5-ILD and ARS-ILD. [Conclusions] Change in serum SP-D levels differed between MDA5-ILD and ARS-ILD. The elevation of SP-D levels during therapy predicted poor prognosis of RP-ILD in MDA5-ILD, but not in ARS-ILD.

W49-5

Clinical significance of serum YKL-40 and identification of the YKL-40-expressing cells in polymyositis and dermatomyositis

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Conflict of interest: None

[Objective] YKL-40 is a chitinase-like protein. The level of YKL-40 is known to be elevated in several autoimmune diseases. However, YKL-40 has no clear clinical significance in myositis itself. The purpose of this study is to clarify the clinical significance of YKL-40 in Polymyositis (PM) and Dermatomyositis (DM) without interstitial lung diseases (ILD). [Methods] We evaluated 36 patients diagnosed with PM/DM from 2006 to 2020 at the Hyogo College of Medicine and 26 healthy controls (HC) and conducted a retrospective review of their clinical records. Immunostaining was performed using peroxidase detection techniques. [Results] Serum level of YKL-40 was significantly higher in patients with myositis than in HC. Endothelial cells and inflammatory cells stained positive for YKL-40 in PM/DM biopsy specimens. [Conclusions] Increased serum YKL-40 levels are associated with disorders characterized by various types of inflammation. Endothelial cells and inflammatory cells may account for the elevation of serum YKL-40 levels. Immunohistochemical staining may suggest that there is a population of YKL-40-positive macrophages. Next, we need to investigate the function of YKL-40-expressing cells.

W49-6

Myositis exacerbation after administration of pembrolizumab in a patient with polymyositis and lung cancer

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Conflict of interest: None

A 55-year-old woman with systemic lupus erythematosus (SLE) and polymyositis (PM) was diagnosed with lung adenocarcinoma 6 years ago. The patient was treated with prednisolone (PSL) monotherapy for SLE and PM, after the diagnosis of adenocarcinoma. Treatment with intravenous immunoglobulin (IVIg) improved myositis, although exacerbations of PM were often. The adenocarcinoma remained in remission after surgery, chemotherapy, and radiation therapy, until recurrence was revealed using positron emission tomography-computed tomography. Consequently, the patient received pembrolizumab (PD-1 antibodies) for the lung adenocarcinoma. Six months after pembrolizumab initiation, elevated CK levels were detected, and the patient experienced muscle weakness. Determining whether myositis was an immune-related adverse event (irAE) of pembrolizumab or a PM relapse was challenging. We selected IVIg as a treatment for myositis; as a result, muscle symptoms improved without increasing the PSL dose. ICIs present with challenges when administered in patients with autoimmune diseases, as they can cause irAEs. We report a case of myositis exacerbation after administration of ICIs in a patient with autoimmune disease and malignant tumour.

W50-1

Clinical features of patients with anti-MDA5 positive dermatomyositis involving laryngopharyngeal manifestation

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Conflict of interest: None

[Objective] To investigate the clinical features of patients with anti-MDA5 positive dermatomyositis involving laryngopharyngeal manifestation. [Methods] We retrospectively examined the clinical features of patients with untreated anti-MDA5 positive dermatomyositis who visited

our department from January 2011 to August 2020 and had laryngopharyngeal involvements. Poor outcome was defined as death or need for home oxygen therapy at discharge. [Results] Among 18 patients with anti-MDA5 positive dermatomyositis (mean age, 49.4 years), nine had pharyngeal involvements (five with sore throat, six with hoarseness, and three with dysphagia). Nasopharyngolaryngoscopy revealed inflammatory involvements including laryngitis or peritonsillitis in five and vocal cord hemiparesis in two. All patients with laryngopharyngeal involvements had active myositis, whereas only three had myositis in those without laryngopharyngeal involvements. In addition, CK and ferritin were significantly higher in patients with pharyngeal involvements. The existence of laryngopharyngeal manifestation was not associated with the poor outcome. [Conclusions] Laryngopharyngeal involvement in anti-MDA5 positive dermatomyositis was not rare, and was associated with inflammation of throat and activity of myositis.

W50-2

Successful treatment of tofacitinib (TOF) for rapidly progressive-interstitial lung disease (RP-ILD) with anti-melanoma differentiation-associated 5 gene antibody-positive (anti-MDA-5 ab-positive) clinically amyopathic dermatomyositis (CADM): Two cases report and literature review

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Conflict of interest: None

[Introduction] Anti-MDA-5 ab-positive CADM has a poor prognosis due to RP-ILD. Currently, treatment protocols for triple therapy of high-dose steroid therapy, calcineurin inhibitor, and intermittent intravenous cyclophosphamide (IVCY) are becoming widespread, but treatment is often difficult. This time, we experienced two cases in which TOF was introduced and remission was obtained. [Case 1] 64-year-old man, cough and erythema such as heliotrope rash appeared. He was admitted with a diagnosis of RP-ILD with anti-MDA-5 ab-positive CADM. PSL1 mg/kg, tacrolimus (TAC), and IVCY were started for ILD. When TAC was discontinued due to the development of reversible cerebral vasospasm syndrome, ILD worsened. Although TOF was introduced, the dose was reduced because of complications. He passed without relapse. [Case 2] 52-year-old man, cough and rash appeared. He was admitted to the hospital with a diagnosis of RP-ILD with anti-MDA-5 ab-positive CADM. Although PSL1 mg/kg, TAC, and IVCY were started, ILD was gradually worsening. However, ILD improved after TOF was introduced. [Conclusions/clinical significanxe] RP-ILD with anti-MDA-5 ab-positive CADM can be fatal and requires early intervention. We have shown that TOF may be effective in the presence of clinical signs of relapse of RP-ILD.

W50-3

Anti-ARS antibody-positive polymyositis-associated interstitial pneumonia complicated by COVID-19 infection: A case report

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Conflict of interest: None

A 72-year-old man with anti-ARS antibody-positive polymyositis complained of exertional dyspnea. One month prior to admission (when he was treated with prednisolone 10 mg and tacrolimus 2 mg), a chest computed tomography (CT) scan showed a worsening of the pre-existing interstitial pneumonia. The mechanic's hands and weakness of the proximal muscle appeared 22 days before admission. He had progressive dyspnea. A day before his admission, he complained of fever and cough. After admission, a CT scan showed an expansion of the ground-glass opacity area, and blood tests showed elevated CRP and KL-6 levels. He was initiated on therapy with 70 mg prednisone. The next day, the patient tested positive for SARS-CoV2 on PCR, but his oxygen saturation was maintained stable since admission. On the 3rd day of hospitalization, his oxygen saturation worsened, so he was intubated, and the administration of favipiravir was started. ECMO was performed from hospitalization day 5 to day 19. On hospitalization day 28, his condition improved when no oxygen administration was required. In these times of the COVID-19 epidemic, attention should be paid to COVID-19 infection, even in the case of a typical phenotype of exacerbation of connective tissue disease-associated interstitial pneumonia.

W50-4

A case of anti-synthetase syndrome accompanied with pulmonary hypertension

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Conflict of interest: Yes

[Case] A 77-year-old woman, who had suffered from interstitial lung disease (ILD) for 2 years, presented Gottron's sign, mechanic's hands, and shawl sign accompanied with muscle weakness 2 months before she visited our department. Her laboratory examinations revealed the positivity of anti-aminoacyl tRNA antibody, which was confirmed as anti-EJ antibody. Muscle biopsy from triceps brachii muscle showed perifascicular necrosis. A respiratory function test revealed her moderate restrictive ventilatory impairment. An echocardiography detected the possibility of pulmonary hypertension (PH), and a cardiac catheterization revealed high mean pulmonary artery pressure (mPAP), 33 mmHg, and pulmonary capillary wedge pressure within a normal rage. Her diagnosis was made as anti-synthetase syndrome (ASS) accompanied with PH. ILD was improved by a 4-week treatment with steroid-pulse therapy, high-dose prednisolone, and tacrolimus, moreover, mPAP was also improved to 19 mmHg. She has not experienced any recurrences of PH. [Clinical significance] Cases with inflammatory myopathies rarely develop PH. While mixed pathogenesis has been indicated in collagen disease-related PH, our case indicates that immnosuppressive therapies should be preceded treatments with vasodilator agents for ASS-related PH.

W50-5

A case of dermatomyositis complicated with progressive acute heart failure

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Conflict of interest: None

A 59-year-old Japanese woman developed pruritic erythema on her face and back and muscle weakness. Serologic and radiographic tests revealed elevated myogenic enzymes and anti-nuclear antibody (x640) and anti-MDA5 antibody and interstitial lung disease (ILD). She was diagnosed as dermatomyositis (DM) and underwent combined immunosuppressive agents using corticosteroid, tacrolimus, and cyclophosphamide pulse and high-dose immunoglobulin, which gave satisfactory symptomatic relief. With gradual tapering of corticosteroid, progressive respiratory distress and lower extremity edema appeared. Echocardiogram showed global ventricular dysfunction and an endomyocardial biopsy showed myocardial degeneration and fibrosis, consistent with congestive heart failure due to DM-related myocarditis. Her symptoms responded to diuretic, cardiotonic, and additional immunosuppressive agents. Cardiac involvement in DM is an underrecognized complication and represents a poor prognostic predictor. Myositis may occur subclinically and progress into overt irreversible cardiac failure. It mostly does not correlate with other myopathic and cutaneous manifestations or ILD. Regular screening for cardiac function is important for prompt diagnosis and treatment for the fatal cardiovascular complication in DM.

W50-6

A case of anti-PL-7 antibody-positive polymyositis with pericarditis

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Kaita Sugiyama, Atsuma Nishiwaki, Mitsuhiro Iwata, Kumiko Akiya, Hitomi Haraoka, Noboru Kitamura, Masami Takei
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Conflict of interest: None

A 71-year-old man with Rheumatoid arthritis was referred to our hospital with slight fever and backache, which resulted in diagnosis of acute pericarditis with cardiac enlargement, pleural effusion, and inflammatory reaction. As echocardiography showed cardiac tamponade, pericardiocentesis/drainage were performed. The blood test showed slightly elevated myogenic enzyme and anti-ARS antibody positive, whose anti-PL-7 antibody was positive. He had myalgia in dorsal muscles, where MRI T2-weighted image showed hyperintense signal. As diagnosis of polymyositis with a complication of acute pericarditis, he had started to be on prednisolone 25 mg/day, and pericardial effusion, inflammatory response and myogenic enzyme level were improved. [Discussion] Although pericarditis is rare as a complication of polymyositis, it is noted that anti-PL-7 antibody positive patients are more likely to havePericarditis. Therefore, measurement of anti-PL-7 antibody should be considered to patients with pericarditis, especially who have myalgia or arthralgia.

W51-1

A case of anti-MDA-5 antibody-positive rapidly progressive interstitial pneumonia that responded to multidisciplinary treatment, including ventilator management and concomitant tofacitinib

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Conflict of interest: None

[Case] A 70-year-old woman. She had a skin rash on her extremities for 3 weeks prior to hospitalization. She had a fever for 2 weeks and a dry cough. There was a typical skin rash with dermatomyositis such as Gottron's sign, and there were no muscular symptoms. The patient was later brought back with anti-MDA-5 antibody 3000 index. The patient was treated with steroid pulse therapy, prednisolone (PSL) 60 mg, tacrolimus (TAC), and intravenous cyclophosphamide from the first day. However, interstitial pneumonia (IP) progressed, and ventilator management and simple plasma exchange (PE) were administered on days 3 -11. Subsequently, the PSL was increased, and on days 35-42, ventilator management was combined with PE. Tofacitinib (TOF) was introduced on day 43, and prophylactic ganciclovir and micafungin were administered in the short term. She was transferred to the other hospital on day 104 for rehabilitation. [Clinical significance] The prognosis of patients with RP-ILD-associated CADM who do not respond to initial treatment is considered to be severe. This is a very serious case requiring ventilator management, but ICU management, combination of TOF and prophylactic medication are considered to have been effective.

W51-2

A case of Pembrolizumab induced myasthenia gravis and myositis

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Conflict of interest: None

A case of Pembrolizumab induced myasthenia gravis and myositis A 79-year-old male patient with multiple metastases to the lung, liver and bone from right renal pelvis cancer was treated with Pembrolizumab in department of urology. A month after the first administration, he presented with weakness in limb and neck, dyspnea and ptosis. These symptoms were regarded as immune-related adverse events (irAE) and he was referred to our department. Edrophonium test was negative and repetitive nerve stimulation test did not show the result of waning, on the other hand serum CK was elevated and T2-weighted MRI showed high intensity on bilateral thigh muscles. He was diagnosed as having Pembrolizumab-related myositis and was treated with high doses of corticosteroids and immunoglobulin. His symptoms improved promptly. After all, he was diagnosed as myasthenia gravis (MG) complicated with myositis because anti-AchR antibody proved to be positive. As several cases of PD-1 inhibitors induced severe myasthenia gravis and myositis have been reported recently, it is important for rheumatologists to be aware of this condition.

W51-3

Efficacy of simple plasma exchange in anti MDA5 antibody positive dermatomyositis patient complicated by fungal infection: A case report

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Conflict of interest: None

A 52-year-old man was admitted for finger stiffness, skin rash, shoulder and hip pain, and low-grade fever. Gottron's papules on the MP joints and scratch dermatitis on the precordium and back were found. Laboratory findings show elevated CK 252 U/L, ALD 11.4 U/L, Ferritin 1281 ng/mL. Muscle weakness was not clear, and a diagnosis of clinically asymptomatic dermatomyositis was made. Anti-MDA5 antibody was positive, and mild interstitial pneumonia was also found. Prednisolone, tacrolimus, and IVCY have been started. The initial treatment was effective, but the patient was complicated by a fungal infection. VRCZ was introduced as an antifungal drug, and simple plasma exchange therapy was performed as a treatment for dermatomyositis. After the treatment change, the symptoms were promptly alleviated, and ferritin was significantly reduced. Before and after plasma exchange, serum IL-6 decreased from 2.08 pg / mL to below the detection limit. Although there is currently no consensus on the treatment of refractory cases of anti-MDA5 antibody-positive dermatomyositis, simple plasma exchange was significantly effective in this case. It was suggested that reducing inflammatory cytokines as well as autoantibodies by plasma exchange may contribute to the therapeutic effect.

W51-4

Pulmonary hypertension in antimelanoma differentiation-associated gene 5 antibody positive clinically amyopathic dermatomyositis (CADM)

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Conflict of interest: None

[Case] A 28-year-old female who was diagnosed with anti-MDA5 antibody-positive CADM at another hospital was referred to our hospital. Oral glucocorticoid was started on an outpatient basis. However, her skin rash ulcerated, so she was admitted to the hospital for immunoglobulin. Shortly before the admission, dyspnea on exertion appeared, and a chest CT showed mildly worsening of the lung field shadow and diffusion capacity of the lung (DLco) was low, so steroid pulses and immunosuppressant were administered. Lung field shading improved and forced vital capacity was normal, but DLco was further reduced. Echocardiography showed a gradual increase in tricuspid regurgitation velocity, and a right heart catheterization (RHC) was performed at X+4 months and diagnosed as PH. Steroid pulses, rituximab, and mycophenolate, bosentan were added, and she was discharged with home oxygen therapy. X+8 months RCH findings were normalized. The skin ulcer was also improved and disappeared. The skin ulcers improved and disappeared. [Discussion] Anti-MDA5 antibodies are known to be associated with severe skin lesions and rapidly progressive ILD but reports of PH complications are rare. This case is interesting in that the skin lesions and PH are concurrent and immu-

nosuppressive agents are successful.

W51-5

Anti-mitochondrial antibody-positive myositis with skin thickening

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Conflict of interest: None

Anti-mitochondrial antibody (AMA)-positive myositis is one of the idiopathic inflammatory myositis, characterized by chronic progress and cardiac involvement. We experienced a case of AMA-positive myositis with skin thickening. A 63-year-old man had been suffered from skin thickening of the left leg 5 years before hospitalization to our hospital. Two years later, skin thickening had gradually expanded to the trunk, accompanied with muscle weakness, weight loss, dysphagia, and dyspnea on exertion. Physical examination revealed skin thickening from left leg to trunk, and muscle weakness. Serum CK, CK-MB and troponin I levels were elevated, and echocardiogram showed left ventricular diffuse hypokinesis. Skin biopsy revealed increased collagen fiber and positive alcian blue staining. Myocardial biopsy also revealed positive alcian blue staining. AMA was positive, and muscle biopsy suggested immune-mediated necrotizing myopathy. He was diagnosed as AMA-positive myositis, and treated by high-dose glucocorticoid and intravenous immunoglobulin, which improved the symptoms. This case implies skin thickeing caused by AMA-positive myositis, and the importance of detailed examination on skin.

W51-6

A Case of Anti SAE Antibody Positive Dermatomyositis with Erythroderma

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Conflict of interest: None

A 57-year-old woman with 4-month history of erythema followed by dysphagia and difficulty of climbing stairs was sent to our department with suspicion of dermatomyositis (DM). The findings of DM such as Gottron sign on fingers, elbows and knees, nailfold bleeding, facial erythema, scratch like dermatitis, and muscle weakness of lower muscle. The laboratory data showed CK 349 U/mL, CRP 0.3 mg/dL, positive antinuclear antibody (speckled) at titers of 1:320, positive antiSS-A antibody (Ab) (≧ 240 U/mL), however, antiARS, MDA5, Mi2, TIF1γ Ab were negative. STIR MRI indicated high signals in bilateral gluteal and thigh muscle. No evident of malignancy, ILD, and cardiomyopathy was found in whole body CT scan, echocardiography, gastrointestinal endoscopy. Skin biopsy revealed thickening of the stratum corneum, vacuolar degeneration, mucin deposition on the epidermis, and melanin dripping. Muscle biopsy showed perifascicular atrophy, and the diagnosis of DM was made. Oral prednisolone of 60 mg daily was initiated and her condition got better. Additional inspection of anti SAE 1/2 Ab was positive. Anti-SAE Ab appear in 1.5% of DM in Japan, characterized by an extensive rash that precedes myositis and is often associated with dysphagia. we think this case is important to diagnostic strategy of DM.

W52-1

Current status of treatment for Takayasu's arteritis -a nationwide retrospective observational study JPVAS-

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Conflict of interest: None

[Objective] To clarify the current status of Takayasu's arteritis (TAK) treatment in Japan. [Methods] We retrospectively examined the clinical status and achievement rate of remission for 3 years from the start of treatment for 129 patients newly diagnosed with TAK from 2007 to 2014 at 24 facilities. [Results] The average age of the patients was 35±18 years, and the male/female ratio was 1:5. At onset, cranial symptoms were observed in 23%, cervical symptoms in 47%, upper limb symptoms in 25%, respiratory symptoms in 24%, and bruit in 30%. CRP was 6.1±5.4 mg/dL, WBC 8900±3100/mm3, ESR 76±37 mm/h, HLA-B52 positive in 63%, and AR in 30%. Positive image findings were found in the order of bilateral carotid arteries, bilateral subclavian arteries, aortic arch, and thoraco-abdominal aorta. The initial dosage of PSL was 35±13 mg/day. An additional immunosuppressive (IS) agent was given to 63% of the patients during treatment. Within 2 years of treatment, 92% of patients reached remission. When the right subclavian artery was affected, remission was achieved later than in the non-affected group ($p<0.05$). No difference were observed in remission rate regardless of age of onset or IS agent initial use. [Conclusions] The current status of medical treatment for TAK has been clarified.

W52-2

Efficacy of tocilizumab for patients with relapsing Takayasu arteritis

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Conflict of interest: None

[Objective] At JCR2019, we have reported the case with Takayasu arteritis (TA), in which arterial lesions progressed even after the inflammation subsided with glucocorticoid therapy, and tocilizumab (TCZ) was finally effective to improve arterial stenosis. This study aimed to clarify the clinical features of TA patients in our department. [Methods] Clinical information on TA patients was evaluated retrospectively on an electrical medical record basis. [Results] Twenty-seven patients with TA (23 women) were recruited, and the age of disease onset was 22 (13-71) (years, median). The initial dosage of prednisolone (PSL) usage was 30 (0-60) (mg/day, median), and steroid pulse therapy was performed in 9 cases (33%). Eighteen patients (66%) relapsed after initial PSL treatment, and they were treated with immunosuppressants or TCZ. The period until a relapse was 16.5 (1-54) (months, median). There was no significant difference in the initial clinical parameters between relapsed or non-relapsed groups. TCZ was administered to 9 patients in the relapsed group (3 cases were treated in combination with immunosuppressants), and 8 cases (88.8%) achieved remission after TCZ therapy. [Conclusions] TCZ was effective in remission induction of relapsing TA patients.

W52-3

The utility of cerebral blood flow SPECT scan in Takayasu's arteritis

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Conflict of interest: None

[Objective] To assess the clinical utility of cerebral single-photon emission computed tomography (SPECT) in patients with Takayasu's arteritis. [Methods] We retrospectively investigated the patients with Takayasu's arteritis who visited to our department from 2012 to 2020. Eight patients, who had the carotid artery lesions, were examined by ^{123}I-IMP cerebral blood-flow SPECT scan. We analyzed the association between the findings of SPECT (resting cerebral blood flow and cerebrovascular reserve capacity) and clinical information. Results: All patients were female and the mean age was 31.4 ± 18.0 years. In the patients, who

have maintained remission by treatment with corticosteroid monotherapy, cerebrovascular reserve capacity tended to decrease compared to the patients with relapse (%increase: non-relapse 50.5% vs relapse 23.9%, p = 0.11). The cerebrovascular reserve capacity did not correlate with CRP or ESR. In a patient, who was examined by the SPECT scan before and after induction therapy, the cerebrovascular reserve capacity was improved after the treatment. [Conclusion] In patients with Takayasu's arteritis treated with steroid monotherapy, decreased cerebrovascular reserve capacity in SPECT scan might predict relapse.

W52-4

A study of long-term tocilizumab treatment for Takayasu arteritis in our hospital

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Conflict of interest: None

[Objective] There are few reports of long-term tocilizumab (TCZ) treatment for Takayasu arteritis in Japan., and we report here on the use of tocilizumab and its treatment in our department. [Methods] As of October 2020, a total of 8 data-acquirable TAK cases at our hospital and other hospitals who had been on TCZ for more than 12 months were evaluated for prednisolone (PSL) dosage and the presence of relapse or adverse events. [Results] The mean age at TCZ induction was 42.1 years, the mean PSL dose at the time of TCZ induction was 21.3 mg/day. The average duration of treatment was 26.6 months as of October 2020, with the exception of one patient who discontinued PSL at the patient's request, who was able to continue TCZ, and five patients whose treatment interval was extended to two weeks or longer. No relapse has been observed. One case of diverticulitis and three cases of hematopenia were reported, but all of them improved with the temporary discontinuation of TCZ or the extension of the interval between doses, and the patient is doing well with continued TCZ treatment. [Conclusions] TCZ can reduce relapse of TAK and may lead to steroid reduction and prolongation of TCZ intervals.

W52-5

Usefulness of tocilizumab in treatment of Takayasu arteritis

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Conflict of interest: None

Objectives: An official introduction of tocilizumab (TCZ) to use in treatment of Takayasu arteritis (TA) has recently been changing therapeutic strategy of this disease. To clarify the usefulness of TCZ we investigate clinical profiles of the patients with TA. Methods: We retrospectively studied medical records of the TA patients who had been treated in our hospital. Results: Six patients were enrolled in this study (1 man and 5 women classification of disease type: 1 in type I, 4 in type IIa and 1 in type V). All of the patients were treated with oral corticosteroid, and 3 of these simultaneously received immunosuppressants. TCZ was given to 3 patients who had shown recurrence or persistence of arteritis while tapering oral corticosteroid, leading to improvement of clinical symptoms in parallel with a decrease in inflammatory reactions and lack of uptake on PET. Both corticosteroid and immunosuppressants could be tapered or discontinued successfully. One patient with aortic valve insufficiency at the onset of TA showed stable cardiac function under low-dose corticosteroid and TCZ. Conclusions: TCZ is a potent therapeutic option in treatment of TA with regard to successful tapering or cessation of corticosteroid and immunosuppressants.

W53-1

Proposal of a method for diagnosis as an optimization of Cranial type imaging diagnosis of giant cell arteritis: presentation of useful of vascular echo for early diagnosis and proposal of vascular echo method for spread

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Conflict of interest: None

[Objective] Giant cell arteritis (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 then evaluated the effect of optimizing diagnostic imaging and methods for patients with suspected GCA who visited our hospital during 2019. Vascular mapping was carried out using vascular ultrasonography for three-dimensional computed tomography angiography (3D CTA) and other imaging methods as references. [Results] The number of biopsies performed decreased from 50% (10 of 20 patients) from 2012 to 2018 to 15% (3 of 20 patients) in 2019. Two cases in the present study had positive findings in both biopsy and vascular ultrasonography, and we found out common sign and we called up down sign. We present ultrasonography is the best imaging method to diagnose early GCA. No patients with GCA developed blindness or stroke during 2019. We are going to report new patients who are required for differential diagnosis in 2020-2021. [Conclusions] We propose that vascular ultrasonography should be performed as the first examination for the diagnosis of GCA by the creation of vascular mappings when GCA is suspected in order to prevent blindness and stroke.

W53-2

PET-CT and clinical findings in elderly patients with large vessel vasculitis

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Conflict of interest: None

[Objective] Patients with elderly onset large vessel vasculitis (LVV) often struggle with disease classification. We aimed to clarify the characteristics of elderly patients with LVV who have lesions in large vessels based on PET-CT findings. [Methods] Seventy-two LVV patients who had had PET-CT imaging history and had no findings of temporal artery inflammation were included in this study. Blood vessels with FDG accumulation by PET-CT were considered as affected blood vessels, and the strength of FDG accumulation in all twenty-three blood vessels was evaluated with a semi-quantitative score (0-3) for each blood vessel. We divided by age of 50 years into two groups: young-onset and elderly-onset LVV, and we compared the number of affected blood vessels and total score. [Results] PET-CT affected blood vessels and total scores in the elderly-onset group were significantly higher than those in the young-onset group. In addition, some of the patients with HLA-B52 allele in the elderly-onset group had higher PET-CT total scores and they formed a cluster. [Conclusions] Based on PET-CT imaging, young-onset and elderly-onset LVV were clearly distinguished from each other, and some HLA-B52 allele carriers in elderly-onset patients presented a different distribution of affected vessels.

W53-3

Disease-specific gene expression in CD4 positive cells and CD14 positive cells of peripheral blood cells in patients with giant cell arteritis

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Conflict of interest: None

[Objective] $CD4^+$ T cells and $CD14^+$ monocyte might play an important role in pathogenesis in giant cell arteritis (GCA). This study aims to find disease-specific gene expression in patients with GCA. [Methods] Patients with GCA newly diagnosed at Tama-Hokubu Medical Center, Tama Medical Center, and Tamananbu Chi-iki Hospital were included. We set patients with rheumatoid arthritis who achieved DAS28-CRP remission as the control group. $CD4^+$ cells and $CD14^+$ cells were separated from peripheral blood, and mRNA ware extracted. We performed microarray using Aligent's kit and compared gene expression analysis between the GCA and control groups. [Results] Six patients in the GCA group (mean 74.2 years old) and four patients (71.8 years old) in the control group were included. Hierarchical cluster analysis and principal component analysis showed that different gene expression patterns in both $CD4^+$ cells and $CD14^+$ cells in GCA groups compared with that of the control group. Inflammatory cytokine genes and some oncogenes in $CD4^+$ cells and chemokine-related genes in $CD14^+$ cells expressed higher in the GCA group than in the control group. [Conclusion] We observed diseases specific gene-expression patterns in $CD4^+$ cells and $CD14^+$ cells in the GCA group.

W53-4

Clinical characteristics in patients with giant cell arteritis Division of rheumatology, Nagano Red Cross Hospital

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Nagano Red Cross Hospital

Conflict of interest: None

[Objective] The aim of this study is to elucidate the clinical characteristics in patients with giant cell arteritis (GCA). [Methods] We retrospectively reviewed medical records of GCA patients in our hospital from October 2015 to September 2020. [Results] Ten patients were enrolled in this study. Initial symptoms were headache (8 cases), impairment of vision (2 cases), and central nervous involvement due to stroke (2 cases). Halo signs of temporal artery ultrasound were observed in 6 cases. Temporal artery biopsies were performed in 5 cases, and inflammatory cell infiltration mainly composed of polynuclear giant cells and lymphocytes was observed in all cases. Remission induction therapy was started with prednisolone (PSL) in 9 patients and steroid pulse therapy in 3 patients. Relapse was observed in 3 cases. Eight of 10 cases maintained remission with PSL alone and other 2 cases maintained with PSL plus methotrexate. [Conclusions] Although no halo sign was observed by ultrasound, there were two cases in which GCA was diagnosed by temporal artery biopsies. Therefore we thought that temporal artery biopsy was important for diagnosis of GCA. And if CRP level in a patient with impairment of vision, or stroke is markedly elevated, we should cite GCA as a differential diagnosis.

W53-5

Tocilizumab as remission induction therapy for Giant Cell Arteritis disease

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Conflict of interest: None

[Purpose] We investigated the efficacy and safety of Tocilizumab (TCZ) in induction therapy and maintenance therapy of Giant Cell Arteritis (GCA). [Methods] Nine patients (mean age 66.9) with GCA (C-GCA 2, LV-GCA 7) were treated with TCZ 164 mg/W in 5 patient, 164 mg/2W in 3, 400 mg/2W in 1. No other immunosuppressants were used. The clinical manifestations included headache, jaw claudication, double vision in C-GCA patients, and fever, abdominal pain in LV-GCA patients. Three patients had polymyalgia rheumatica (PMR). The mean initial dose of PSL was 21.9 mg. The average observation period were 18.9 months. [Results] All patients responded well to TCZ. Relapse was seen in 2 cases after 10 months and 12 month, added increasing PSL. The average PSL dose after 1 year is 3.5 mg. Remission had been maintained in all cases at the time of final observation, and 6 were able to discontinue PSL. Leukocytopenia was observed in one case, but improved by extending the interval of TCZ. [Conclusion] TCZ seems effective, safety and useful for reducing the cumulative dose of steroids for the treatment of GCA.

W53-6

Effectiveness of tocilizumab monotherapy for treatment of giant cell arteritis and importance of ultrasound imaging

Haruki Matsumoto[1], Yuya Fujita[1], Tomoyuki Asano[1], Shuzo Sato[1], Jumpei Temmoku[1], Makiko Furuya[1], Naoki Matsuoka[1], Eiji Suzuki[1,2], Hiroshi Watanabe[1], Kiyoshi Migita[1]
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Conflict of interest: None

An 89-year-old man was referred to our department for frequent bilateral temporal headache. On admission, his clinical examination was unremarkable except for the palpable distended temporal artery with tenderness. Laboratory data showed elevated inflammatory markers. Color doppler sonography (CDS) showed wall thickening of the bilateral temporal arteries with luminal stenosis. Pathological findings of superficial temporal artery revealed the formation of granuloma with lymphocyte infiltration and multiple giant cells at arterial wall, accompanied with the wall structure destruction. From these findings, we established diagnosis of giant cell arteritis (GCA) in this patient. Because of his age and cardiovascular risk, he received biweekly subcutaneous injection of Tocilizumab (TCZ). TCZ was effective for his symptoms, laboratory data and CDS imaging. Although glucocorticoids have traditionally been the mainstay of GCA treatment, the importance of Interleukin-6 has recently been reported in the pathogenesis of GCA. Thus, TCZ can be a key drug for treatment of GCA. In addition, CDS is useful for diagnosis of GCA and rapid assessment of vascular damage for evaluating therapeutic effect in GCA.

W53-7

Tocilizumab Use in Giat Cell Artertis: Sigle Center Experience

Hiromichi Tamaki, Takanori Ito, Sho Fukui, Takehiro Nakai, Genki Kidoguchi, Hiroki Ozawa, Satoshi Kawaai, Yukihiko Ikeda, Ayako Kitada, Yuri Ohara, Atsushi Nomura, Hisanori Shimizu, Ken-ichi Yamaguchi, Masato Okada
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Conflict of interest: Yes

[Objective] Tocilizumab (TCZ) was approved for Giant Cell Arteritis (GCA) in August 2017 in Japan. However, data for its use in Japan is still lacking. Here, we aimed to investigate TCZ use for GCA in Japan. [Methods] This is a retrospective chart review of the patients with GCA at St. Luke's International Hospital in Tokyo. The patients with GCA who used TCZ and who were followed for at least 12 months were reviewed. [Results] Thirteen patients were identified (4 men and 9 women). The median age at initiation of TCZ was 72 years. TCZ was used for recurrence in 10 patients. TCZ was used for concerns of glucocorticoids toxicity in 3 patients with new onset GCA. The median dose of prednisolone at the initiation of TCZ was 15 mg and that at 6 months was 3.75 mg ($p=0.02$ [Wilcoxon signed rank test]). That at 12 months was 0 mg ($p=0.03$ [Wilcoxon signed rank test]). One patient discontinued TCZ due to liver enzyme elevation and another discontinued due to leukopenia. One transiently stopped TCZ but the patient did not develop leukopenia after restarting TCZ with discontinuing another culprit medication. Prednisolone was discontinued in 7 out of eleven patients at 12 months. Relapse occurred in one patient. [Conclusion] Tocilizumab seems to have significant steroid sparing effect.

W54-1

Increased circulating cell-free DNA in eosinophilic granulomatosis with polyangiitis: implications for eosinophil extracellular traps and thrombosis

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Conflict of interest: None

[Objective] cf-DNA levels were elevated in EGPA and correlated with eosinophil count and D-dimer. Then, eosinophil extracellular traps (EETs), the cell death called EETosis, plays important role in Allergic disease. We also reported EETs showed greater stability against DNase in vitro, and associated with cfDNA levels in EGPA. However the presence of EETs/EETosis in EGPA or thrombi remains unclear. [Methods] Tissue samples from 9 EGPA patients were examined by immunofluorescence and transmission electron microscopy. [Results] Tissues were immunostained with CD31 and citrullinated histone H3, a marker for ETs. Comparing with H&E staining, several chromatolytic cells containing net-like CitH3 and DNA indicated the presence of EETs in small vessel thrombi. Additionally, biopsy samples were double-immunostained for the eosinophil-specific proteins, cgal-10 and MBP, to detect intact and EETotic cells. EETotic eosinophils (gal-10-/MBP+) were observed in small vessel thrombi. The ultrastructural morphological characteristics of EETosis were confirmed by TEM. [Conclusions] EETs/EETosis were observed in thrombi of EGPA. These results suggested that EETosis-mediated cytolytic eosinophils in thrombi might be responsible for the increases in circulating cf-DNA in EGPA patients.

W54-2

Anti-neutrophil extracellular traps (NETs) antibody that recognizes myosin light chain 6 has an inhibitory activity against DNase I-mediated degradation of NETs

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Conflict of interest: None

[Objective] In anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, a vicious cycle of neutrophil extracellular traps (NETs) and ANCA occurs, and antibodies to NETs (ANETA) are produced in some patients. Part of ANETA inhibit the activity of DNase I, a key regulator of NETs, and thus resulting in an amplification of the NETs-ANCA vicious cycle. We attempted to determine the antigen of ANETA that possesses an inhibitory activity against the degradation of NETs. [Methods] Neutrophils and NETs were affixed to glass slides and reacted with ANETA pre-absorbed with MPO. Soluble proteins of neutrophils were electrophoresed and western blotting (WB) was performed using ANETA-positive sera as probes. [Results] ANETA reactivity was not absorbed by MPO, thus suggesting that ANETA was an ANCA different from MPO-ANCA. An ANETA specific band was identified as myosin light chain 6 (MYL6) by nano LC MS/MS analysis. The reactivity of recombinant MYL6 with ANETA was confirmed by WB. In addition, the degradation of NETs was observed by adding anti-MYL6 antibody and DNase I to NETs, and anti-MYL6 antibody significantly inhibited the degradation of NETs by DNase I. [Conclusions] MLY6 was identified as an antigen of ANETA, which has the inhibitory activity against the degradation of NETs.

W54-3

Association of HLA-class II alleles with relapse in MPO-ANCA positive vasculitis

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Conflict of interest: None

[Objective] A substantial proportion of patients with ANCA-associated vasculitis (AAV) experience relapse. In the European population, *HLA-DPB1*04:01*, the susceptibility allele to granulomatosis with polyangiitis, has been associated with the risk of relapse. In this study, we examined whether *HLA-class II* alleles are associated with relapse in AAV in a Japanese population. [Methods] Among 264 AAV patients enrolled in cohort studies of remission induction therapy, 199 MPO-ANCA positive, PR3-ANCA negative patients who achieved remission during the observation period were studied. The carrier frequencies of *HLA-DRB1* and *DQB1* alleles were compared between the patients with and without relapse, and the relapse-free survival rate in each allele carriers and non-carriers was compared using a Cox proportional hazards model. [Results] Carrier frequencies of *DRB1*09:01*, *DRB1*08:02*, *DQB1*03:03* and *DQB1*04:02* were increased in AAV patients with relapse compared with those without relapse. Relapse-free survival rate was significantly lower in *DRB1*09:01*, *DQB1*03:03* carriers when conditioned on age, sex, clinical classification and treatment. [Conclusions] These results suggested that *HLA-class II* alleles may be associated with relapse in MPO-ANCA positive AAV.

W54-4

Patient with ADA2 Deficiency Diagnosed at Age 27 and Monocytes Analysis

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Conflict of interest: None

[Introduction] ADA2 deficiency (DADA2) is an autosomal recessive disease caused by mutations in *CECR1* gene. Clinical features of ADA2 are similar to those of polyarteritis nodosa (PAN). The mechanism of vasculitis is unknown, but it has been reported that monocytes from DADA2 patients displayed higher production of TNF-α compared with healthy controls. Herein, we report DADA2 patient and her monocytes functional analysis. [Case Report] The patient is a 27 year-old female. She has no notable family history. She had erythema from 1 year old and had repeated strokes from 13 years old. At the age of 15, she suffered a renal infarction and was diagnosed with a PAN. Prednisolone (PSL) and azathioprine (AZP) were started. At the age of 27, a genetic test revealed that a mutation in complex heterozygotes in ADA2. Then she introduced etanercept (ETN). Monocyte analysis revealed increased TNF-α and IL-6 production. Even one month after the introduction of ETN, monocyte TNF-α and IL-6 production did not change. [Conclusion] Genetic testing should be done when PAN-like symptoms occur from a young age. Monocyte TNF-α and IL-6 production enhancement may be associated with pathophysiology, analysis over time is underway.

W54-5

The Effect of IL-5 blockade on Serum IL-5 Level and Peripheral Eosinophil Count in the Seven refractory cases of Eosinophilic Granulomatosis with Polyangiitis (EGPA)

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Conflict of interest: None

[Objective] To investigate the effect of IL-5 inhibition on the symptoms and the laboratory parameters in the active disease of EGPA [Methods] Seven patients with the refractory disease were given 300 mg mepolizumab every month. We retrospectively studied their treatment for EGPA, and serum IL-5 and peripheral eosinophil counts before and during mepolizumab therapy. [Results] Eligible patients' median age was 54. The pur-

poses of mepolizumab were deterioration of the disease for five patients and eosinophilia for five (three patients had both). PSL dose at the initiation of mepolizumab was 6.5±2.7 mg/day. Eighteen months (median) passed before the first administration of mepolizumab. Median eosinophil counts were 600/μL. Clinical symptoms were ameliorated in all patients. During mepolizumab therapy, eosinophil counts were significantly reduced to 31.4±17.7/μL. Serum IL-5 was increased in two patients before the administration of mepolizumab, and it decreased under the cut-off level in two patients. In contrast, increased IL-5 level was observed in two patients during mepolizumab therapy. In five patients, PSL doses were decreased at least for 1 mg/day. [Conclusions] IL-5 inhibition improved symptoms and eosinophilia in EGPA, whereas it gave various effects on the serum IL-5 level.

W55-1

The impact on patient outcomes of the recent treatment strategy for ANCA associated vasculitis

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Conflict of interest: None

[Objective] Recently, the treatment strategy of ANCA associated vasculitis (AAV) has changed with the intensive corticosteroid (CS) tapering and RTX therapy. We studied the impact on patient outcomes of the recent treatment strategy for AAV. [Methods] By using the database of our multi-center vasculitis cohort study, we recruited AAV patients except for EGPA, who were followed for more than two years. We compared two groups, which were divided based on dates of diagnosis. [Results] The former group (2012/1~2015/5) had 57 patients, and the latter (2015/6~) had 59 patients. The median ages were 69 years old and 74 years old, respectively. There were no differences in sex, ANCA status and BVAS scores. The latter had less MPA (59.7% vs 35.6%) more unclassified AAV (8.8% vs 28.8%). For initial remission induction, the latter used less CY (40% vs 14%), but more RTX (2% vs 22%). The latter group tapered CS more intensively (median PSL dose (mg/day): 10 vs 8 (0.5 y), 9 vs 4 (1y), 6 vs 3 (2y)). Remission, relapse and survival rates were comparable. VDI were decreased (averages: 1.7 vs 1.1 (0.5 y), 1.8 vs 1.2 (1y), 2.2 vs 1.3 (2y)). [Conclusions] We found that the recent AAV treatment strategy with intensive CS tapering and RTX inhibited the progression of vasculitis organ damages.

W55-2

Usefulness of tissue inhibitor of metalloproteinase 1 as a predictor of relapse and sustained remission in patients with antineutrophil cytoplasmic antibody-associated vasculitis

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Conflict of interest: None

[Objective] We previously identified serum TIMP-1 as a biomarker of disease activity in AAV with a targeted proteomics approach. In this study, we investigated whether TIMP-1 is clinically useful as a predictor of relapse and sustained remission in AAV patients with MPA and GPA during maintenance therapy. [Methods] The relationship between serum TIMP-1 levels and clinical outcomes in AAV patients receiving maintenance therapy was assessed using the follow-up data of the RemIT-JAV-RPGN study and data collected from AAV patients on maintenance therapy in our hospital (the MAAV-EU study). [Results] In the RemIT-JAV RPGN study, serum levels of TIMP-1 were significantly higher in mildly active AAV patients 6 months after the initiation of remission-induction therapy than in remission patients. Regarding maintenance therapy, elevated TIMP-1 levels in remission patients were associated with relapse and/or difficulty reducing the glucocorticoid dosage after 6 to 12 months. In the MAAV-EU study, serum levels of TIMP-1 were elevated in relapsed patients 6 months before relapse, earlier than the increase in serum levels of CRP. [Conclusions] We herein demonstrated that TIMP-1 is useful as a predictor of relapse and sustained remission in maintenance therapy for AAV.

W55-3

Examination of relapse and death risk in ANCA-related vasculitis at our hospital

Tohru Michitsuji[1], Naoki Iwamoto[1], Takuya Tomokawa[1], Tomohisa Uchida[1], Shota Kurushima[1], Shinya Nishihata[1], Yoshika Tsuji[1], Momoko Okamoto[1], Yushiro Endo[1], Toshimasa Shimizu[1], Remi Sumiyoshi[1], Tomohiro Koga[1], Shin-ya Kawashiri[1], Takashi Igawa[1], Kunihiro Ichinose[1], Mami Tamai[1], Hideki Nakamura[1], Tomoki Origuchi[2], Atsushi Kawakami[1]

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Conflict of interest: None

[Objective] In ANCA-related vasculitis (AAV), mortality risk have been reported in the past. But there are only a few studies considered by organ disability and severity. [Methods] This report is a retrospective cohort study of cases of AAV in our department from April 2000 to June 2019. 130 cases were included (88 with microscopic polyangiitis, and 42 with polyangiitis granulomatosis). The risk of death 12 months later and the risk of relapse 12 months later were analyzed using logistic regression analysis. [Results] Serum creatinine level, blood hemoglobin level, age of onset, and steroid monotherapy were extracted as risk factors for death after 12 months. Serum creatinine level and age of onset were extracted as risk factors for relapse after 12 months, too. Similar studies were conducted in the rapidly progressive glomerulonephritis group, alveolar hemorrhage group. In the rapidly progressive glomerulonephritis group, age was a risk factor for both death and relapse. In the diffuse alveolar hemorrhage group, only age was extracted as a risk for both relapse and death. [Conclusions] It was suggested that the age of onset is involved in the factors predicting mortality and relapse after 12 months of AAV. This time, we will analyze and report on other factors such as severity.

W55-4

Analysis of clinical features in relapsing MPO-ANCA-positive eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] Eosinophilic granulomatosis with polyangiitis (EGPA) is characterized by precedent bronchial asthma, eosinophilia and vasculitis, with about half of the cases being MPO-ANCA positive. However, clinical features of relapsed cases with EGPA are not well investigated. Therefore,

we have examined the relapse of MPO-ANCA -positive EGPA. [Methods] Ten patients with MPO-ANCA -positive EGPA (4 male and 6 female) who were admitted to our hospital after 1998 were followed up. The relapse was defined as the occurrence of >1 BVAS items caused by active vasculitis after having achieved remission. We analyzed the clinical features at the time of relapse with respect to the presence or the absence of MPO-ANCA and eosinophilia. [Results] During the study period, 17 relapses were observed, with an average time interval from the onset for 34.5 months. At the time of relapses, serum MPO-ANCA was positive in 15/17 (88%), associated with (10/17; 59%) or without (7/17; 41%) eosinophilia. There were two relapses with negative MPO-ANCA titers (2/17 relapses), one of which associated with eosinophilia. [Conclusions] The patients with MPO-ANCA-positive EGPA may see relapses within several years by variable clinical findings and even in the absence of an increase in MPO-ANCA titers and eosinophilia.

W55-5

Predictive factors of cytomegalovirus viremia during the clinical course of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis: a single center observational study

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Conflict of interest: None

[Objective] To elucidate predictive factors of cytomegalovirus (CMV) viremia for anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) patients, we conducted a single-center, retrospective, observational study. [Methods] Among 35 patients with newly diagnosed AAV between January 2013 and December 2019, factors associated with the development of CMV viremia were investigated via a logistic regression analysis. [Results] The CMV antigenemia test was performed in 25 patients (71%), of whom 15 (60%) were diagnosed with CMV viremia. Of these 15 patients, five developed a CMV infection. The total protein, hemoglobin, and platelet count at the time of the CMV antigenemia test were significantly lower in patients who developed CMV viremia. In addition, total protein, hemoglobin, and platelet count also presented significantly decreasing trends in the following order: patients who did not develop CMV viremia, patients who developed CMV viremia without any symptoms, and patients who developed CMV infection. All AAV patients with CMV recovered by appropriate treatment. [Conclusions] The total protein, hemoglobin, and platelet count may be useful markers for the prediction of CMV viremia and infection after the start of induction immunosuppressive therapy for patients with AAV.

W55-6

Echocardiographic features of acute-phase microscopic polyangiitis

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Conflict of interest: None

[Objective] Microscopic polyangiitis (MPA) is a type of ANCA associated vasculitis wherein various organs are affected. However, echocardiographic findings of MPA have been unclear. Here, we investigate the echocardiographic features of acute-phase MPA patients. [Methods] This single-center case-control study included 15 MPA patients who underwent echocardiography before or within 2 weeks of starting steroid for induction or reinduction therapy. The echocardiography parameters of thepatients were compared with those of the 30 age- and sex-matched controls. [Results] Significant difference in theleft ventricular end-diastolic diameter, left ventricular end-systolic diameter, and left ventricular ejection fraction was not observed between the two groups. However, the MPA group showedsignificantly higher left atrial diameter ($p = 0.033$), left atrial volume ($p = 0.001$), and left atrial volume index ($p = 0.001$) as well as higher early diastolic filling velocity (E-wave, $p = 0.015$; E/A, $p = 0.043$; E/e', $p = 0.041$), diastolic pulmonary venous flow velocity (D-wave, $p = 0.013$), and trans-tricuspid pressure gradient ($p = 0.019$). [Conclusions] Acute-phase MPA patients revealed diastolic dysfunction of the left ventricle. This finding indicates the importance of cardiac assessment in MPA.

W55-7

Clinical features of 10 patients with eosinophilic granulomatosis with polyangitis (EGPA) in our department

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Conflict of interest: None

[Objective] To clarify the clinical features of eosinophilic granulomatosis with polyangitis (EGPA) in our department [Methods] We have retrospectively examined symptoms, laboratory findings, organ lesions, and treatments of 10 patients with EGPA among the patients who visited our department in the past 1 year. [Results] 3 males and 7 females, the onset ages were 33 to 73 years. All patients had a history of preceding bronchial asthma. All had neuropathy, with rash in 9 cases, gastrointestinal lesions in 2, and renal lesions in 2. Only 3 cases had MPO-ANCA positive. IgG4 was measured at onset in all 5 cases with high values. Skin biopsy was performed in 8 cases and pathological findings consisted with EGPA, but sural nerve biopsy in 2 cases did not prove vasculitis. All patients were treated with steroids, 8 with other immunosuppressive drugs, IV-Ig in 1 and mepolizumab in 3. Initial treatment was successful and steroids were gradually reduced in all cases, but neurological symptoms still remain in 9 cases. [Conclusions] In our department, the clinical features of EGPA are as follows: The diagnoses were almost made by skin biopsy, and the treatment responses are good, but neuropathy is likely to remain. It is suggested that IgG4 may be a biomarker of EGPA.

W56-1

Efficacy of Rituximab for Otitis Media with ANCA Associated Vasculitis

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Conflict of interest: None

[Objective] We clarify efficacy of rituximab (RTX) for otitis media with ANCA associated vasculitis (OMAAV). [Methods] Seventy-three patients with granulomatosis with polyangiitis (GPA) were admitted to Niigata University Hospital from 1989 through 2019. Efficacy of RTX for GPA with or without otitis media were analyzed. [Results] RTX was used for six cases with otitis media and three cases without otitis media. CRP and Birmingham Vasculitis Activity Score prior to administration of RTX were 3.64±1.04 mg/dl, 12±5.9 in otitis media group and 1.04±0.43 mg/dl, 11±4.9 ($P=0.19$, 0.81, respectively). Five patients (83%) with otitis media and one patient (33%) without otitis media were in remission with RTX ($P=0.17$). GPA was relapsed in no patient with otitis media (0%) and one patient without otitis media (50%) during RTX therapy ($P=0.12$). The persistency of RTX was 67% in otitis media group and 33% in non-otitis media group ($P=0.41$). Cyclophosphamide was used prior to RTX in eight of all nine cases. The effect of RTX appeared a few months after injection of RTX in 50% of otitis media group. [Conclusions] Efficacy of RTX for GPA with otitis media was not inferior to that for GPA without otitis media. The effect of RTX for OMAAV can appear a few months after administration of RTX.

W56-2

Interim analysis results of post-marketing surveillance of mepolizumab in patients in Japan with eosinophilic granulomatosis with polyangiitis

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Conflict of interest: Yes

[Objective] A post-marketing surveillance was conducted to evaluate the safety and efficacy of mepolizumab in patients with eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] The target population included all patients who received mepolizumab for the treatment of EGPA in Japan. The study period was from May 2018 and the follow-up period per patient was 96 weeks. The safety endpoint was the occurrence of adverse events, and the efficacy endpoint was the overall efficacy assessment and clinical symptoms. [Results] As of September 23, 2020, 1,165 patients were enrolled and 380 case report forms were collected as the data for 12 weeks. 58.4% were female, mean age was 59.3, duration of disease was 3.6 years, and 93.4% of patients had comorbidities. Mean observation period was 192 days. Adverse events were reported in 25.0% of patients. As for safety specification, hypersensitivity/infection/malignant tumor were reported in 5.5% (EGPA1.3% etc.), 8.2% (Nasopharyngitis1.3% etc.) and 0.3%, respectively. The proportion of patients who did not have clinical symptoms were 10.7% at baseline and 33.6% at 48 weeks. [Conclusions] Interim analysis data on safety and efficacy endpoints in the post-marketing surveillance of mepolizumab for EGPA were reported. (Funding: GSK study, 208505)

W56-3

Comparison between mepolizumab and azathioprine for maintenance therapy of eosinophilic granulomatosis with polyangiitis: a single-center retrospective study

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Conflict of interest: None

[Objective] Glucocorticoid (GS) and azathioprine (AZA) are recommended in maintenance therapy of eosinophilic granulomatosis with polyangiitis (EGPA). The efficacy of mepolizumab (MEPO) were found in MIRRA study, but the efficacy of low-dose MEPO (LD-MEPO) was not found because the dose response study was not performed. We compared the efficacy and safety of LD-MEPO with AZA in the maintenance therapy. [Methods] We retrospectively examined patients with EGPA who received maintenance therapy of LD-MEPO or AZA from 2009 to 2020. We divided them into 2 groups, those treated with LD-MEPO and AZA, and evaluated the efficacy and safety. Relapse was defined as BVAS≧1. [Results] We evaluated 15 patients with MEPO group and 17 patients with AZA group. The mean observation period was 2.5 years. In the clinical features before the therapy, higher percentage of BVAS≧1, less doses of GS, and higher percentage of patients with immunosuppressive drugs, were observed in MEPO group ($p<0.01$, <0.01 and <0.01, respectively). No significant difference was found in cumulative relapse rate ($p=0.5$). We found higher continuance rate, and less percentage of adverse events in MEPO group ($p=0.02$ and <0.01, respectively). [Conclusions] LD-MEPO might be effective and safe in maintenance therapy for EGPA.

W56-4

Investigating the appropriate timing of introduction of mepolizumab in patients with eosinophilic polyangiitis granulomatosis

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Conflict of interest: None

[Objectives] To clarify the steroid dose reduction status of EGPA patients who were introduced with MEP at the time of relapse. [Methods] We retrospectively investigated the medical records of 27 EGPA patients who used MEP at our hospital. [Results] The mean age at the start of MEP was 53.9 years, the mean morbidity was 54.8 months, the ANCA positive rate was 25.9%, the prednisolone (PSL) dose rate was 100%, and the mean dose was 12.7 mg / day. The timing of the start of MEP was analyzed in the group introduced during the relapse period ($N = 10$) and the group introduced at other times ($N = 17$). In the relapse period introduction group, the average PSL amount at the time of relapse was 7.6 mg / day. Compared with the PSL amount at the time of relapse, the average PSL amount at 52 weeks was 4.4 mg / day ($P = 0.0313$). It was confirmed that the PSL weight was further reduced. In the group in which MEP was introduced at other times, the average PSL amount at the time of MEP introduction was 13.3 mg / day. After the introduction of MEP, the average PSL amount at 52 weeks was 3.5 mg / day ($P = 0.0005$), confirming that the PSL amount could be reduced by introducing MEP. [Conclusions] MEP is effective in introducing the relapse period.

W56-5

The usefulness of RTX in remission induction therapy for 41 patients with ANCA-associated vasculitis (AAV) and the influence of RTX on biomarkers

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Conflict of interest: None

[Objective] To compare the efficacy and safety of cyclophosphamide (CY) and rituximab (RTX) as remission induction therapy for AAV. In addition, the influence of biomarker with RTX will be discussed. [Methods] 41 patients with MPA or GPA were divided into two groups, and the remission rate, relapse rate, and adverse events were evaluated. We also measured biomarkers (serum TIMP-1, BAFF, and MMP-9) in the RTX group. [Results] The remission rate (BVAS=0 and PSL≦7.5 mg/day) at 6 months was 45% in the CY group and 52% in the RTX group. Relapse were 3 cases in each groups respectively. Serious infections were observed 2 in the CY group and 3 in the RTX group. TIMP-1 was significantly decreased ($p<0.001$), BAFF was significantly increased ($p=0.012$), and MMP-9 tended to be decreased ($p=0.47$). TIMP-1 levels in pre-treatment were positively correlated with BVAS ($rho=0.61$, $p=0.007$). The 2 patients with elevated TIMP-1 after treatment had significantly higher ANCA levels in post-treatment ($p=0.005$). BAFF levels after treatment were significantly negatively correlated with IgG levels ($rho=-0.67$, $p=0.006$). [Conclusions] The efficacy and safety of CY and RTX were comparable. Furthermore, our results suggest an association between novel serum biomarkers and disease activity in RTX treatment.

W56-6

Clinical Features of Eosinophilic Granulomatosis with Polyangiitis Treated with Mepolizumab as Remission Induction Therapy

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Conflict of interest: None

[Objective] We aimed to elucidate the clinical features of patients with eosinophilic granulomatosis with polyangiitis (EGPA) treated with mepolizumab as remission induction therapy. [Methods] Cases of EGPA treated with mepolizumab as remission induction therapy were collected from medical records, and their clinical features were retrospectively studied. The same number of EGPA cases treated without mepolizumab were also collected and compared to those treated with mepolizumab. [Results] Four cases each were collected, and high-dose corticosteroids were administered to all the cases. Among the cases treated with mepolizumab, the mean age was 57 years, the mean blood eosinophil count was 16,304/μl, the mean BVAS was 22, and the mean Five Factor Score was 1.5 at baseline. The mean time to remission was 2.3 months, and the mean dosage of

prednisolone at 16-weeks was 12.5 mg/day among the cases treated with mepolizumab. No significant difference were observed between each group in these features. There was no significant mepolizumab-related adverse event. [Conclusions] No distinctive features were identified in EGPA cases treated with mepolizumab. Further cases and longer observation are needed to determine the role of mepolizumab as remission induction therapy in EGPA.

W56-7

Safety of Rituximab induction therapy for elderly patients with ANCA-related vasculitis

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Conflict of interest: None

[Objective] To evaluate the safety of rituximab (RTX) therapy in elderly ANCA-related vasculitis (AAV) patients aged 75 years or older. [Methods] AAV patients who were treated at our hospital from January 2016 to April 2020 and were over 75 years old at the start of treatment are examined. These patients were divided into the RTX group and the non-RTX group, and the safety up to 6 months after the start of treatment was compared. [Results] The target patients were 7 and 9 patients in the RTX group and the non-RTX group, respectively. The median age of onset (years) was 80 (IQR 77-83) and 78 (IQR 75-83), the median BVAS was 14 (IQR 10.5-18) and 7 (IQR 5-16) and the median prednisolone dose (mg / kg) at the start of treatment was 0.96 (IQR 0.91-1.00) and 0.86 (IQR 0.60-0.98), respectively. The dose of RTX was 375 mg / mm^2 in all patients, however, the number of administrations was reduced in many cases. Bacterial infections requiring antibiotics intravenously were found in 0 case and 2 cases. Cytomegalovirus reactivation was observed in 3 cases and 0 case. One case of herpes zoster was seen in each group. [Conclusions] Even in patients aged 75 years or older, it may be possible to use RTX relatively safely with reducing the number of its administrations.

W57-1

Thrombotic risk in antiphospholipid antibody-positive patients with anti-neutrophil cytoplasmic antibody-associated vasculitis

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Conflict of interest: None

[Objective] It was reported 17-52% of anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) patients were antiphospholipid antibody (aPL)-positive in foreign countries. We aimed to evaluate the proportion of aPL-positivity and its thrombotic risk in Japanese AAV patients. [Methods] We retrospectively assessed AAV patients diagnosed from 2013 to 2020 at our hospital. Positivity of aPL was defined as positivity of either anti-cardiolipin antibody, anti-cardiolipin β2GPI complex antibody or lupus anticoagulant. The thrombotic risk was examined by the Kaplan-Meier method and the Cox regression model. [Results] A total of 93 patients with a median age of 73 years were included in the study. The median follow-up period was 28.5 months. Eleven patients (11.8%) had malignancies and 26 (27.9%) were aPL-positive. Seventeen thrombotic events occurred in 15 patients (16.1%). Positive-aPL patients tended to have thromboses by the Log-rank test (p=0.088). Cox regression model identified aPL-positivity as a thrombotic risk factor when adjusting age, glucocorticoid dosage and malignancies (Hazard ratio 2.95, 95% confidence interval 1.02-8.54). [Conclusions] The proportion of aPL-positive patients was 27.9%, and aPL-positivity increased the thrombotic risk in Japanese AAV patients.

W57-2

Otitis Media with ANCA-Associated Vasculitis (OMAAV): a Case Series of 30 Patients

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Conflict of interest: None

Objectives: OMAAV is a new disease entity developed for early diagnosis and treatment of ANCA-associated vasculitis (AAV) presenting with otitis media. We aimed to characterize clinical features and courses of OMAAV. **Methods:** We reviewed clinical records of 30 Japanese adult patients who were hospitalized in our department in a study period from April 2005 through December 2019 and fulfilled the OMAAV Diagnostic Criteria 2015 proposed by Harabuchi et al. **Results:** The mean age at OMAAV onset was 64.9±10.9 years. Twenty-seven (90%) patients were treated with 50±11 mg/day of prednisolone, and 18 (60%) patients were administered immunosuppressants for remission induction. All patients achieved remission. Nine (30%) patients experienced a relapse of AAV, and 2 (7%) patients died of infection, in a median follow-up period of 35 months (range, 16-82 months). The shorter duration between the onset and the start of treatment tended to result in better hearing improvement. The relapse rate was significantly higher in patients where the duration between the onset and the start of treatment was more than 3 months than those less than 3 months. **Conclusion:** Our results suggest that early treatment contributes to lower relapse rates and better hearing outcomes.

W57-3

Efficacy of mepolizumab for treatment of peripheral neuropathy associated with eosinophilic granulomatosis with polyangiitis assessed by the nerve conduction study

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Conflict of interest: None

[Objective] Peripheral neuropathy is one of the intractable complications associated with eosinophilic granulomatosis with polyangiitis (EGPA). The efficacy of mepolizumab for treatment of EGPA has been reported but its effect on peripheral neuropathy remains unclear. Additionally, the therapeutic efficacy of mepolizumab has not been evaluated by objective and quantitative analyses. Here, we used nerve conduction study (NCS) to report the efficacy of mepolizumab for treatment of peripheral neuropathy complicated with EGPA. [Methods] Four patients with peripheral neuropathy complicated with EGPA resistant to glucocorticoids therapy were included in this study. The therapeutic efficacy was evaluated by conventional physical examination and NCS was performed before and after administration of mepolizumab. [Results] After mepolizumab administration, the steroid dose was reduced in all patients with no deterioration in their symptoms. A comparison of NCS before and after mepolizumab administration revealed that three patients showed an improvement in the amplitude of compound muscle action potentials and one patient showed no improvement. [Conclusions] NCS results confirmed the effectiveness of mepolizumab in the treatment of intractable peripheral neuropathy complicated with EGPA.

W57-4

Clinical Characteristics of ANCA-Associated Vasculitis Patients with Protein-losing Enteropathy (PLE)

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Conflict of interest: None

[Objective] Protein-losing enteropathy (PLE), a rare condition characterized by the loss of proteins in gastrointestinal tract, is associated with a variety of systemic autoimmune diseases, most famously systemic lupus erythematosus (SLE). Clinical characteristics of ANCA-associated vasculitis (AAV) patients with PLE have not been reported. We performed a

retrospective chart study to describe the clinical characteristics of AAV patients with PLE. [Methods] We reviewed medical records of patients diagnosed with AAV who began treatment at the University of Tokyo Hospital between June 2003 and June 2020. [Results] Medical records of 70 AAV patients were reviewed, and there were four patients with PLE (2 MPA, 1 GPA, and 1 EGPA). The pattern of organ involvement was similar between the patients with PLE and without PLE, but patients with PLE had hypocomplementemia more frequently. Medians of CH50 were 15.4 vs 58.2 U/mL (p=0.0468), those of C3 were 68 vs 117 mg/dL (p=0.0377), and those of C4 were 7.5 vs 26 mg/dL (p=0.0499). [Conclusions] PLE is a rare complication of AAV. The presence of hypocomplementemia in AAV patients with PLE suggests that a complement dependent mechanism similar to SLE may be involved in the pathogenesis of PLE in AAV.

W57-5

Clinical study of 4 cases of microscopic polyangiitis with myocardial abnormalities detected cardiac magnetic resonance

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Conflict of interest: None

[Objective] Microscopic polyangiitis (MPA) is known to be associated with cardiac lesions, but there are few reports on the study of cardiac lesions in MPA using cardiac magnetic resonance (CMR). We examined the clinical features of MPA patients who underwent CMR and experienced 4 patients with cardiac lesions. [Subjects / Methods] The average of age was 76.5 years in 3 females and 1 male. One had palpitations and three had no cardiac symptoms. All four cases showed an increase in NTproBNP. [Results] Three of the four patients had nephritis, and two of them had rapidly progressive glomerulonephritis. CMR showed elevated T1 mapping in all 4 patients, indicating the presence of diffuse myocardial abnormalities. One patient with cardiac symptoms showed delayed gadolinium imaging localized to the endocardium and a high signal on T2-weighted images at the same area. Myocardial abnormalities was found in a region different from the area controlled by the coronary arteries. [Conclusion] It was confirmed by CMR that myocardial abnormalities had been already observed even in cases where there were no cardiac symptoms. It is considered that there are cases in which detailed examination including myocardial lesions is required for evaluation of organ complications of MPA.

W57-6

Relationship between the extent of palpable purpura and systemic symptoms in patients with IgA vasculitis

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Conflict of interest: None

[Objective] We examined the impact of the extent of palpable purpura on systemic symptoms and laboratory findings. [Methods] 38 cases of IgA vasculitis who visited our department between 2010 and 2019 were included in the study. [Results] The mean age was 44.2±22.2 years, 6 patients were less than 15 years old, and the male to female ratio was 22:16. Joint symptoms were seen in 21 patients (55.3%), urinary abnormalities were detected in 18 (47.4%), and abdominal symptoms were observed in 25 (65.8%). The prevalence of abdominal findings was significantly higher in patients whose purpura extended beyond the lower extremities (n=24) than in those whose purpura was localized to the lower extremities (n=14) (79.2% vs 42.9%, P=0.035). In addition, the CRP and D-dimer values at the initial examination were significantly higher in the former group. Moreover, there was a positive correlation between the CRP value and the D-dimer value (r=0.63, P=0.0001), both of which were significantly higher in patients with abdominal findings. Finally, D-dimer levels were negatively correlated with factor XIII (r=-0.40, P=0.040). [Conclusion] In IgA vasculitis, purpura over the lower extremities and high initial CRP and D-dimer levels were considered to be potential risk factors for abdominal symptoms.

W57-7

Two Cases of Small-Vessel Vasculitis Associated with Fibrotic Nodules in the Kidneys

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Conflict of interest: None

[Case 1] A 67 year-old woman presented with multiple nodules in the kidneys. Six months later, she developed a fever, scleritis, sinusitis, and pulmonary nodules. MPO-ANCA was positive, and she was diagnosed clinically with granulomatosis with polyangiitis. A biopsy of the renal nodules showed fibrotic tissue with infiltration of inflammatory cells, including IgG4-positive plasma cells, and stenosis of the vascular lumen, possibly due to vasculitis. [Case 2] A 73 year-old women presented with purpura, alveolar hemorrhage, and Mononeuritis multiplex. There was evidence of necrotizing vasculitis upon skin biopsy, and she was diagnosed with ANCA-negative microscopic polyangiitis. She attained remission with steroids and cyclophosphamide. She was taking low-dose steroids and azathioprine, when a nodule was noted in the right kidney 39 months later. Three months later, she developed hypertrophic pachymeningitis and was considered to have a relapse of AAV. A biopsy of the renal nodule showed sclerosed glomeruli surrounded by fibrotic tissue with inflammatory cells, including IgG4-positive plasma cells, and granulomas. [Clinical Significance] ANCA-associated vasculitis may be associated with fibrotic nodules in the kidneys with infiltration of IgG4-positive plasma cells.

W58-1

Examination of parotid gland ultrasonography (US) and blood test findings in cases with dry mouth

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Conflict of interest: None

[Objective] We examined blood test findings related to parotid gland US findings in dry mouth patients. [Methods] The subjects were 134 patients with dry mouth (54 ± 14 years old, 5 males, 129 females). The US grades of the parotid gland were classified into G0 to G4 according to the report of Ariji et al. (G0: 46%, G1: 15%, G2: 10%, G3: 9%, G4: 19%). [Results] The antibody examination was ACA-negative SSA-negative (DN group) were 19%, ACA-negative SS-A-positive (SSA group) were 65%, and ACA-positive (ACA group) were 16%. The grades of SSA group were G0: 34%, G1: 21%, G2: 14%, G3: 11% and G4: 20%. The grades of ACA group were G0: 29%, G1: 10%, G2: 5%, G3: 24% and G4: 33%. When divided into G0 / G1 / G2 cases and G3 / G4 cases, G0 / G1 / G2 cases were 69% and G3 / G4: 27 cases were 31% in the SS-A group. G0/ G1 / G2 cases were 43%, G3 / G4 cases were 57% in the ACA group, G3 / G4 cases were significantly higher in the ACA group (p=0.041). In the SSA group, IgG and lymphocyte fraction were significantly higher than in the ACA group, and the neutrophil fraction was significantly lower. IgG increased and the neutrophil fraction decreased as the grade progressed. [Conclusions] A high rate was observed in G3 and G4 in the ACA group, which was considered to reflect the fibrosis.

W58-2

Evaluation of power Doppler signals in salivary gland ultrasonography in Sjogren's syndrome

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Conflict of interest: None

[Objective] Gray scale (GS) in salivary gland ultrasonography (SGUS)

is reported to be useful in diagnosis of Sjogren's syndrome, and it has correlations between disease activity and complecations. On the other hand, there are few reports of power Doppler signal (PDS) in SGUS, so we investigated correlations with several parameters of Sjogren's syndrome. [Methods] Forty patients with primary and secondary SS were included. GS, PDS of parotid glands (PG) and submandibular glands (SG) were evaluated from grade 0 to 3, and correlations with ESSDAI, ESSPRI, OHIP-14, IgG, CH50, C3 C4, RF, SS-A, SS-B were investigated. [Results] GS scores of PG was correlated with IgG, C3, SS-B, and GS of SG with IgG, C3, SS-B, GS of PG as were reported previously except C3. PDS scores of PG was correlated with SS-A, SS-B, glandular/cutaneous/hematological involvement of ESSDAI, GS of PG, and GS/PDS of SG. PDS of SG was correlated with ESSPRI, PD of PG, and PDS positive group was correlated with SS-A. [Conclusions] PDS of PG was correlated with GS and some organ involvement. On the other hand, PDS of SG was independent of GS, and reflected patient's subjective symptoms. Combination of GS and PDS of PG and SG might be useful in prediction of prognosis or estimation of treatments in SS.

W58-3

Clinical feature using ESSDAI and salivary gland ultrasonography in patients of early-onset and late-onset primary Sjögren's syndrome

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Conflict of interest: None

[Objective] Primary Sjögren's syndrome (pSS) is a common disease in middle-aged and elderly patients, but the etiology and pathogenesis identity of early-onset pSS (EOpSS) and late-onset pSS (LOpSS) are unknown. The aim of this study was to compare EOpSS and LOpSS using clinical findings with ESSDAI and salivary gland ultrasonography (SGUS) to examine the identity in the both groups. [Methods] Twenty-six EOpSS (age≦40) and 30 LOpSS (age≧65) patients were studied. The clinical findings were evaluated ESSDAI and OMERACT SGUS score at the first visit to our hospital. [Results] The frequency of positive RF, anti-SS-A and anti-SS-B antibodies was not different in the two groups, but ESSDAI (7.30 vs 4.23, p=0.002), constitutional (1.50 vs 0.60, p=0.03), articular (1.54 vs 0.40, p=0.0002) and biological domain (1.35 vs 0.90, p=0.04) were higher in the EOpSS than in the LOpSS. No difference in salivary secretion was found between two groups, but the OMERACT SGUS score lower in EOpSS than in LOpSS (2.00 vs 2.70, p=0.0002). [Conclusions] EOpSS had higher disease activity and milder salivary gland degeneration than LOpSS, and the pathogenesis of the two groups was different. However, the two groups did not differ in serological findings and were unlikely to have different etiologies.

W58-4

The crosstalk between BAFF-signaling and sodium channel is involved in activation of monocytes of patients with primary Sjogren's syndrome

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Conflict of interest: None

[Objective] We investigate the possible involvement of sodium channels, such as Nav 1.7 in BAFF signaling pathways in monocytes of patients with primary Sjogren's syndrome (pSS). [Methods] The proportion of BR3 and Nav1.7 positive monocytes were analyzed by FACS using whole blood samples from patients with pSS (n = 28), active RA (n = 15), active SLE (n = 37) and healthy controls (HC; n = 15). The expression levels of BR3 and Nav1.7 in peripheral monocytes were analyzed by qPCR. BAFF-stimulated peripheral monocytes were cultured with an inhibitor against Nav1.7. The amount of IL-6 in the culture supernatants was measured by ELISA. [Results] FACS and qPCR analysis revealed that the expression levels of Nav1.7 and BR3 in pSS monocytes was significantly higher than those of active RA, active SLE and HC. Interestingly, the expression level of Nav 1.7 in pSS monocytes was significantly and positively correlated with that of BR3 in the cells ($p = 0.02$). Moreover, a specific inhibitor against Nav 1.7 suppressed IL-6 production by sBAFF-stimulated peripheral monocytes in a dose dependent manner. [Conclusions] Our data suggest that localization of Nav1.7 in peripheral monocytes contributes to activation of BAFF signaling in monocytes of pSS patients.

W58-5

Inhibitory effect of HTLV-1 on the production of B-cell activating factors in established follicular dendritic cell-like cells

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Conflict of interest: None

[Background] The low frequency of ectopic germinal center in the labial salivary glands of patients with HTLV-1 antibody-positive Sjogren's syndrome (SS) suggests HTLV-1 has some effects on follicular dendritic cells (FDC). [Objectives] To investigate the effect of HTLV-1-infected cell line on the expression of BAFF and CXCL13 in FDC-like cells. [Methods] Cell-surface markers of FDC-like cells isolated from human tonsils were examined by immunofluorescence (IF) and flow cytometry (FCM). After co-culturing FDC-like cells and HCT-5, the expression of BAFF and CXCL13 was examined by IF and ELISA. Serum BAFF and CXCL13 of HTLV-1 seropositive/seronegative SS patients were measured by ELISA. [Results] Day 2 cultured cells showed expressions of CD14, CD23 and ICAM-1. Day 14 cells expressed FDC (CNA.42) and fibroblast cell marker. Intracellular BAFF and CXCL13 were constitutively expressed, but these expressions were decreased in direct co-cultures. These findings were not observed in indirect co-cultures. Supernatant BAFF under IFN-γ stimulation was decreased by the addition of HCT-5. Serum BAFF and CXCL13 in the HTLV-1-seropositive SS were lower than that of seronegative SS. [Conclusions] Direct contact of HTLV-1-infected cells might suppress the expression of BAFF and CXCL13 in FDCs.

W58-6

Activation of signaling pathways of Toll-like receptor 4 contribute to elevated expression of BAFF receptor in monocytes of patients with primary Sjögren's syndrome

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Conflict of interest: None

[Objective] We investigate possible involvement of signaling pathways of TLR4 in enhanced expression of BR3 in monocytes of patients with primary Sjögren's syndrome (pSS). [Methods] The expression levels of BR3 and TLR4 in peripheral monocytes of pSS patients (n = 18) and healthy controls (HC, n = 13) by qPCR and FACS. LPS-stimulated THP-1 were cultured with or without TAK-242, a specific inhibitor for TLR4 signals and the expression of CD14, CD16 and BR3 in the cells were analyzed by FACS. The expression of TLR4 signaling molecules in LPS-stimulated THP-1 were analyzed by Western blotting. [Results] The expression of BR3 and TLR4 in peripheral monocytes were upregulated in pSS as compared with HC. Interestingly, FACS analysis showed that both BR3 and TLR4 were localized in $CD14^{++}CD16^{+}$ monocytes. The expression of BR3 was elevated in $CD16^{+}$ THP-1 when the cells were stimulated with LPS. In addition, TAK-242 inhibited expression levels of BR3 and CD16 in LPS-stimulated THP-1 cells in a dose dependent manner. Moreover, western blotting revealed that the expression of MyD88 and phosphorylated IRAK4 were upregulated in LPS-stimulated THP-1. [Conclusions] Our results collectively suggest that TLR4 signaling pathways are involved in the elevated expression of BR3 and CD16 in human monocytes.

W59-1

Automatic diagnosis support for IgG4-related disease based on machine learning

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Conflict of interest: None

[Objective] In recent years, the application of artificial intelligence (AI) to medicine has been accelerated. In order to solve regional disparities in physicians and medical departments, we are developing a system that allows diagnosis of rare diseases anywhere in the world. Therefore, we used machine learning to investigate whether the clinical diagnosis of IgG4-related disease (IgG4-RD), which is also rare disorder, is possible based on the questionnaires, physical examination and blood tests. [Methods] Patients with IgG4-RD and non-IgG4-RD at several university hospitals were included in the study, and the diagnosis of IgG4-RD was made according to the comprehensive diagnostic criteria or the criteria for each organ. Non-IgG4-RD were defined as rheumatic diseases other than IgG4-RD, or healthy controls. Basic data, subjective symptoms, other symptoms, and blood test results were analyzed using decision tree and random forest methods. [Results] Both methods showed good sensitivity and specificity in the diagnosis of IgG4-RD. [Conclusions] In this study, we attempted to predict the diagnosis of IgG4-RD based on machine learning. The results of this analysis suggest that the introduction of AI may help to resolve regional disparities in the diagnosis of rheumatic diseases.

W59-2

Relationship between relapse of IgG4-related disease and self-management of medication at our hospital

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Conflict of interest: None

[Objective] We examined the relationship between relapse of IgG4-related disease (IgG4-RD) and self-management of glucocorticoids (GC) in order to lead to effective nursing intervention for maintaining therapeutic effects. [Methods] This study included 104 patients (Pts) with IgG4-RD being treated on GC treatment at our hospital. A questionnaire survey using Medication Assessment Tool was conducted to examine the relationship between basic attributes, medication status and relapse. [Results] The mean age of Pts (58% male) was 67.0 years. The average dose of prednisolone was 6.3 mg / day and the mean treatment duration was 5.2 years. There were 28 Pts with relapse. Eight Pts stopped and 5 Pts self-adjusted taking GC at their own discretion. Dacryoadenitis had a significantly higher complication rate in Pts with relapse. Significantly more Pts with relapse answered that they need less medicine and it is not good to rely on medicine. Those results may indicate low acceptance to GC. [Conclusions] Poor subjective symptoms and inability to realize the efficacy of the drug could cause low acceptance to GC in Pts with IgG4-RD. It is necessary for nurses to cooperate with doctors and pharmacists to provide medication support while confirming the Pts acceptance of medication.

W59-3

Clinical significance of positive disease-specific autoantibodies in diagnosing IgG4-related disease using the 2019 ACR/EULAR classification criteria in daily clinical practice

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Conflict of interest: None

[Objective] This study aimed to validate the 2019 ACR/EULAR classification criteria for IgG4-related disease (IgG4-RD) as well as identify characteristics of patients showing false-negative results. [Methods] We retrospectively analyzed 162 IgG4-RD patients and 130 mimickers. The sensitivity, specificity, and fulfillment rates for each criterion were calculated, and intergroup comparisons were performed to characterize the false-negative cases. [Results] The classification criteria had a sensitivity of 72.8% and specificity of 100%. Of the 44 false-negative cases, 20 fulfilled one exclusion criterion, and 27 did not achieve sufficient inclusion criteria scores. The false-negative cases had fewer affected organs, lower serum IgG4 levels, and were less likely to have received biopsies than the true-positive cases. Notably, positive disease-specific autoantibodies were the most common exclusion criterion fulfilled in 18 patients, only two of whom were diagnosed with a specific autoimmune disease complicated by IgG4-RD. [Conclusions] Positive disease-specific autoantibodies may have limited clinical significance for the diagnosis of IgG4-RD using the ACR/EULAR classification criteria in daily clinical practice.

W59-4

Proposal of the diagnostic criteria for IgG4-related kidney disease (IgG4-RKD) 2020 by the IgG4-RKD working group of the Japanese Society of Nephrology

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Conflict of interest: None

[Objective] To develop a new version of the diagnostic criteria for IgG4-RKD. [Methods] Although the diagnostic criteria for IgG4-RKD 2011 were highly specific (90.0%), their sensitivity was relatively low (72.7%) because some true IgG4-RKD patients, that lacked storiform fibrosis upon renal histology and biopsy-proven IgG4-related extra-renal lesions, were misclassified as mimickers. We developed some revised versions of the criteria and examined the sensitivity and specificity for each revised version in the cohort used in the validation study. On this basis, we selected the version showing the best performance. [Results] Among some revised version, the version in which the item “imaging or clinical findings compatible with extra-renal organ (s), i.e. 1) bilateral lacrimal gland swelling or 2) bilateral submandibular or parotid gland swelling or 3) imaging findings compatible with type 1 autoimmune pancreatitis, or 4) imaging features of retroperitoneal fibrosis” was added as an extra-renal organ (s) item, showed the highest performance (sensitivity 90.9% and specificity 90.0%). [Conclusions] We developed the revised version that has considerably improved test performance after addition of the new extra-renal organ item (imaging and clinical findings).

W59-5

Analysis for relapse of IgG4-related disease after corticosteroid therapy

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Conflict of interest: None

[Objectives] To clarify the clinical features of patients with IgG4-related disease (IgG4-RD) who experienced relapse after steroid therapy. [Methods] We examined patients with definite IgG4-RD by comprehensive diagnostic criteria 2011, who had started to be treated with steroid between Jul 2008 and Sep 2017, and had been followed up for ≧ 36 months (M). We investigated 1) relapse rate, 2) comparison of clinical features and therapy between relapsed and non-relapsed cases, and 3) clinical course of relapsed cases, retrospectively. [Results] 32 patients (62.8± 12.1 years old (YO), 20 males/12 females, IgG4 1001±974 mg/dl) were examined. 1) Ten cases (31.3%) experienced the relapse. 2) The relapsed cases tended to be younger than non-relapsed cases (56.9±11.3 vs 65.5± 11.6 YO, P=0.067). Gender, observation period, the lag between disease onset and initiation of therapy, serum IgG4, affected organs, IgG4/IgG+plasmacytes ratio in tissues, and initial steroid dose and duration were similar between groups. 3) Relapses occurred 55.0±41.0 M later from initiation of therapy, at mean PSL dose of 4.4±4.0 mg/day, and in one of the initially affected organs. [Conclusion] Relapses occurred in 31.3%. Predictive factors for relapse were not revealed, thus long-term cautious observation would be needed.

W59-6

Analysis of clinical characteristics of idiopathic retroperitoneal fibrosis

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Conflict of interest: None

[Objective] To analyze the clinical features of idiopathic retroperitoneal fibrosis (IRF) in our hospital. [Methods] Forty-two patients diagnosed with IRF at our institution between April 2008 and August 2020 were retrospectively analyzed in this study. [Results] The median age of onset was 69.0 years, and 30 cases (71.4%) were males. The median follow-up period was 26.0 months. The 14 cases (34.1%) developed systemic symptoms, back pain in 12 cases (29.3%), abdominal pain in 12 cases (29.3%). The CT images showed peri-arterial lesions in 34 cases (80.9%), peri-ureteric lesions in 10 cases (23.8%), pelvic plate-like lesions in 8 cases (19.0%), and hydronephrosis in 31 cases (73.8%). Twenty-three cases (54.7%) showed the increase of serum IgG4 (median 348 mg/dl, 174.5-853.5 mg/dl) at diagnosis. The level of serum C3 and C4 in IgG4-elevated IRF group were significantly lower than in IgG4-non elevated IRF group (p=0.03 and p=0.002, respectively). However, there were no statistically significant differences in the radiographic features, treatment response, and relapse rate between the two groups. [Conclusions] Serum level of IgG4 at diagnosis seems not to be involved in clinical features of IRF. IgG4-elevated IRF and IgG4-non elevated IRF may share a common pathological condition.

W60-1

Pathogenic roles and therapeutic potential of the CCL8-CCR8 axis in LAT Y136F knock in mice as a model of IgG4-related disease (IgG4-RD)

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Conflict of interest: None

[Objective] To clarify pathogenic roles and therapeutic potential of CCL8-CCR8 axis in the animal model of IgG4-RD (LAT mice). [Methods] LAT or littermate (LM) mice were sacrificed at 6 weeks of age. 1) Salivary glands (SG) were examined by HE, MT and IF staining. The focus and fibrosis score were assessed in a blind manner. 2) mRNA expression of Ccl8 and Ccr8 in spleen, cLN and SG was examined by qPCR. 3) We injected anti CCL8 neutralizing antibody (Ab) or control IgG (Ctrl) (N=3, each) intravenously to 5-week-old LAT mice. One week after injection, SG were examined. 4) We stimulated mouse fibroblast cell line (NIH/3T3) with rCCL8 in vitro. mRNA expression of Col1a2 was examined by qPCR. [Results] 1) The infiltration of mononuclear cells including $CD4^+$T and $B220^+$B cells was detected in SG of LAT mice. The focus and fibrosis score of SG were significantly higher in LAT mice than in LM. 2) mRNA expression of Ccl8 and Ccr8 in SG as well as Ccl8 in spleen was significantly higher in LAT mice than in LM. 3) The focus, fibrosis score, and $CD4^+$T cells in SG were significantly lower in Ab treated mice than in Ctrl treated mice. 4) mRNA expression of Col1a2 was significantly increased in a rCCL8 dose dependent manner. [Conclusions] CCL8-CCR8 axis could be a potential therapeutic target for IgG4-RD.

W60-2

Analysis of T/B cells specific differentially expressed genes by RNA-Seq in affected organs of patients with IgG4-related disease

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Conflict of interest: None

[Objective] To clarify T/B cells specific differentially expressed genes (DEGs) by RNA-Seq in affected organs of patients with IgG4-related disease (IgG4-RD). [Methods] Pathologically confirmed submandibular glands (SMGs) and PBMC were collected from treatment naïve definite IgG4-RD patients (N=3), subsequently $CD3^+$T and $CD19^+$B cells were sorted by MACS. We compared the gene expression of 1) $CD3^+$T cells and 2) $CD19^+$B cells by RNA-Seq between SMGs and PBMC, and performed principal component analysis (PCA) and pathway analysis for DEGs using web tool (reactome). [Results] 1) Gene expression patterns of $CD3^+$T cells of SMGs differed from those of PBMC in PCA. 170 up-regulated and 41 down-regulated DEGs were identified in SMGs compared with PBMC. 170 up-regulated DEGs in SMGs related with nuclear events, Treg-development, IL-10, IL-4, IL-13 signaling, and co-stimulation by CD28 in pathway analysis. 2) Gene expression patterns of $CD19^+$B cells of SMGs differed from those of PBMC. 437 up-regulated and 96 down-regulated DEGs were identified in SMGs. 437 up-regulated DEGs in SMGs related with complement, FCGR, BCR, FCERI signaling, and Leishmania infection. [Conclusions] RNA-Seq clarified up-regulated DEGs in T/B cells of affected organs, which might contribute to the pathogenesis of IgG4-RD.

W60-3

Clinical significance of high serum IgA levels in IgG4-related disease

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Conflict of interest: None

[Objective] This study aimed to clarify the clinical significance of high serum IgA levels in IgG4-related disease. [Methods] We retrospectively investigated the clinical features of 170 patients with IgG4-RD according to the presence/absence of elevated serum levels of IgA (>410 mg/dl). The diagnosis of IgG4-RD was made by experts, based on the fulfillment of the comprehensive diagnostic criteria and/or each organ-specific diagnostic criteria. [Results] Elevated serum levels of IgA were seen in 18 (10.6%). In the patients with serum IgA elevation, serum CRP levels were higher and the prevalence of relapse was lower than those without it. However, there were not significant differences in the other clinical features including the number of involved organs and inclusion scores of ACR/EULAR classification criteria. In the Cox regression analysis, the elevated serum IgA levels had not a significant association with but a tendency of lower incidence of relapse [hazard ratio (HR) 0.997, 95% confidence interval (CI) 0.994-1.000] during the clinical course. [Conclusions] The present study suggests that IgG4-RD patients with high serum IgA levels can be diagnosed and treated in the same way as those without it although they may be characterized by mild increase in serum CRP levels.

W60-4

Investigation of serum IgG4 measurement by the magnetic bead assay panel method (multiplex method) comparing with nephelometry

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Conflict of interest: None

[Objective] Although nephelometry has been used, the multiplex method is relatively easy to use and available to measure IgG4 with small amounts of serum. Therefore, we evaluated the accuracy of the latter method in comparison with the standard nephelometry method. [Methods] We collected 947 samples from residential health checkups, measured IgG4 levels by both methods and evaluated the accuracy of multiplex IgG4 which is equivalent to 135 mg/dl, the normal cutoff of serum IgG4 levels by the nephelometry method. Using the calculated nephelometry-IgG4, we measured serum IgG in 3620 samples of Goto City residential health checkup, and compared them with background information, including smoking, body weight, and alcohol consumption. [Results] The results showed a strong positive correlation between serum IgG4 and nephelometry (135 mg/dL), and the ROC curve showed a cutoff value of 797,000 ng/mL for multiplex IgG4, with a sensitivity of 90.0% and specificity of 96.7%. The detected cut-off value was 90.0% sensitivity and 96.7% specificity. The IgG4 level of the residents' health checkup in Goto Island was weakly associated with the amount of smoking and BMI. [Conclusions] It was shown that the multiplex method may be an alternative to nephelometry for a small amount of blood samples.

W60-5

IgG4 related diseases (IgG4-RD) and tubarial salivary glands

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Conflict of interest: None

[Objective] Tubarial salivary glands (TSGs) are one of the salivary glands newly identified in September 2020 around the eustachian tube. It is still unclear if TSGs are affected by IgG4-RD or not. To address this, we examined the 18F-FDG accumulation of TSGs in patients with IgG4-RD. [Methods] We retrospectively reviewed the clinical characteristics of IgG4-RD patients who underwent 18F-FDG-PET/CT scans. At first, we evaluated 18F-FDG accumulation to TSGs in 16 patients with IgG4-related dacryoadenitis / sialadenitis (IgG4-DS) and 14 patients without IgG4-DS at the disease onset. In the second analysis, we further collected additional 51 patients with or without IgG4-DS and examined the clinical manifestations and laboratory findings related to 18F-FDG accumulation of TSGs. [Results] The accumulation of 18F-FDG to TSGs in patients with IgG4-DS was significantly higher than without IgG4-DS. The patients with 18F-FDG accumulation to TSGs had more major organ involvements (IgG4-DS, autoimmune pancreatitis, retroperitoneal fibrosis, tubular interstitial nephritis) and showed higher serum IgG4 and soluble IL2 receptors levels. [Conclusions] TSGs in the patients with IgG4-DS accumulated higher amount of 18F-FDG. The results suggested that TSGs could be affected by IgG4-RD.

W60-6

The relationship between Multifocal fibrosclerosis (MFS) and IgG4 related disease - from 7 cases of experience

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Conflict of interest: None

Here we summarized 7 cases of IgG4 related disease patients who have variable skin lesions in our department. In this presentation, we mainly focus on 3 patients who presented unusual cutaneous manifestations. Left side of the face were mainly affected and the skin lesions including fibrosis and sclerosing changes which generate great influences in their daily life. 1 patient combined with IgG4 related pancreatitis and retroperitoneal fibrosis and another one case with cardiovascular lesions. Histopathological finding revealed fibrosis and focal lymphocytic and plasma cell infiltration. About the treatment, 2 patients responded well to IVCY combination with agents for hyperlipidemias, and one for PSL with antihyperlipidemic drug. Our cases suggest MFS is a subtype of IgG related disease.

W61-1

Analysis of Current Status of Diagnosis and Treatment of Behçet's Disease Using Large Medical Databases

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Conflict of interest: Yes

[Objective] Oral ulcers (OU) are the most common initial symptoms in Behçet's disease (BD). We conducted a retrospective cohort study using large-scale medical databases (JMDC and MDV) to understand the current status of BD diagnosis and treatment including OU symptoms in Japan. [Methods] Patients (pts) with BD records were extracted (JMDC; 2005-2018, MDV; 2010-2018). The presence of BD symptoms in MHLW criteria prior to BD diagnosis and duration to the definitive diagnosis were analyzed. [Results] 1,061 (JMDC) and 7,471 (MDV) pts were included. Internal medicine was the most common department in which definitive diagnosis was made (JMDC 66.7%, MDV 30.4%). Time from the initial symptoms to definitive diagnosis was 7.75±14.68 months (JMDC) and 3.34±14.68 months (MDV). The time to diagnosis in pts with OU as the first symptom tended to be longer than pts with other symptoms. [Conclusions] When BD symptoms including OUs were observed, it was considered that earlier visit by pts and proactive diagnosis by doctors would lead to faster diagnosis and treatment. There may be an opportunity for physicians to diagnose earlier if they connect OU as a cardinal manifestation of BD. It is also possible that other symptoms occurred after OU may help the definitive diagnosis.

W61-2

Residual disease activity revealed by the Behçet's disease registry study

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Conflict of interest: None

Objective: As part of the Behçet's Disease (BD) registry study, we aimed to examine and compare the disease activity among multicenter, and assess the prognostic factor using the Behçet's Disease Current Activity Form (BDCAF), overall disease activity measure in BD. **Methods:** Initially, BDCAF was assessed on BD patients at Yokohama City University (YCU), Hokkaido University, Kitasato University, and Niigata University from February 2019 to September 2020. The second BDCAF were surveyed 1 year after the first survey from July to September 2020. **Results:** A total of 249 patients were included in the initial survey, 199 at

YCU and 50 at the others. The mean of age was 50.2 years and disease duration was 8.2 years. The median BDCAF score was equal to 2.0 (IQR 1.0-3.0) for both YCU and non-YCU. 100 patients were assessed at the second survey. Although the BDCAF score was statistically lower than the first score, the median score was 2.0 (IQR 1.0-3.0) indicating 2 symptoms remained. The ocular and intestinal attack were scattered even when the initial score was less than 1. **Conclusion:** Through the BD registry, we found that disease activity remained in many patients and persisted after 1 year. Even in patients with low disease activity, the attack of critical organ involvement was observed.

W61-3

The efficacy and safety of apremilast for the treatment of refractory oral ulcers of Behçet's disease at this hospital

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Conflict of interest: None

[Objective] To determine the efficacy and safety of the apremilast for refractory oral ulcers (OU) of Behçet's disease (BD) at this hospital. [Methods] A total of 10 patients who were received apremilast for refractory OU in BD between September 2019 and August 2020 were included in the study. To assess the efficacy and safety of treatment up to 12 weeks retrospectively. [Results] Active lesions other than OU were found in 5 cases of arthritis, 1 case of genital ulcer, and 4 cases of skin lesions. Concomitant drugs were included prednisolone (PSL) in 5 patients (50%), 6.38 ± 3.3 mg/day, colchicine in 8 patients (80%), immunosuppressive drugs in 1 patient (10%), and biologic agents in 1 patient (10%). After 12 weeks, apremilast was continued in all cases, and OU improved in 8 patients (80%, p=0.013). Arthritis improved in 2 patients (40%, p=0.48), but genital ulcers and skin lesions did not improve. 5 patients continued to receive PSL, 5.6 ± 3.1 mg/day (p>0.99). Adverse events during the study were abdominal involvements (n=3). One patient was treated with a reduced dose of apremilast and the other 2 patients improved with symptomatic therapy only. [Conclusions] Apremilast is effective and tolerated in the treatment of refractory OU in BD.

W61-4

Characteristics of vascular lesions in Behcet's disease and factors associated with relapse

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Conflict of interest: None

[Objective] To characterize vascular lesion in Behcets disease and examine factors associated with flare-ups. [Methods] 225 patients with Behcet's disease visited our hospital from January 1, 2007 to December 31, 2017. 32 patients had vascular lesions. Among them, 29 case (complete and inadequate type) were studied retrospectively. [Results] Of the 29 cases, 16 were male, and the mean age of diagnosis was 36.3 years. and first vascular lesion appearance was 39.8 years. Intestinal lesions were found in 7 and neurological leisions in 2. There are venous thrombus and obstruction in 15, arterial aneurysm in 7, arterial wall thicking in 6, arterial thrombous and obstruction in 5, arterial dissection in 2. In 16 cases, vascular lesions preceded the diagnosis of Behcet's disease.16 cases had a single appearance of vascular leisions and 13 cases had a relapse. In both groups, a high percentage of inflammatory findings were found. But there were a few cases of new leisions with negative CRP. Also rates of intestinal and eye lesions, and use of TNFinhibiter were higher in the single-appearance group than another group. [Conclusions] Vascular lesions in Behcet's disease can occur before or after diagnosis. Early treatment with TNFinhibiters may reduce the relapse of vasucular lesions.

W61-5

Effect of Apremilast on Behçet's disease

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Conflict of interest: None

Objective: To evaluate the effects of apremilast, which was indicated for Behçet's disease, on oral ulcers and other domains and cytokine expression. Methods: We studied the improvement rate of oral and genital ulcers, skin lesions, arthritis, and eye lesions, as well as the changes in serum cytokines (IFN-γ, IL-10, IL-8, and TNF-α) before and after treatment. Results: The mean age of 12 patients (2 males and 10 females) was 46.3 ± 11.7 years and the mean duration of disease was 9.8 ± 9.4 years. All patients had oral ulcers, five had genital ulcers, six had skin lesions, four had arthritis, and two had eye lesions. Oral ulcers improved in 11 patients, and resolution of oral ulcers was maintained in 10 patients. The improvement rates of genital ulcers, skin lesions and arthritis were 100%, 66% and 25%, respectively. Changes in serum cytokines were different from those previously reported in psoriasis. Adverse events were gastrointestinal symptoms such as nausea and diarrhea in 4 patients and sensorineural deafness in 1 patient. Medication was discontinued in one patient. Conclusions: Apremilast is a useful treatment option for oral ulcers caused by Behçet's disease and may be effective for other domains. Effects on serum cytokines are different from those in patients with psoriasis.

W61-6

Clinical course of 3 cases with trisomy 8 and Behcet's disease-like symptoms

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Conflict of interest: None

[Overview] Behcet's disease (BD)-like intestinal lesions associated with trisomy 8-positive MDS have been reported. We experienced 3 cases with BD-like symptoms such as fever, oral aphthae, arthritis, and skin symptoms, which were strongly suggested to be related to trisomy 8. Case 1: Female in her 50s with Sjogren's syndrome and trisomy 8-positive MDS presented fever and oral / skin / joint lesions. A moderate dose of PSL was effective, but PSL could not be reduced by adding treatments such as colchicine, TAC, ABA, GOL, HCQ, and TOF. Case 2: Male in his 60s with HLA-B51 and trisomy 8 presented fever and oral / intestinal lesions. Colchicine was ineffective, and IFX and ADA partially improved intestinal lesions, but PSL could not be reduced to less than 10 mg. Case 3: Male in his 70s with trisomy 8-positive MDS presented fever and oral / genital / intestinal lesions. Colchicine, INF, ADA, CsA, and TCZ had no therapeutic effect, and peritonitis persisted and died. [Discussion] Trisomy 8 cases with symptoms similar to Behcet's disease present with a variety of symptoms, not limited to intestinal lesions, and may resist conventional treatments.

W62-1

Efficacy and safety of tacrolimus in patients with juvenile idiopathic arthritis - single-center retrospective study

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Conflict of interest: Yes

[Objective] The anti-rheumatic drug covered by insurance for juvenile

idiopathic arthritis (JIA) is only methotrexate (MTX) in Japan, is recognaized as urgent problem. We aimed to evaluate the tacrolimus for JIA and to serve as a data for expanding the indication of tacrolimus to JIA. [Methods] We retrospectively reviewed the singlecenter survey data of patients with JIA treated with tacrolimus between 2019 and 2020. Patients' characteristics, disease activity (JADAS-27, MMP-3), short-term (3-month) and long-term (1-year) outcomes, and adverse events were evaluated. This study was approved by the Human Research Ethics Committee of the Tokyo medical and dental university Hospital. [Results] Patients included 12 boys and 21 girls (median at administration: 14 years). The JIA classification was systemic in 6 cases, oligoarthritis in 8 cases, and polyarthritis in 19 cases. Twenty-two patients were using biologics and 21 were using MTX before administered. Nine cases were changed from MTX because of side effects. The median values of JADAS-27 and MMP-3 at administration / 3-month / 1-year were 10.5 / 3 / 2 and 53.4 / 46 / 39.15, respectively, which were significantly improved (p <0.05). [Conclusions] Tacrolimus was a safe and effective second-line therapy for JIA.

W62-2

Analysis of Clinical Practice of Juvenile Idiopathic Arthritis and Rheumatoid Arthritis Patients aged 16 to 30 years old using CoNinJa and NinJa

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Conflict of interest: None

[Objective] We investigated the actual practice of medical care of JIA and RA patients aged 16 to 30 years old and the actual medical care of drugs used. [Methods] Using data from CoNinJa (Children's version of National Database of Rheumatic Diseases in Japan) and NinJa (National Database of Rheumatic Diseases in Japan) in 2016, we cross-sectionally compared the registered cases of articular JIA and RA from 16 to 30 years of age. [Results] We examined 179 cases of JIA and 152 cases of RA. Compared with RA cases, JIA cases had lower disease activity (DAS 28 - ESR, median 1.36 vs. 2.01, $p < 0.01$). Biological agents were used more frequently in JIA cases (Utilization 63.1% vs. 25.7%, $p < 0.01$). There were more off-label use of biologics in JIA than RA. [Conclusions] In Japan, there is a medical subsidy system for JIA, but not for young RA. It is necessary to establish the medical subsidy system which can positively use the expensive biologics for the young RA case. And insurance adaptation extension of the drug in JIA seemed to be the necessity.

W62-3

Identification of novel biomarker candidates in the serum for systemic juvenile idiopathic arthritis using next-generation proteomics

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Conflict of interest: None

[Objective] Systemic juvenile idiopathic arthritis (sJIA) is an autoinflammatory disease caused by high production of inflammatory cytokines. IL-18 are reportedly not always associated with frequent relapses or complication with macrophage activation syndrome (MAS). Therefore, novel biomarkers that reflect the disease activity are needed. Our study investigated the proteins associated with sJIA disease activity using next-generation proteomics. [Methods] We performed a deep proteome analysis of serum samples from nine patients with sJIA using highly sensitive mass spectrometry and identified proteins that varied according to the disease phase. [Results] We selected 158 upregulated proteins (URPs) that were highly expressed in the active phase from total of 2,727 proteins. Pathway analysis revealed that the URPs included proteins related to the NF-κB pathway and proteasome proteins. The levels of the six most highly expressed proteins from URPs (LAP3, CNDP2, BMP10, GNPDA1, TYMP, GBP1) clearly reflected the disease activity, suggesting that those proteins might be useful in assessing the sJIA disease activity. [Conclusions] We identified a novel group of proteins that may be clinically useful for diagnostic and therapeutic purposes and might help determine the pathogenesis of the disease.

W62-4

Follow-up study of Tocilizumab phase II/III trials in patients with systemic juvenile idiopathic arthritis: an interim report

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Conflict of interest: None

[Objective] In 2002, tocilizumab (TCZ) was the first medication in the world to be investigated in Japan for systemic juvenile idiopathic arthritis (sJIA). A follow-up study was conducted to determine the long-term prognosis of patients participating in the phase II/III trial. [Methods] The results of the study were collected from 8 collaborating hospitals. [Results] By October 2020, 68 patients (30 males and 38 females) were enrolled from 6 hospitals. There were no deaths among all patients, who were 25.5 years at evaluation, 3.6 years at the time of onset, 9.0 years at the time of first dose of TCZ, and 3.5 years from onset to first dose of TCZ. The final diagnosis was 66 patients with sJIA (21 (31.8%) of which were chronic arthritic sJIA). 11 (16.2%) patients continued to be treated at the same hospitals, 13 (19.1%) had treatment-free remission, and 46 were transferred to other hospitals. 6 of the 11 patients who continued to attend at the investigating hospitals were receiving TCZ. The 13 patients with remission off medication did not have chronic arthritic sJIA. [Conclusions] Approximately 80% of patients were still under medical care. Additional evaluations are planned to clarify the pathophysiology and problems of sJIA in the transitional and adult-hood of the disease.

W62-5

Redox-active protein thioredoxin (TRX)-1 reflects the activity of pediatric rheumatic diseases

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Conflict of interest: None

[Objective] Although oxidative stress markers have been used for disease prevention and diagnosis of presymptomatic diseases in the elderly, there have been no reports on oxidative stress in pediatric rheumatic diseases. Evaluation of oxidative stress markers may help to understand the pathogenesis of pediatric rheumatic diseases, including their severity and relapse. [Methods] Redox-regulated protein thioredoxin (TRX) was measured in sera collected from 25 cases of pediatric rheumatic diseases treated at Okayama University Hospital during the acute phase and the remission phase. [Results] TRX was significantly elevated in the acute phase and decreased in the stable phase ($p<0.05$). TRX was significantly elevated in the acute phase of JIA except in the systemic type ($p<0.001$). No significant differences were observed in other diseases. In JIA except in the systemic type, TRX showed a similar trend to ferritin, but did not correlate with MMP3. In JIA except in the systemic type, TRX seemed to correlate with systemic inflammation. [Conclusion] Oxidative stress markers were shown to be potentially useful biomarkers for monitoring the activity of

pediatric rheumatic diseases.

W62-6

Comparison of clinical characteristics between childhood-onset and adult-onset systemic lupus erythematosus: Results from a prospective cohort study of young patients with systemic lupus erythematosus in Japan (PLEASURE-J)

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Conflict of interest: None

[Objective] To identify difference of characteristics between childhood-onset (<18 years, cSLE) and adult-onset (≧18 years, aSLE) systemic lupus erythematosus (SLE). [Methods] We analyzed the patients in a prospective SLE cohort study (Pleasure-J study). [Results] The patients with cSLE and aSLE were 26 (male=2) and 128 (male=15). The median age at diagnosis (IQR) of cSLE and aSLE were 15 years (13.0-16.8) and 27 years (22.0-31.0). The median SLE Disease Activity Index 2000 (SLEDAI-2K) of cSLE and aSLE were 16 (8-21) and 14 (9-21). The aSLE had more arthritis than cSLE (p=0.002). C4 and CH50 were lower in cSLE than aSLE (p=0.029 and p=0.038). Renal biopsy was done in cSLE more than in aSLE. Among patients who had renal biopsy, all of patients with cSLE and 97% of patients with aSLE presented with lupus nephritis (LN). There was no significant difference of severity of LN. As initial treatment, methylpredonisolone pulse and mycophenolate mofetil were more likely to be given in cSLE than aSLE. Calcineurin inhibitors were given more in aSLE than cSLE. More initial dose of prednisolone/kg were given to cSLE than aSLE. [Conclusions] There were no significant differences of organ damage and SLEDAI-2K. The cSLE group had more aggressive therapy. We need to analyze more participants.

W63-1

Is the severity classification useful for predicting outcomes in patients with Adult Still's disease?

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Conflict of interest: Yes

[Objective] To investigate the usefulness of the severity classification in predicting outcome of patients with Adult Still's disease (ASD). [Methods] By a retrospective multicenter study, we collected clinical information on 142 patients with ASD. Patients were classified into mild, moderate, and severe groups according to the severity classification, and clinical features, treatments, and prognosis were compared among these groups. [Results] Forty-nine (34.5%), 37 (26.1%), and 56 patients (39.4%) were classified into mild, moderate, and severe group, respectively. Patients in the severe group had higher frequency of high fever, pleuritis, pericarditis, MAS, and DIC, and showed higher levels of white blood cells, neutrophils, CRP, aspartate transaminase, lactose dehydrogenase, and ferritin. Biological agents, calcineurin inhibitors and mPSL pulse therapy were more frequently used in severe group. Furthermore, in the severe group, ASD-related survival was tended to reduce, and drug-free remission rate was lower than mild plus moderate groups (P=0.0996 and P=0.0231, respectively). [Conclusions] Severity classification is useful for predicting outcomes in ASD patients.

W63-2

Clinical characteristics and treatment of elderly-onset Adult-onset Still's disease ~from multicenter cohort of Nagano prefecture ~

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Conflict of interest: None

[Objective] To determine the clinical characteristics and treatment status of patients with elderly-onset Adult-onset Still's disease (AOSD) using a multicenter cohort of Nagano prefecture. [Methods] We retrospectively analyzed clinical features and treatment about 55 patients with AOSD between 2008 and 2019. Patients were divided into two groups based on the age of disease onset (65 years and older or not). [Results] Twenty four patients (43.6%) experienced their first symptom at age ≧65 years. The disease activity of elderly-onset patients was not different with younger-onset patients, however, the higher frequency of hemophagocytic syndrome and disseminated intravascular coagulation and higher levels of white blood cells, C-reactive protein, and serum ferritin were seen compared with younger-onset patients. In recent years, elderly-onset patients using some immunosuppressant or tocilizumab had increased. Moreover, the number of days to glucocorticoid halving and the frequency of infections was reduced. [Conclusions] Elderly-onset patients with AOSD had been increased. The disease activity of them was as same as younger-onset patients, and the frequency of therapeutic option other than glucocorticoid is increasing.

W63-3

Analysis for clinical features of elderly onset adult Still's disease

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Conflict of interest: None

[Objective] To clarify the clinical features of elderly onset adult Still's disease. [Methods] We examined patients with definite adult Still's disease based on Yamaguchi's criteria, who developed the disease between Jan 2010 and Sep 2020. We retrospectively compared 1) patient background and symptoms, 2) laboratory data, and 3) treatment and prognosis, between young onset (YO) group (<65 years old) and elderly onset (EO) group (≧65 years old). [Results] 35 patients (47.0±21.4 years old, 10 males/25 females) were examined (YO group: 27/EO group: 8 patients). 1) Typical rush (63.0 vs 12.5%) and splenomegaly (59.3 vs 0%) were significantly less frequent, while atypical rush (25.9 vs 100%) was significantly more frequent in EO than in YO group. 2) WBC count was significantly higher and serum IL-6 was significantly lower in EO than in YO group. Serum ferritin was comparable between two groups. Initial PSL dose, concomitant immunosuppressants and biologics, and relapse were comparable between two groups, whereas infections were significantly more frequent in EO than in YO group. [Conclusions] In EO group, atypical rush was more frequent, typical rush and splenomegaly were less frequent, WBC count was higher, serum IL-6 was lower, andinfections were more frequent than in YO group.

W63-4

Clinical features of patients with elderly onset of adult Still disease

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Conflict of interest: None

Objective: We aimed to identify the features of patients with elderly onset of adult Still disease (ASD). Methods: We collected 82 patients with ASD (median age, 52 years; female, n= 66) who were diagnosed at Ohta-Nishinouchi Hospital or Fukushima Medical University Hospital or Nagasaki University Hospital and related facilities. We assigned the patients to groups depending on whether they developed ASD at age ≧ 65 (elderly group; n= 20) or < 65 years (young group; n= 62) and compared their clinical findings. Results: Lymphadenopathy and sore throat were significantly less prevalent in the elderly, than the young group (15% vs. 54.8%, p= 0.0019 and 35% vs. 80.6%, p= 0.0004, respectively). The number of applicable items in the Yamaguchi classification criteria of ASD was significantly low, with a median of six and seven items in the elderly and young groups, respectively (p= 0.0062). Median values for C reactive protein and ferritin in the elderly group were 12.2 mg/dL and 9423 ng/mL. Steroid pulse therapy was administered to 55%, of the elderly group and tocilizumab was administered to 25% of them. Conclusion: Sore throats and lymphadenopathy were less prevalent among patients with elderly onset ASD, and few items in the classification criteria were applicable to them.

W63-5

Functional Analysis of Monocyte/Macrophage Pyroptosis and GSDMD as a Novel Biomarker in AOSD and sJIA

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Conflict of interest: None

[Objective] Elevated serum IL-18 in AOSD and sJIA suggests inflammasome activation. GasderminD N-terminal (GD-N) forms pores in cell membrane and plays a key role in Pyroptosis. IL-18 and ferritin (Fer) are released extracellularly via the pore. Herein, we focused on GD-N and analyzed the mechanism in AOSD&sJIA. [Method] The IRBs approved this study. Serum GD-N of active and inactive AOSD/sJIA, Behcet's disease and macrophage (M&φ) activation syndrome were measured by ELISA. Peripheral blood monocytes (Mo) were isolated and stimulated with GM-CSF for 9 days to differentiate into M1M&φ. Using these cells, the cell number after culturing and the Fer/GD-N concentration in the culture supernatant (cSN) were measured. [Results] We examined 48 AOSD and 9 sJIA. Serum GD-N was significantly higher in active AOSD, and positively correlated with serum Fer/IL-18. The cultured M&φ decreased with time in active AOSD, suggesting M&φ death was enhanced in active AOSD. M1M&φ derived from active AOSD released much of Fer and GD-N in the cSN. Besides, GD inhibitors antagonized Fer release into the cSN by Nigericin-induced Pyroptosis of Mo. [Conclusion] Serum GD-N increased in active AOSD&sJIA, indicating that Mo/M&φ pyroptosis was enhanced, and as a result, hyperferritinemia may occur.

W63-6

Clinical significance of serum interleukin-18 level in the differential diagnosis of adult onset Still's disease and hemophagocytic syndrome

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Conflict of interest: None

[Objective] Adult onset Still's disease (AOSD) is a systematic inflammatory disease that is associated with activation of macrophage. It has been suggested that IL-18 is associated with the pathogenesis of AOSD. AOSD shares several clinical and laboratory variables with hemophagocytic syndrome (HPS). So, It is difficult to differentiate these diseases. We evaluate the clinical significance of serum IL-18 level to differentiate AOSD and HPS. [Methods] 45 patients with AOSD and 30 patients with HPS, who were admitted to our hospital between January 2012 and September 2020, were enrolled. AOSD patients were diagnosed according to Yamaguchi criteria. Serum concentration of CRP, LDH, GOT, GPT, ferritin, sIL-2R, IL-6 and IL-18 was determined in both ASD and HPS. [Results] The serum IL-18 level in AOSD patients was significantly higher than that in HPS patients ($p<0.0001$), and that of sIL-2R was lower ($p<0.0001$). Between ASD and HPS, serum concentrations of CRP, LDH, GOT, GPT, ferritin, and IL-6 were not significantly different. IL-18 serum levels in AOSD patients positively correlated with serum ferritin levels ($r=0.7$, $p<0.0001$). [Conclusions] We argue that IL-18 can be a biomarker for differential diagnosis between AOSD and HPS and be associated with activation of macrophage.

W64-1

Analysis of factors affecting drug-free remission of adult-onset Still's disease (AOSD)

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Conflict of interest: None

[Objective] To elucidate the clinical features involved in drug-free remission of adult-onset Still's disease (AOSD). [METHODS] Of the AOSD patients diagnosed from January 2006 to September 2016, 124 patients (90 females and 34 males) who were followed up for more than half a year were included. A Cox proportional hazard model was used. [Results] The median age at diagnosis was 47.5 years. The median observation period was 3.8 years (6 months to 13 years). Drug-free remission was observed in

44 patients (35.5%). In univariate analysis, male, under 60 years old, no organ complications (MAS, DIC, serositis), no MAS, no joint pain, no fever, rash, no lymphadenopathy, no pleurisy, reddening promotion, AST high value, and total protein high value, no steroid pulse, no MTX, no cyclosporine were extracted. As a result of multivariate analysis of these items, male (HR=3.25, P=0.013), under 60 years old (HR=3.49, P=0.018), no organ complications (HR=10.77, P=0.009), No MTX administration (HR=4.60, P=0.017) and no cyclosporine administration (HR=3.64, P=0.003) were independent related factors. [Conclusion] It was revealed that young men do not have organ complications or use of immunosuppressive drugs as factors involved in achieving drug-free remission.

W64-2

Associated factors of poor treatment response for initial glucocorticoid therapy in patients with adult-onset Still's disease

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Conflict of interest: None

[Objective] Treatment intensification is required in adult onset Still's disease (AOSD) patients resistant to initial treatment. The aim of this study was to identify risk factors with poor clinical response. [Methods] We enrolled 71 AOSD patients (mean age 51.6 years) in a retrospective, monocentric cohort. The patients who received two and more pulse glucocorticoid (GC) therapy or any immunosuppressive drugs within 4 weeks due to progression or flare were defined as poor treatment response for initial GCs therapy. [Results] Initial poor treatment response was observed in 29 (40.8%) of the 71 AOSD. Patients with poor response had higher white blood cell (WBC) counts, serum ferritin level, serum LDH level, systemic feature score based on clinical symptoms (mSFS), and had more macrophage activated syndrome than in the remaining 42 control patients. Multivariable analysis revealed WBC count was the associated factor of the poor response (odds ratio per 1000/μl increment: 1.12, 95%CI 1.04-1.29), while thrombocytopenia, ferritin, LDH, and mSFS did not reach statistical significance. [Conclusions] The initial treatment intensity within 4 weeks in AOSD could be determined based on the WBC counts at the initiation of the treatment.

W64-3

The clinical course of adult onset Still's disease in our hospital

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Conflict of interest: None

[Objective] We characterized the therapeutic response and clinical course of AOSD. [Methods] We retrospectively investigated the clinical course of AOSD patients treated in our hospital between January 2010 and September 2020. [Results] Subjects were 21 women and 3 men with a mean age of 55.5 ± 15.5 years. 3 cases went into remission spontaneously, 4 cases were treated by steroid monotherapy, and 17 cases were resistant to steroid therapy. Of these, 13 patients were administered MTX and 5 were administered CyA. 6 of these 17 patients were administered TCZ because these immunosuppressants were ineffective. Two patients received plasma exchange therapy. Compared with 10 patients who achieved remission with MTX and/or CyA, 6 patients who required TCZ had significantly higher peak ferritin levels (11986 ± 13531, 62290 ± 73466 ng/ml: p = 0.03). 23 patients had clinical remission and 1 patient died. Overall, 8 patients experienced recurrence. In 6 cases with TCZ administration, recurrence has not been recognized. [Conclusions] Very high ferritin levels may indicate resistance to conventional treatment, and TCZ appeared to be effective in these refractory AOSD.

W64-4

Clinical characteristics and treatments of patients with adult-onset Still's disease who developed thrombocytopenia after tocilizumab administration

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Conflict of interest: None

[Objective] We explored the clinical characteristics of patients with adult-onset Still's disease (SD) who developed thrombocytopenia after tocilizumab (TCZ) administration, and their treatments. [Methods] We retrospectively studied 28 patients treated from January 2009 to October 2020. [Results] We prescribed TCZ to 18 cases at first onset of SD and to 10 cases at disease relapse. Patients who developed thrombocytopenia had received lower steroid pulses than others, shorter time span from onset or relapse date to TCZ introduction, and higher ferritin levels. In patients with mild thrombocytopenia, steroids were gradually decreased and then the patients recovered. When thrombocytopenia was severe or the ferritin level was elevated, we did not reduce the steroid level, but reduced the TCZ dose interval to weekly, inducing only transient changes. [Conclusions] When TCZ was introduced relatively soon after SD onset, and ferritin level was elevated, thrombocytopenia tended to develop. However, even if thrombocytopenia was marked, reduction of the interval between TCZ administrations while maintaining the steroid dose constant allowed recovery.

W64-5

A review of 19 cases treated with tocilizumab for adult Still's disease

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The University of Tokyo Hospital

Conflict of interest: None

[Objective] The effectiveness of tocilizumab (TCZ) for adult Still's disease (ASD) has been widely recognized. Whereas, the timing of TCZ introduction differs depending on the case. In this study, we investigated the risk of inducing hemophagocytic syndrome (HPS) and the steroid sparing effect depending on the timing of TCZ introduction. [Method] We retrospectively analyzed 19 cases of ASD treated with TCZ from 2011 to 2020. The high ferritin group (HFG: 500 ng/mL or more) and the low ferritin group (LFG: less than 500 ng/mL) were defined by the ferritin level at the time of TCZ introduction. [Results] There was no significant difference in age, sex and the presence of HPS before treatment between HFG (n =11) and LFG (n = 8). The ferritin level before treatment and at TCZ induction was significantly higher in HFG (pretreatment: $P = 0.048$, TCZ induction: $P = 0.0074$). The steroid dose (PSL equivalent) at the time of TCZ introduction was significantly higher in HFG ($P = 0.015$), but the difference disappeared 3 months after TCZ introduction ($P = 0.225$). Only one patient in LFG had newly developed HPS after the introduction of TCZ. [Conclusions] Introducing TCZ relatively early phase of ASD, where hyperferritinemia remains, may result in safe steroid dose reduction.

W64-6

The order of drug withdrawal after remission of ASD treated with TCZ may not be related to maintenance of remission

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Conflict of interest: None

[Objective] We aimed to report on the clinical characteristics of the use of tocilizumab (TCZ) for adult Still's disease (ASD). [Method] Twelve patients (ave. 53.7 years old at TCZ introduction, 9 females) of ASD with

Yamaguchi's diagnostic criteria, administered TCZ in our department by August 2020, were included. [Results] CRP and ferritin at TCZ induction were 3.41±3.47 mg/dL and 3340.0±3537.3 ng/mL, respectively, which declined rapidly after administration. Eleven patients were treated with steroids (PSL 39.6 ± 28.2 mg/day at TCZ induction). Drug-free remission was observed in 4 patients. We had three cases in which TCZ was stopped prior to other drugs and three cases in which TCZ was stopped after cessation of other drugs, and relapse was observed in two cases, respectively. Patients with repeated relapses after treatment with prior TCZ discontinuation maintained remission for a longer period of time after prior cessation of other medications and final cessation of TCZ. [Conclusions] TCZ are beneficial for inducing remission in ASD and should be administered in sufficient quantities. The order of drug withdrawal after remission of ASD treated with TCZ may not be related to maintenance of remission, while it should be adjusted according to the course of the individual case.

W65-1

Anti-type 2 collagen antibodies at the time of diagnosis are predictors of flare in relapsing polychondritis

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Conflict of interest: None

[Objective] We aim to investigate whether the relapse rates differ between anti-type 2 collagen (C2) positive and negative patients in relapsing polychondritis (RP). [Methods] We analyzed 19 patients diagnosed with RP between April 2006 and June 2020 in our hospital. The rates of relapse during the follow-up period of 2 years were compared between the anti-C2 positive and negative groups. [Results] Anti-C2 antibodies were measured at the time of diagnosis in 13 patients. The anti-C2 positive and negative group included 7 and 6 patients respectively. The median age was younger in the anti-C2 positive group (50.3 years vs 68.8 years, p=0.234). The anti-C2 positive group was significantly more likely to have respiratory tract manifestations (n=5 (83.3%) vs n=1 (14.3%), p=0.0291). The median dose of corticosteroids (predonisone equivalent) was higher in the anti-C2 positive group (47.5 mg vs 5.0 mg, p=0.0173). Methotrexate was more often used in the anti-C2 positive group (n=4 (66.7%) vs n=0 (0%), p=0.021). The anti- C2 positive group tended to relapse with greater frequency (n=5 (83.3%) vs n=2 (28.6%), log rank test p=0.0374). [Conclusions] It is suggested that anti-C2 antibodies at the time of diagnosis are predictors of flare in RP.

W65-2

Comparison of the clinical features of TAFRO syndrome and idiopathic multicentric Castleman's disease

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Conflict of interest: None

[Objective] We compared the clinical features of TAFRO syndrome (TAFRO) and idiopathic multicentric Castleman's disease (iMCD). [Methods] We retrospectively compared 5 TAFRO and 6 iMCD patients of our hospital. We used diagnostic criteria for TAFRO by Masaki or Iwaki and criteria for iMCD by CDCN. [Results] There were 4 (80%) male TAFRO patients and 3 (50%) male iMCD patients. The age of onset was 47 [42-48] (median [IQR]) and 49 [38-60] years old, respectively. Before treatment, the CRP score was 10.2 [3.8-17.9] vs 6.3 [5.5-9.9] mg/dL, the platelet number was 3.8 [2.6-13.8] vs 23.6 [20.5-38.3] x10^4/μL, and the level of IgG was 1432 [1152-1572] vs 4321 [2766-4777] mg/dL, respectively. RNA immunoprecipitation identified anti-SS-A antibody in 4 of 5 TAFRO patients, but not in iMCD patients. ELISA test showed similar results. TCZ was used in 5 cases (83%) with iMCD and the disease activity was well controlled after induction. On the other hand, of the 4 TAFRO cases (80%) treated with TCZ, 2 cases showed insufficient response, and then were effectively treated with RTX. [Conclusions] Compared with iMCD, the TAFRO patients were positive for anti-SS-A antibody and showed different response to TCZ. These results suggest that autoimmunity may play a role in the pathogenesis of TAFRO.

W65-3

Analysis of serum biomarkers in idiopathic multicentric Castleman's disease

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Conflict of interest: None

[Objective] We will identify biomarkers that discriminate iMCD-NOS and iMCD-TAFRO or predict the treatment responsiveness. [Methods] We performed a comprehensive analysis of serum proteins using the L-Series Human Antibody Array L-507 on the 4 iMCD-NOS and 2 iMCD-TAFRO patients from which pre- and post-tocilizumab treatment samples were obtained. Using sera from 28 healthy controls, 8 iMCD-NOS and 6 iMCD-TAFRO patients, we validated the validity of IGFBP-1, identified as a protein with a high rate of reduction after treatment, by ELISA. [Results] In the 4 patients who responded well to treatment with tocilizumab, with the reduction of IGFBP-1 was high in all 4 cases by L-507 serum protein arrays. In iMCD cases, serum IGFBP-1 was significantly higher (p=0.0016) before the introduction of treatment compared to healthy controls. In addition, iMCD-TAFRO was significantly higher than iMCD-NOS (p=0.024). Furthermore, post-treatment serum IGFBP-1 was decreased in many cases. [Conclusions] Serum IGFBP-1 may play a particularly important role in the pathogenesis of iMCD-TAFRO and may be useful in discriminating between iMCD-NOS and iMCD-TAFRO. In the future, we will accumulate more cases, compare it with other inflammatory diseases, and examine the difference in response to treatment.

W65-4

Clinical characteristics of patients with pustulotic arthro-osteitis

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Conflict of interest: None

[Objective] The clinical characteristics of pustulotic artho-osteitis (PAO) in Japanese patients have not been fully established. We reviewed clinical characteristics of the patients with PAO. [Methods] We investigated the patient background, disease activity index, mSASSS, comorbidities, HLA typing, and treatment in 8 patients with PAO. [Results] The patient's background was as follows; male: 3 cases, smoking history; 5 cases, hypertension: 4 cases, osteoporosis: 3 cases, aortic regurgitation: 2 cases. Six patients had spinal lesion on imaging (mSASSS≧1), but two complained of back pain due to axial lesions. There were stenoclavicular arthritis in 6 cases, sacroiliac arthritis in1 case, peripheral arthritis in 2 cases, enthesitis in 1 case. None of them had focal infection. HLA-A33 was found in three cases, and B51 and B52 were in two cases each. The treatment for PAO was as follow; methotrexate; 2 case, glucocorticoid; 2 cases, non-steroidal anti-inflammatory drugs; 3 cases, salazosulfapyridine 2 cas-

es, guselkumab 2 cases. [Conclusions] Histories of smoking and hypertension were prominent and sternoclavicular arthritis were common in the patients with PAO. Most of the cases had spinal lesions, suggesting that the search for spinal lesions by imaging may be necessary in PAO.

W65-5

Inflammatory arthritis associated with immune-related adverse events of immune checkpoint inhibitors

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Conflict of interest: None

[Objectives] To investigate the clinical features of inflammatory arthritis (IA) associated with immune-related adverse events (irAE) of immune checkpoint inhibitors (ICI). [Methods] 166 patients with cancer who were introduced ICI between January 2017 and December 2019 were evaluated. [Results] Of the 166 patients who received ICI, 7 patients, 5 males and 2 females, were clinically diagnosed as IA. 4 patients were treated with pembrolizumab and 3 were treated with nivolumab. Mean time of the onset from starting of ICI was 3.0 months. In all patients, ICI showed anti-tumor effects at the onset of the irAE. Arthritis were seen mainly in upper extremities. NSAIDs was effective in one patient and other 6 patients were required glucocorticoid treatment. One patient needed to increase glucocorticoid and received disease-modifying anti-rheumatic drugs, but others could decrease glucocorticoid. All patients continued ICI treatment. [Conclusions] IA induced by ICI was seen in during an early time and could be managed with treatment, such as with glucocorticoids. Early diagnosis and treatment is critical in the management of IA associated with ICI.

W65-6

Biomarkers of Difficulty in Tapering Glucocorticoid in Polymyalgia Rheumatica: The Importance of Fibrinogen

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Conflict of interest: None

[Objective] Clinical markers of polymyalgia rheumatica (PMR) in cases of relapse or difficulty in maintenance of remission were investigated. [Methods] Symptoms, examinations, and treatments were analyzed. Difficulty in tapering glucocorticoid (GCC) was defined as increasing prednisolone (PSL) dose, adding other immunosuppressants due to worsening symptoms, or inability to reduce PSL to ≦ 5 mg/day even 1 year after treatment. [Results] Eighty patients were enrolled (70% female; median onset age 73 years). Median C-reactive protein (CRP) and fibrinogen levels and erythrocyte sedimentation rate (ESR) were 8.81 mg/dL, 620 mg/dL, and 88.5 mm/h, respectively. The rate of difficulty in tapering GCC was 40%. There were no significant differences in liver enzyme, CRP, or ESR levels according to difficulty in tapering GCC, but fibrinogen level was significantly different between the difficulty and non-difficulty groups (664.4 vs. 599 mg/dL, respectively, $P = 0.02$). With a fibrinogen cutoff level of 531.4 mg/dL, the sensitivity and specificity of prediction on ROC curve analysis were 100%, and 40%, respectively. [Conclusion] Fibrinogen is an important marker for difficulty in tapering GCC in PMR.

W66-1

A family of infantile episodic limb pain

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Conflict of interest: None

[Case] 25-year-old woman [Main complaint] Paroxysmal one-limb pain [Current medical history] From birth, there was a seizure that caused pain in one of the upper limbs, lower limbs, or limbs. Seizures occur once every one or two weeks, peak in two hours, and then improve in six hours. The onset time is not fixed, but it often occurs before bedtime. Fatigue, overeating, drinking and cold are the inducing factors. [Family history] Father, uncle and cousin, grandfather and his sister have similar symptoms. Seizures decrease to about once every six months after the age of 20. [Progress] A diagnosis of childhood limb pain attack was made based on the characteristic symptoms and autosomal dominant inheritance. A heterozygous p. R222H mutation was found in the gene responsible for this disease, SCN11A, from the patient and his father. [Discussion] This disease is a disease reported and established by Okuda H et al. In 2016 (PLoS One. 2016; 11 (5): e0154827). It is a disease that can be diagnosed only by the characteristic current medical history and family history. However, many patients may remain undiagnosed due to low disease awareness and a reduced frequency of limb pain attacks after puberty.

W66-2

An adarimumab effective case of Hidradenitis suppurativa with systemic manifestations requiring differentiation from Behçet's disease

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Conflict of interest: None

[Case] A 26-year-old male patient was referred to our hospital with relapsing multiple oral ulcers, folliculitis, polyarthralgia, occasional fever and genital ulcer with bleeding and skin defect for two years. Colonoscopic examination revealed no mucocutaneous ulcers. These manifestations were tried to control with 30 mg of oral prednisolone under the diagnosis of incomplete types of Behçet's disease (BD) at the previous hospital, however, perianal abscess had been active even after using azathioprine and minomycin. The skin ulcers with fistula distributed on hip and axillary regions were considered Hidradenitis suppurativa (HS), which required several times of incisional drainage. Therefore, Adarimumab (ADA) was administered for HS, polyarthralgia, fever and continuous CRP increasing, resistant to immunosuppressive drugs (cyclosporin, tacrolimus and methotrexate). ADA use improved all the symptoms, and led to remission and discontinuation of steroid. [Discussion] HS is a chronic, recurrent, inflammatory and refractory skin disease. Although pathogenetic association between two diseases has been discussed, few cases HS complicated with BD were reported, in fact. Here we report an ADA-response HS case accompanying systemic manifestations, initially diagnosed as BD.

W66-3

A case of Erdheim-Chester disease that required differentiation from giant cell arteritis and IgG4-related disease

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Conflict of interest: None

A 77-year-old man was admitted to a nearby hospital for dyspnea and fever. Eight years ago, he was pointed out for aortic dissection and was followed by a cardiovascular surgeon. A follow-up chest CT showed aortic wall thickening, pericarditis, and right pleuritis, 2 months before admission. He was transferred to our Department of Cardiology for diagnosis. Giant cell arteritis (GCA) was suspected, and he was referred to our department. Laboratory data showed that CRP 6.92 mg/dL and IgG4 227 mg/dL. GCA or IgG4-related disease (IgG4RD) were considered. However, the pleuritis and pericarditis were rare complications of GCA, and the high inflammatory response was atypical for IgG4RD. An FDG-PET revealed an increased accumulation of FDG in the aortic wall, pleura, pericardium, humerus, and testis. Erdheim-Chester disease (ECD) was suspected. The left testis was removed, and the histopathological examination confirmed a diagnosis of ECD. ECD is a rare disease belonging to non-Langerhans cell histiocytosis. Patients with ECD often present with aortic lesions which are similar to GCA and IgG4RD. Rheumatologists should be aware of ECD.

W66-4

A case of suspected Crow-Fukase syndrome

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Conflict of interest: None

Case: Male in his 60s, At the age of 37, he developed polymyositis and mononeuritis multiplex and received steroid treatment. In X-4, he was referred to our department on suspicion of relapse of polymyositis. Although there was an increase in CK, MRI showed no evidence of myositis, electromyography showed no myogenic changes, and myositis-related autoantibodies were negative. Motor neuropathy was suspected on a peripheral nerve conduction study. The condition was stable, but fatigue appeared from the end of August X. In October, I visited an outpatient clinic because of dyspnea. Pleural effusion and ascites were observed on CT, and platelets 44000 / μl, CRP5.83 mg / dl, CK 153 U / L, aldolase 21.8 U / L IgG188 mg / dl, IgA57 mg / dl, IgM2787 mg / dl M proteinemia were suspected on blood sampling., Crow-Fukase syndrome was suspected because it was judged to be polyneuropathy associated with M proteinemia. Although the platelet antibody was negative, the bacteria were positive for Helicobacter pylori, so eradication was performed, PSL 30 mg / day was started, and platelet transfusion was performed as appropriate. We report a rare case of Crow-Fukase syndrome suspected of relapse of polymyositis

W66-5

Familial cases of CTLA4 Haplodeficiency successfully treated with Abatacept

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Conflict of interest: None

[Introduction] CTLA4 haploinsufficiency is an immunodeficiency due to reduced expression of CTLA4 protein by heteromutation of CTLA4. We report two cases within a family successfully treated with Abatacept (ABT). [Case 1] 47-year-old male. At age 19 years, he had thrombocytopenia, and at age 32 years, he developed autoimmune hemolytic anemia. At 41 years of age, he was diagnosed with CTLA4 haploinsufficiency. At age 44 years, he showed granulomatous interstitial nephritis. As nonspecific colitis with T-cell infiltration were observed at age 45 years, ABT was started. After administration of ABT, enteritis, renal function, and cytopenia were improved. [Case 2] 21-year-old son of Case 1. He had eczema from infancy. At 17 years of age, thrombocytopenia, hepatic dysfunction, hypogammaglobulinemia, and diarrhea were observed. ABT was started at age 20 years, and eczema, diarrhea, thrombocytopenia, and hepatic dysfunction were completely resolved. As he had hypogammaglobulinemia persistantly, subcutaneous gammaglobulin therapy was continued. [Conclusion] In CTLA4 haploinsufficiency, organ damage was caused by inflammation and the immune response due to T-cell infiltration. ABT should be use from early stage of the disease to prevent organ damage.

W66-6

Refractory multicentric reticulohistiocytosis successfully treated by denosumab

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Conflict of interest: None

A 46-year-old man presented with papules and nodules in his face, ears, sculp, and fingers and was diagnosed as sarcoidosis and the skin biopsy showed consistent findings. He developed wide-spread pain and underwent FDG-PET/CT and musculoskeletal ultrasound, both of which showed inflammation in multiple joints. He had inadequate responses to glucocorticoids, methotrexate, etanercept, and golimumab. After 1 year of treatment, radiographs and CT scan revealed rapid progression of bone destruction. We reassessed the skin biopsy specimen and identified granuloma mostly comprised of epitheloid cells with eosinophilic cytoplasm, which led to the diagnosis of multicentric reticulohistiocytosis (MRH). Bisphosphonate was added and the dose of golimumab was increased to show no effects. In contrast, treatment with denosumab, which was switched from bisphosphonate, significantly improved both arthritis and skin lesions and halted structural damage progression. Although glucocorticoids were tapered off, the patient's symptoms have not flared. MRH is a rare disease that causes multiple subcutaneous masses and arthritis mutilans in joints throughout the body. Pathophysiology underlying MRH remains unknown and there is no established treatment. Our case will be discussed with literature review.

W67-1

Clinicopathological features of lymphoproliferative disorders in Rheumatoid Arthritis (RA-LPD)

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Conflict of interest: None

[Objective] In order to elucidate clinicopathological features of rheumatoid arthritis (RA) complicated by lymphoproliferative disorders (LPD). [Methods] 57 cases of RA-LPD diagnosed between 2005 and 2020 were retrospectively analyzed. [Results] The clinical features of patients were as follows: 68.5±10.1 y/o; male to female ratio 17:40; duration of RA 21.1±5.6 y; stage 3.34±1.01; class 2.34 ± 0.61. MTX and biologics were used in 98.2%, 47.4% respectively. Duration, maximum dosage, accumulation dosage of MTX was 7.91±5.46 y, 9.45±3.85 mg/w, 3903.2±3066.5 mg. Diffuse large B-cell lymphoma was 40.4%, polymorphic LPD 12.8%, Hodgkin lymphoma 10.6%. EBV was detected in 49.1%, and EBV positivity was not associated with prognosis. Lymphoma stage was 2.43 ± 1.25, and 46.8% had extra-nodal involvement. Performance status was 2.30 ± 0.73. CRP (4.19±5.52 mg/dL) and ESR (51.1±34.3 mm) was elevated without exacerbation of joint symptom and MMP-3 at the time of the LPD onset. All patients discontinued MTX, and 44% of patients received chemotherapy and/or surgery. 38.6% of patients died with a median follow-up of 5.13±3.92 y. [Conclusions] RA-LPD is likely to occur in male RA patients of older age. RA-LPD should be considered when exacerbation of inflammation without joint symptoms is observed.

W67-2

Usefulness of FDG-PET/CT for predicting spontaneous regression in MTX associated lymphoproliferative disorder

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Conflict of interest: None

[Objective] Recently, there are many reports from Japan about methotrexate associated lymphoproliferative disorder (MTX-LPD). We are investigating the predictive factor of spontaneous regression (SR) in MTX-LPD. On the other hand, FDG-PET/CT is used for diagnosis of LPD including malignant lymphoma. However, there are few reports that image findings predicted SR in MTX-LPD. We investigate the usefulness of FDG-PET/CT for predictive factor of SR in MTX-LPD. [Methods] We enrolled 24 RA patients who diagnosed MTX-LPD and performed FDG-PET/CT from 2005 to 2019. We divided these cases into spontaneous regression cases (SR group; 15 cases) and cases that treated with chemotherapy after MTX discontinuation (CTx group; 9 cases), and compared the difference as follow subjects between two groups; biomarker (serum LDH and sIL-2R) at LPD onset, SUVmax to evaluate malignant tumor activity by FDG-PET/CT, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) which refer to metabolically active volume of the tumor seg-

mented FDG-PET/CT. [Results] The level of sIL-2R was significantly lower in SR group. In addition, MTV and TLG by FDG-PET/CT was significantly lower in SR group. [Conclusions] We suggested that serum sIL-2R, MTV and TLG were useful for predict of SR in MTX-LPD.

W67-3

Analysis of clinical signs and abnormalities leading to the diagnosis of MTX-LPD with rheumatoid arthritis. A single center experience of 40 cases

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Conflict of interest: None

[Background] Methotrexate-associated lymphoproliferative disorders (MTX-LPD) is one of the important side effects of methotrexate, which is the anchor drug for rheumatoid arthritis (RA). The half of MTX-LPD achieved remission only by discontinuation of MTX, therefore early diagnosis is important. [Objective] We clarified the clinical signs and abnormalities which led to the diagnosis of MTX-LPD. [Methods] We investigated retrospectively the medical records of 40 patients of MTX-LPD with RA (pathological diagnosis 35, clinically diagnosis 5) from January 2008 to July 2020. [Results] The most opportunity of diagnosis was subjective symptom, twenty-three patients (57.5%). Five patients (12.5%) had a fever. Next was upper gastrointestinal endoscopy in medical check-up, four patients (10%). Four patients (10%) were diagnosed by abnormal findings in routine Chest X ray. Three patients (7.5%) were incidentally found lymphadenopathy in computed tomography. A patient (2.5%) was diagnosed by blood test abnormality, high LDH. Subjective symptoms were mass and superficial lymphadenopathy. [Conclusions] It is suggested we should do physical examination, interview and routine imaging test for RA patients treated with MTX.

W67-4

Analysis of iatrogenic immunodeficiency-related lymphoproliferative disorders in our hospital

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Conflict of interest: None

[Objective] To grasp the actual situation of iatrogenic immunodeficiency-related lymphoproliferative disease (OIIA-LPD), we analyzed the cases in our hospital. [Methods] Referring electoronic medical record in our hospital, we extracted 38 patients with connective tissue disease who were diagnosed with OIIA-LPD by pathological examination, and analyzed underlying disease, types and duration of drugs, pathology, and Progress after the drug withdrawal. [Results] The median age of onset was 67.5 (60-73) years, and the male-female ratio was 7:31. The underlying disease was RA 34, SLE 4 (3 with RA), DM 1, adult-onset Still's disease 1, Behçet's disease 1, and PBC 1 (with RA). The drug used was MTX 36, TAC 4 (MTX combination 3, MMF combination 1), CYA 2 (MTX combination 1), MMF 1, and biologics (IFX, ETN, GLM, ABT, ADA, TCZ). In Pathological findings, DLBCL (17 cases) was the most common, followed by HL (8 cases). After drug withdrawal, 24 patients had reduced lesions. In these cases, the number of peripheral blood lymphocytes tended to increase after the drug withdrawal. The median overall survival was 2.55 (0.8-5.6) years. [Conclusion] In addition to MTX, Using calcineurin inhibitors can cause OIIA-LPD. The number of peripheral blood lymphocytes may be effective as a predictor of prognosis.

W67-5

Study of the risk factor of steroid-induced osteonecrosis for patients with systemic lupus erythematosus and idiopathic inflammatory muscle disease

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Conflict of interest: None

[Objective] We define the risk factors of steroid-induced osteonecrosis for patients with systemic lupus erythematosus (SLE) and idiopathic inflammatory muscle disease (IIM). [Methods] SLE and IIM patients who received steroid pulse therapy or prednisolone ≧50 mg (or 1 mg/kg)/day from October 2010 to September 2020 were retrospectively evaluated. [Results] Osteonecrosis developed in 9 of 42 SLE patients. The total observation period was 126.9 years, thus, 7.09/100 person-years. The osteonecrosis group had higher triglycerides (p=0.01) and lower HDL cholesterol (p=0.04) at the onset of the disease. Smoking tended to be higher (p=0.06). Comparing cumulative steroid doses since the start of treatment, there was a significant increase at 90 (p=0.02), 180 (p=0.04), and 360 (p=0.04) days. The cumulative amount per body weight at the onset was significantly higher at 30 days (p=0.04). Osteonecrosis developed in 9 of 39 IIM patients. The total observation period of 114.6 years, 7.86/100 person-years. There was a higher risk of smoking (p=0.04) and dyslipidemia (p=0.07). [Conclusion] Smoking and dyslipidemia may be a risk for the development of osteonecrosis, and high cumulative steroid doses early in the treatment of SLE are also a risk for the development of osteonecrosis.

W67-6

Examination of nutritional status of patients with rheumatoid arthritis in NinJa 2019

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Conflict of interest: Yes

[Objective] To examine the nutritional status of patients with rheumatoid arthritis using the clinical nutrition index CONUT (Controlling Nutrition Status). [Methods] 5277 patients were included. The CONUT score is a nutritional index that scores the serum albumin level, serum total cholesterol level, and total lymphocyte count. Malnutrition levels are classified into normal (0-1) and mild (2-4), moderate (5-8), and severe (8-12) requiring nutritional intervention. The average age of the target patients was 66.8 ± 12.9 years. [Results] The average CONUT score was 1.5 ± 1.4. By age group, it was 1.6 ± 1.5 for 65 years or older (3354 cases) and 1.3 ± 1.2 for under 65 years (1923 cases), which were significantly higher in the 65 years or older group ($p < 0.001$). Malnutrition levels were normal in 56.24%. Mild 40.88%, moderate 2.69% and severe 0.02% requiring nutritional intervention totaled 43.76%. Furthermore, the average CONUT score of the hospitalized group (124 cases) due to infectious disease (pneumonia) was 2.33 ± 2.16, and that of the non-hospitalized group due to infectious disease (5153 cases) was 1.46 ± 1.36, showing a significant difference between the two groups ($p < 0.001$). [Conclusions] Active nutritional intervention is required for patients with rheumatoid arthritis.

W68-1

Usefulness of serum KL-6 and SP-D as therapeutic response predictors in acute exacerbation of connective tissue disease-associated interstitial lung disease

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Conflict of interest: None

[Objective] Connective tissue disease-associated interstitial lung disease (CTD-ILD) has a better response to immunosuppressants than idiopathic pulmonary fibrosis, but there is no standard therapy for acute exacerbation of CTD-ILD. We investigated the associations of serum KL-6 and SP-D with treatment response. [methods] We analyzed the relations of serum KL-6 and SP-D levels, and the rate of increase in KL-6 during 2-4-week period after treatment with the therapeutic response in 75 cases admitted to our department from 2005 to 2020. [results] 51 (17 males) and 24 (12 males) cases showed a good and poor response. The rate of KL-6 increase was significantly higher in the poor than good group ($p<0.001$). In 60 cases undergoing steroid pulse therapy, KL-6 increase rate was significantly lower in the responsive group than non-responsive intravenous bolus cyclophosphamide therapy (IVCY) and the non-IVCY cases ($p=0.046$, $p=0.006$). Serum SP-D was significantly lower among the IVCY than non-IVCY responsive cases ($p=0.01$). [conclusions] In case with little increase in serum SP-D, IVCY can be considered in combination with steroid pulse therapy at an early stage. Even if the serum SP-D level is high, additional treatment should be considered when serum KL-6 continues to increase at 2-4-weeks.

W68-2

Progressive fibrosing interstitial lung disease in connective tissue disease: a single-center, retrospective study

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Conflict of interest: Yes

[Objective] A retrospective, observational, single-center study was conducted to examine the clinical characteristics of progressive fibrosing interstitial lung disease (PF-ILD) in connective tissue diseases related-interstitial lung disease (CTD-ILD) and interstitial pneumonia with autoimmune features (IPAF). [Method] Thirty-four CTD-ILD or IPAF patients, who have been followed for more than 2 years, were enrolled. [Results] Of the 34 patients, 16 patients (47%) developed PF-ILD during the clinical course: the mean age of the patients was 58.3 years and 11 (68.8%) were female. Four of the patients had rheumatoid arthritis, 3 had systemic sclerosis, 3 had myositis, 3 had IPAF, and 3 had other CTDs. All of the patients with PF-ILD showed an increased extent of fibrosis on chest computed tomography scan, and 4 (22.2%) of the patients received nintedanib. PF-ILD patients had higher KL-6 (1769 vs 923 U / ml) and SP-D (220 vs 137 ng / ml) and lower %DLco (55 vs 86%) compared to the non-PF-ILD patients. [Conclusions] Half of the patients with CTD-ILD or IPAF develop PF-ILD and have higher disease activity even at their initial visit. (Nintedanib treatment may improve health outcome and survival in PF-ILD patients.)

W68-3

Risk factors of adverse events from sulfamethoxazole-trimethoprim for prophylaxis of pneumocystis pneumonia in patients with systemic rheumatic diseases

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Conflict of interest: None

[Objective] To elucidate risk factors of adverse events (AEs) from sulfamethoxazole-trimethoprim (SMX/TMP) for prophylaxis of pneumocystis pneumonia (PCP) in patients with systemic rheumatic diseases. [Methods] We reviewed patients with systemic rheumatic diseases admitted to our hospital for induction therapy from 2012 to 2019. Patients who newly started SMX/TMP for PCP prophylaxis were divided into two groups according to the presence or absence of discontinuation of SMX/TMP due to AEs. We evaluated clinical characteristics and conducted multivariate analysis to identify the risk factors of AEs. [Results] We included 316 patients and AEs were detected in 56 (17.8%). Baseline age (60.0±17.7 vs 54.8±17.1, $p=0.039$) and the rate of presence of past history of malignancy ($p=0.04$) were significantly higher in AEs positive group. There were significantly higher rates of AEs in patients with adult still disease (ASD) than those without (70.6%, $p<0.001$). Multivariate analysis revealed older age (OR 1.03, $p=0.012$), presence of ASD (OR 19.5, $p<0.001$), low platelet counts (OR 0.995, $p<0.01$) were selected as independent factor associating with AEs expression. [Conclusions] We need careful attention to AEs of SMX/TMP in patients with elderly, ASD and low platelet counts at baseline.

W68-4

Examination of the relationship between myeloperoxidase-antineutrophil cytoplasmic antibody and interstitial pneumonia in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the relationship between myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) and interstitial pneumonia (IP) in rheumatoid arthritis (RA) patients. [Methods] Medical records and chest high-resolution computed tomography (HRCT) were used to compare 22 MPO-ANCA-positive patients (P group) and 44 MPO-ANCA-negative patients (N group) (controls). [Results] Mean age was 71.1 years; 32% were men and 68% were women. There were no significant differences in smoking, DAS28 score, stage, class, anti-CCP antibody positivity, antinuclear antibody positivity, and prednisolone usage and dose. Rheumatoid factor positivity (95.5% vs 63.6%), IP complication rate (81.8% vs 31.8%), and rate of high KL-6 levels (72.7% vs 22.7%) were significantly higher in the P group versus the N group, respectively. Methotrexate usage was significantly lower in the P group (13.6% vs 75.0%, respectively). The HRCT findings showed that the P group had more non-usual interstitial pneumonia (UIP) patterns (77.8%), while the N group had more UIP patterns (50.0%). In the P group, IP exacerbation and death due to acute IP exacerbation were observed in six (27.2%) and three (13.6%) patients, respectively. [Conclusions] IP may influence prognosis in MPO-ANCA-positive RA patients.

W68-5

Study of patients with connective tissue disease-related pulmonary hypertenstion (CTD-PH)

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Conflict of interest: None

[Objective] Prognosis of CTD-PH is generally poor. Scleroderma-related PH (SSc-PH) tends to have a worse prognosis compared to other diseases, with a 5-year survival rate of about 30%. We conducted a multifaceted comparative study of SSc-PH and nonSSc-PH cases of CTD-PH. [Methods] We conducted a retrospective analysis of patients with CTD-PH at our hospital between 2008 and 2020; the diagnosis and classification of PH was based on the Nice Classificaton 2013 adopted at the 5th World Symposium on Pulmonary Hypertentsion. [Results] 22 patients were extracted; 11 were SSc-PH and 11 were nonSSc-PH. There were 8 and 3 deaths in SSc-PH and nonSSc-PH, retrospectively ($p=0.0861$); mean age at diagnosis of primary disease was 65±61.5 and 29±24.5 years ($p=0.00497$); mean age at onset of PH was 71±64.5 and 39±34.5 years ($p=0.000309$); predictive value of DLCO was 42.0±35.2% and 64.4±54.9% ($p=0.0848$); Cariac Index was 2.55±1.77 L/min/m^2 and 3.41±2.70 L/min/m^2 ($p=0.0418$). [Conclusions] SSc-PH had an older age of onest and lower cardiac output than nonSSc-PH. Although the difference was not statistically significant, the mean pulmonary diffusing capacity of SSc-PH was

lower then that of nonSSc-PH.

W68-6

Predictors of deep vein thrombosis in hospitalized patients with collagen vascular diseases

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Conflict of interest: None

Objective: Collagen vascular diseases (CVD) are one of the risk factors involved in the development of deep vein thrombosis (DVT). However, risk assessment of developing DVT in an inpatient setting with CVD has not been reported previously. With the aid of the Wells score, we investigated the predictors and factors responsible for the development of DVT in hospitalized patients with CVD. Methods: This study enrolled patients with CVD who were admitted to our hospital from January 2018 to June 2020. We screened the patients who were newly diagnosed, and collected the data retrospectively. Results: A total of 71 patients were analyzed. Eleven (15.5%) developed DVT. Among the 11, 4 had microscopic polyangiitis, 3 had eosinophilic granulomatosis with polyangiitis, 1 had systemic lupus erythematosus, 1 had Sjogren's syndrome, 1 had RA, and 1 had polymyositis. The average Wells score of CVD patients with and without DVT were 0.91 and 0.10, respectively. CVD patients with DVT showed significantly higher Wells score on admission than those without DVT. However, age, D-dimer levels, and the initial dose of steroid between the two groups were not significantly different. Discussion: The Wells score on admission is a useful measure for assessing the risk of developing DVT in patients with CVD.

W69-1

Usefulness of anti-GPL core IgA antibody among rheumatoid arthritis patients

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA) patients, it is difficult to differentiate between bronchiolitis due to RA and non-tuberculous mycobacterium pulmonary disease (NTM-PD) on chest CT. The objective of this study is to examine the usefulness of anti-glycopeptidolipid (GPL) core IgA antibody for the diagnosis of NTM-PD. [Methods] RA patients with measurement of anti-GPL core IgA antibody during 2017-2020 and with chest CT reports by radiologists were included in this study. If the reports said suspicion of bronchiolitis due to RA or NTM-PD, these patients were classified as "suspicion of NTM-PD" [Results] Among 327 RA patients (female 260, median age 70 years old), 103 patients were reported to have "suspicion of NTM-PD". NTM-PD was diagnosed in 34 patients, whereas 9 were classified as contamination of NTM. Anti-GPL core IgA antibody showed a sensitivity of 59%, a specificity of 83%, a positive predictive value of 63%, and a negative predictive value of 80% for NTM-PD diagnosis. There was no significant difference in anti-GPL core IgA antibody titers between patients of true positive (n=20) and false positive (n=12) (median titer 3.59 vs 1.51 U/mL, p=0.17). [Conclusions] Anti-GPL core IgA antibody showed a high specificity but had a low sensitivity.

W69-2

Long-term observation treated biologics in 10 rheumatoid arthritis patient complicated with pulmonary MAC disease

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Conflict of interest: None

To estimate long-term safety and efficacy of biologics for rheumatoid arthritis (RA) complicated with pulmonary MAC disease. We assessed 10 RA patients by sequential chest CT (medium follow-up: 92 months). After 75 months diagnosed with MAC disease, 7 patients were administered anti-MAC therapy (CAM, RFP, EB) and 3 patients developed cystic bronchiectasis. Medium RA duration was 14.5 years and RA disease activity was high at DAS-CRP of 4.7. Four patients were prior administered for anti-MAC drugs before startong biologics, thereafter confirmed efficacy of MAC therapy and then started biologics. Other 6 patients were diagnosed with MAC disease after 47 months starting biologics. Biologics was once discontinued, then anti-MAC therapy started and resolved pulmonary MAC was determined and then re-started biologics. All patients were sustained less than low disease activity. Seven patients were required hospitalization due to bacterial or organizing pneumonia. The medium age of recent observation was 75 years-old, and 2 of 10 died due to pneumonia other than MAC infection. Biologic could be safely used during long-term observation. Biologics and anti-MAC drugs should be used, before avoiding multiple cystic change by destructive lung structure, which induced MAC infection.

W69-3

Is it the same the bacteremia in SLE patients as general population?

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Conflict of interest: None

[Objective] We evaluated that the characteristics and prognostic factor for bacteremia patients with systemic erythematosus (SLE). [Methods] The database was built from the results of our ordered blood culture tests from 2009 to 2020. During the 2799 sets of blood culture tests, 388 sets were positive results, of which 75 were SLE cases. [Results] Of the 75 cases, 59 survived and 16 died. Thirty-five cases were diagnosed that hospital-acquired infection. The infection routes were following; 19 cases of urinary tract, 18 of skin and musculoskeletal, 14 of abdominal, 12 of catheter infection, 5 of respiratory tract, 2 of blood stream infection of unknown cause, 2 of meningitis, and 2 of postoperative infection. The results of gram's staining were following; 30 cases of Gram-positive cocci, 2 of Gram-positive rod, 1 of Gram-negative cocci, 38 of Gram-negative rod, and 4 of fungal infection. The comparison between survival group and dead group showed statistically different in age (median: 53 vs 69), Glasgow coma scale (15 vs 12), and SOFA score (2 vs 4). [Conclusions] We evaluated the SOFA score and GCS were useful prognostic factor for survival rate in bacteremia patients with SLE, such as the general population.

W69-4

Study of the clinical features of 79 new cases of tuberculosis (TB) in patients with rheumatoid arthritis (RA) registered in the NinJa for 17 years

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Conflict of interest: None

[Objective] To evaluate the characteristics of the newly developed tuberculosis (TB) in the registered patients in ***NinJa*** cohort study for rheumatoid arthritis (RA). [Patients and Methods] We calculated the standardized incidence ratio (SIR) of TB from the clinical data on National Database of Rheumatic Disease by iR-net in Japan (***NinJa***) prospectively from 55 facilities for 17 years. [Results] Among 171,318 patients registered from 2003 to 2019, 79 patients developed TB and the SIR of TB was 1.80 (95%CI: 1.40-2.20). 14 patients (17.7%) were treated with biologic agents, and 25 patients (31.6%) were treated with MTX. The mean age of them was 71.3 years old and the mean duration of RA before the onset of TB was 10.0 years. Extrapulmonary TB is high in 16 cases (20.3%), and is high in Bio and MTX-administered cases, and extrapulmonary TB is on the rise. [Conclusions] As in our previous reports, the prevalence of TB in RA patients was on a downward trend. By this study, in elderly, in patients

with RA of long-term morbidity is the high risk of the newly developed TB. Attention should be paid to the increase in extrapulmonary TB, which is often difficult to diagnose.

W69-5

Clinical features of 16 patients with rheumatic disease complicated by pulmonary aspergillosis

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Conflict of interest: None

[Background] In rheumatic diseases, fungal infections are often life-threatening due to the administration of immunosuppressive drugs in the presence of pre-existing lung diseases. In particular, invasive pulmonary aspergillosis (IPA) and chronic progressive pulmonary aspergillosis (CPPA) are often difficult to treat with antifungal drugs. [Method] We retrospectively reviewed data from all the 16 patients with rheumatic disease, diagnosed as IPA or CPPA, and treated at our hospital between January 2010 and April 2020. [Results] The mean patient age was 74 years. Those who died tended to have received a higher dosage of steroids at the time of antifungal drug administration (30.9 mg vs 17.6 mg; $p<0.05$). When the levels of serum albumin, IgG, white blood cell count, neutrophil count, and CRP level before the initiation of antifungal drug were examined, only the albumin levels were significantly lower in the dead cases than in living cases (2.33 mg/dl vs 3.05 mg/dl; $p<0.005$). [Conclusion] Pulmonary aspergillosis with rheumatic disease was often associated with pre-existing lung disease. There was also a tendency for the prognosis to be poorer when the current disease was active and immunosuppressive treatment was intensified, or when serum albumin level was lower at the time of onset.

W69-6

Two cases of non-tuberculous mycobacterial tenosynovitis treated successfully without surgical operations

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Conflict of interest: None

[Background] Non-tuberculous mycobacterial tenosynovitis may mimic rheumatic diseases. We present 2 cases of non-tuberculous mycobacterial tenosynovitis which were successfully treated without surgical operations. [Case 1] A 69-year-old man presented with swelling on the palmar side of the right hand after a minor trauma without systemic illness. T-SPOT was negative, but the MAC-specific glycopeptidolipid (GPL) core antibody was positive. Based on a synovial biopsy, mycobacterial cultures revealed *Mycobacterium intracellulare* (*M. intracellulare*). He was treated with Clarithromycin (CAM), Ethambutol (EB), and Rifampicin (REP) during 2 years, resulting full recovery. [Case 2] A 48-year-old woman developed swelling of the palmar side of the left hand without a history of trauma. She was diagnosed as rheumatoid arthritis and dermatomyositis for which she received corticosteroids, immunosuppressants and biologics for six years. T-SPOT and the MAC-specific GPL core antibody were negative. A synobial biopsy and culture was performed which yielded *M. intracellulare*. Antimycobacterial treatment consisting of CAM, EB and REP was performed for 2 years with no recurrence. [Conclusions] Rheumatologists should be aware of mycobacterial infection for the differential diagnosis of tenosynovitis.

W70-1

A retrospective study of 11 patients with systemic autoimmune disease receiving novel adjuvanted subunit herpes zoster vaccine

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Conflict of interest: None

[Objective] To evaluate the clinical characteristics of patients with systemic autoimmune disease who received HZ/su. [Methods] We retrospectively analyzed the clinical characteristics of 11 patients who had received HZ/su in Oita Red Cross Hospital. [Results] The 11 patients comprised 10 with RA (2 males, 8 females) and one with SLE (female). The mean age at the time of the initial vaccination was 71.5 ± 9.5 years. Eight patients had an eGFR <60 mL/min/1.73 m^2, with one patient having an eGFR as low as 16 mL/min/1.73 m^2. With respect to medical therapy, prednisolone was used in 7 patients, with a mean use of 4.7 mg/day. JAK inhibitors were used in 8 patients. No cases of post-vaccination herpes zoster or worsening of the present disease were observed. Adverse events were observed in 5 patients (injection site pain in 2, fever in 3, nausea in 2, and fatigue in 2). All adverse events disappeared within 72 h after vaccination. In 2 patients with RA, anti-varicella zoster virus IgG antibodies were measured before and after vaccination, and in both cases antibody titers were increased. [Conclusion] Eight of the 11 patients were on JAK inhibitors. Eight patients had renal dysfunction; however, no serious adverse effects were observed. The efficacy of the drug will be evaluated over time.

W70-2

The Usefulness of Cytomegalovirus Infection Management Strategy in Patients with Connective Tissue Disease, Based on the 2011 Guideline of the Japan Society for Hematopoietic Cell Transplantation

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Conflict of interest: None

[Objective] Cytomegalovirus (CMV) infection is a life-threatening complication in immunocompromised patients. However, to date, there are no guidelines for CMV infection management in patients with connective tissue disease (CTD). We evaluated the efficacy and safety of the management of CMV infection in CTD patients according to the 2011 guideline of the Japan Society for Hematopoietic Cell Transplantation (JSHCT). [Methods] We retrospectively investigated 184 CTD patients admitted to our hospital and treated with ≧20 mg/day of prednisolone. CMV infection was managed based on the 2011 JSHCT. The primary endpoint was mortality due to CMV infection. We also investigated the risk factors related to CMV reactivation and infection. [Results] CMV reactivation was observed in 89 cases and CMV infection was in 51 cases. Thrombocytopenia was the most common finding of CMV disease. Infected patients tended to be males, had concurrent infections and an earlier antigenemia. No patients died due to CMV disease. No serious organ involvement occurred, except for a case with rectal ulcer. Male, early antigenemia, and steroid pulse therapy were identified as risk factors. [Conclusions] This study demonstrated the usefulness of CMV infection management in CTD patients according to the 2011 JSHCT.

W70-3

Risk factors for cytomegalovirus (CMV) reactivation in patients with connective-tissue disease (CTD), single-center prospective cohort study

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Conflict of interest: None

[Objective] To investigate risk factors relevant with CMV reactivation in patients with CTD. [Methods] Consecutive CTD cases who started immunosuppressive therapy for CTD from February 2017 until February 2019 were enrolled. CMV pp65 antigen was monitored weekly, and the risk factors for CMV reactivation were statistically analyzed. [Results] 157 cases were enrolled; the mean age was 60.8 years old, and female was 71%. The underlying CTDs were vasculitides 48, SLE 27, PM/DM 25, RA

14, and others 43. The mean initial PSL dose was 48.3 mg/day, and mPSL pulse therapy was conducted in 44 (28%). Immunosuppressive therapies were IVCY 55, CNI 27, MMF 16, MTX 4, and biological agents 21 including RTX. No CMV reactivation occurred in 21 CMV-IgG negative cases. Among 136 CMV-IgG positive cases, CMV reactivated in 52 cases (38%) with CMV infection in 5 cases (hepatitis 3, retinitis 1, and hematopoietic injury 1). Multiple regression analysis revealed that history of malignancy, CMV-IgM positivity, HbA1c >6.35%, PSL >0.91 mg/kg/day, and IVCY were relevant risk factor for CMV reactivation in CTD patient with positive CMV-IgG. [Conclusions] No CMV reactivation occurred in CMV-IgG negative cases. The risk factors for CMV reactivation in CMV-IgG positive CTD cases were prospectively detected.

W70-4

Pneumocystis pneumonia (PCP), an autoimmune disease, in our hospital. The importance of sputum Pneumocystis PCR and the need for adequate TMX-SMP prophylaxis

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Conflict of interest: None

[Objective] Pneumocystis pneumonia (PCP) is important in autoimmune diseases such as RA and vasculitis. However, diagnosis is difficult and non-HIV PCP has a poor prognosis, and prevention is also important. [Methods] We studied the diagnosis and prophylaxis of 48 cases of PCP secondary to autoimmune diseases diagnosed at our hospital between 2010 to 2020. [Results] Pneumocystis PCR was used in 29 cases and βD-glucan in 20 cases. 19 cases were diagnosed by PCR of sputum and 10 cases by PCR of bronchoscopic alveolar lavage fluid (BALF). There were 4 cases of both sputum and BALF, 3 cases both positive, 1 case was sputum (-) and BALF (+). There were 10 deaths due to PCP, 6 cases were sputum PCR-positive, 4 cases were not examined by Pneumocystis PCR. All patients diagnosed BALF survived. There were 10 cases of Glocott staining, and only one BALF was positive. Only three cases of prophylaxis with TMP/SMX within one month, all of which were small doses of 80-240 mg/w trimethoprim equivalent. [Conclusions] Pneumocystis PCR measurement of sputum plays a significant role in the diagnosis and prognosis of PCP and important in determining treatment strategy. In addition, prophylaxis with TMP/SMX should be administered in sufficient doses for high-risk cases.

W70-5

The screening test for latent tuberculosis infection in human T-cell leukemia virus type 1-positive patients with rheumatoid arthritis: a retrospective case-control observational study

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Conflict of interest: None

[Objective] The present study aimed to evaluate the use of the T-SPOT. TB assay in human T-cell leukemia virus type 1 (HTLV-1)-positive rheumatoid arthritis (RA) patients. [Methods] Twenty-nine HTLV-1-positive RA patients and 87 age- and sex-matched HTLV-1-negative RA patients (controls) were enrolled from the HTLV-1 RA Miyazaki Registry. The clinical characteristics at performing T-SPOT. TB assay were compared between the groups. Results of the T-SPOT. TB assay for latent tuberculosis infection (LTBI) screening were collected from medical records of patients. The values of HTLV-1 provirus load (PVL) were analyzed based on T-SPOT. TB assay results. [Results] There were no differences in the clinical characteristics of between the groups. Approximately 55% of the HTLV-1-positive RA patients showed invalid T-SPOT. TB assay results (odds ratio: 108, $p < 0.0001$) owing to a spot count of >10 in the negative control panels. HTLV-1 proviral load values were significantly higher in patients with invalid results compared with those without invalid results ($p = 0.003$). [Conclusions] HTLV-1 infection affects T-SPOT. TB assay results in RA patients. Assay results in HTLV-1 endemic regions should be interpreted with caution when screening for LTBI before initiation of biologic therapy.

W70-6

Examination of efficacy and safety of small doses of ST mixture in rheumatism clinic

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Conflict of interest: None

[Objective] Investigate whether a small amount of ST mixture, one tablet twice a week, can prevent the onset of PCP and reduce the side effects of the ST combination. [Methods] Collagen disease patients (N = 355 patients) who had been prescribed ST mixture as of September 2017 were extracted. One ST mixture was divided into a daily normal prevention group (N = 48 people) and one ST mixture 1 tablet 2 days a week in a small dose army (N = 307 people). After that, in the three years until September 2020, the presence or absence of PCP onset in both groups and the frequency of side effects associated with ST mixture were compared. [Results] There was no onset of PCP in either the normal preventive dose group or the low dose group of the ST mixture. However, the side effects associated with the ST mixture were 35.4% in the normal preventive dose group (4 patients with elevated liver enzymes, 3 patients with elevated eosinophils, 6 patients with rash, 4 patients with cytopenia), and 0.9% in the low-dose group (rash). There was a big difference with 3 people). [Conclusions] It was suggested that a small amount of 1 tablet of ST mixture twice a week could be expected to have a sufficient preventive effect on PCP and reduce drug side effects.

W71-1

The risk factor of SARS-CoV2 transmission in patients with rheumatic diseases; analysis of a COVID-19 hospital outbreak

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Conflict of interest: None

[Objective] To investigate the risk factors of SARS-CoV-2 transmission in patients with rheumatic diseases. [Methods] In the hospital outbreak of COVID-19, 39 patients with rheumatic diseases were hospitalized. SARS-CoV2 infection was tested by RT-PCR and serologic test. We investigated patient characteristics, including age, sex, types of diseases, disease severity, treatment, and contact days of health care workers (HCWs) who were confirmed SARS-CoV2 infection later. [Results] In hospitalized patients with rheumatic disease, 10 were antibody-positive (1 was PCR-negative) and 29 were antibody-negative. Among the infected patients, days of contact with HCWs were 13.6±6.9. All patients were treated with corticosteroid (19.1±20.1 mg/day). Among the non-infected patients, days of contact with infected HCWs were 6.1±6.9. 75.9% of patients were treated with corticosteroid (13.7±12.4 mg/day). No significant differences were observed in types of disease, disease severity, and non-steroidal immunosuppressive treatments. [Conclusions] The risk of SARS-CoV2 infection was higher in patients with rhematic diseases who were frequently contacted with infected HCWs. Prevention of contact with asymptomatic and pre-symptomatic SARS-CoV2 infected HCWs was important in all patients with rheumatic disease.

W71-2

Status of infectious complications in outpatients with autoimmune diseases at our hospital in 2019 and 2020, before and after the COVID-19 pandemic

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Conflict of interest: None

[Objective] To examine whether lifestyle changes after the COVID-19 pandemic have any effect on preventing infectious complications in outpatients with autoimmune diseases. [Methods] A retrospective, record linked cohort study among patients who regularly visited our outpatient clinic for rheumatism in 2019 and in 2020 was conducted. In addition, a questionnaire about changes in lifestyle was administered. [Results] Of the 1331 outpatients who visited our hospital in 2019 (mean age 64.1 years old), 63.3% were patients with rheumatoid arthritis, 28.1% had coexisting respiratory disease, 40.8% were treated with prednisolone. A total of 615 infectious complications were reported in 2019. The main ones were 264 common cold, 41 pneumonia, 28 influenza, and 27 herpes zoster. The survey for 2020 is currently being undertaken. To our questionnaire, 1175 out of 1177 patients have responded. The findings have shown that 20% of the patients wore masks before the COVID-19 pandemic, and 75% became more careful about wearing masks after the pandemic. Similarly, 13% of patients disinfected their hands on a daily basis before the pandemic, and 81% began doing so after the pandemic. [Conclusions] Patients are becoming more aware of preventing infection. Its outcome is presently under investigation.

W71-3

RA disease activity during the COIVD-19 pandemic

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Conflict of interest: None

[Objective] During the COVID-19 pandemic, there was a general tendency to refrain from visiting medical institutions. The number of patients introduced to our department from regional medical institutions decreased by 25% year-on-year, and the number of referral patients in their 80s decreased significantly from the previous year to 26%. Even in RA patients in our hospital, there were noticeable cases of suspension or postponement of visits after the state of emergency declared in April. Here we examined the possibility that the tendency to shy away from visiting RA patients due to the COVID-19 pandemic may have affected disease activity. [Methods] We evaluated the CDAI in 356 RA patients who visited our hospital in December 2019, 286 patients who visited our department in April 2020 when the state of emergency was declared, 324 patients who visited in June 2020 after the declaration was lifted, and 346 patients who visited in June 2019, the same month a year ago. Each group difference was tested by the Tukey-Kramer method. [Results] There was no significant difference between the groups. [Conclusions] During the COVID-19 pandemic, RA patients also tended to refrain from visiting the hospital, but there was no significant effect on RA activity.

W71-4

Practical treatment of rheumatic disease at COVID-19 base hospital

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Conflict of interest: None

[Objective] Hyogo Prefectural Kakogawa Medical Center is the base hospital of COVID-19 and there are 3100 patients in rheumatology center. We investigated how the spread of COVID-19 infection affects actual medical care. [Methods] We surveyed the number of outpatients and prescription faxes using telephone re-examination for patients who visited our hospital from January to September 2019. We also investigated patients who were hospitalized for COVID-19 pseudo-symptoms and patients who were receiving infusions of bDMARDs. [Results] The number of outpatients decreased the most from April to May during the state of emergency, and did not decrease again from July to August, when the number of COVID-19 patients actually peaked. The number of prescription faxes was similar. Regarding COVID-19 pseudo-symptom hospitalization, 9 out of 17 patients had infections, 7 had symptoms due to the underlying disease. In patients with bDMARDs, due to anxiety about COVID-19, 9 had postponed the infusion, and 6 out of 9 had relapsed arthritis. [Conclusions] From July to August, patients tended to become accustomed to COVID-19. We were asked for a proper explanation. The symptoms of RA and collagen disease are similar to those of COVID-19, and it is important to promptly identify the pseudo-symptoms.

W71-5

Impact of the COVID-19 epidemic on consultation behavior in RA patients using biologics

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Conflict of interest: None

[Purpose] The epidemic of COVID-19 had a great impact on rheumatoid arthritis (RA) treatment. The purpose of this study was to investigate the outpatient treatment status of RA patients using biologics (BIO) under the COVID-19 epidemic. [Methods] The subjects were BIO-using RA patients at the outpatient from March 31 to 1 month when COVID-19-positive persons were confirmed in Yamagata. [Results] 61 cases had an average age of 66.2 years and an average RA morbidity of 17.3 years. Of the 28 cases who requested face-to-face consultation, 13 cases received self-injection, and 12 cases received outpatient infusion and JAK inhibitors were used in 2 cases. Of the 33 cases who requested a telephone examination, 30 cases were self-injecting, and 2 cases wished to postpone the outpatient infusion date. JAK inhibitor use was in 1 case. The average prescription was 8.7 weeks. In one case of postponement of outpatient infusion, exacerbation of the disease was observed. [Conclusion] Although regular medical examinations and blood biochemical tests are required while using BIO. Although no major complications were found in this survey, it was necessary to decide whether or not to perform a telephone consultation in view of the COVID-19 epidemic and the risk of postponement of consultation.

W71-6

A case of dermatomyositis interstitial pneumonia complicated by COVID-19

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Conflict of interest: None

[Case] A 76-year-old woman was admitted to our department 8 years ago for interstitial pneumonia complicated by dermatomyositis. She was treated with PSL 7 mg and CsA 75 mg. 16 days ago, she developed malaise, and 14 days ago, she was found to be strongly positive for SARS-CoV-2-PCR >10×10ˆ6 copies. She was treated with favipiravir and dexamethasone 6.6 mg, but her respiratory condition deteriorated and she was transferred to our hospital. At the time of transfer, SARS-CoV-2-PCR 6×10ˆ6 copies and the chest HRCT showed GGO and consolidation in all lung fields, with P/F ratio 120 and severe respiratory failure, and the patient was ventilated on the same day. Remdesivir, dexamethasone 6.6 mg, heparin started, CsA 150 mg resumed, and the P/F ratio improved to 200 on the third day, and the patient is still under treatment. [Clinical significance] There have been few reports of COVID-19 complicating CTD in Japan, and IP with DM has similar imaging findings to COVID-19, making it difficult to differentiate between the two diseases. We report the clinical course of the disease as well.

W72-1

Clinical features and analysis of MEFV gene in 32 patients with Familial Mediterranean Fever (FMF)

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Conflict of interest: None

[Objective] We have analyzed 32 patients (23 female/9 male) with FMF to clarify the association between clinical features and mutation of *MEFV.* [Methods] Mutated MEFV, clinical features and laboratory data have been explored. Results] Clinical symptoms such as periodic fever, abdominal pain, headache, arthralgia, chest pain, cervical lymph nodes swelling and myalgia were 32/32, 9/32, 6/32, 6/32, 6/32, 2/32 and 1/32, respectively. Patients with typical compound heterozygous mutations of MEFV (E148Q /M694I in exon 10) were 5 cases. Patients with atypical mutations, except for mutations in exon 10, such as exon 1 (E84K, L110P), 2 (E148Q), 3 (G304R, P369S, R408Q), 5 (S503C) and 9 (I591M) were 8 cases. Patients with no mutations were 12 cases. E148Q mutation have at least abdominal pain (4/5: 80%). There were no significant differences of clinical symptoms and laboratory examinations between 3 groups. Five patients who received canakinumab treatment and 1 patient who received etanercept because of severe diarrhea, alopecia and liver dysfunction were observed. One patient had successfully pregnancy and delivery during canakinumab treatment. [Conclusion] Abdominal pain was associated with E148Q mutatio, and biological treatments in colchicine-intolerable patients with FMF might be necessary.

W72-2

New and rapid functional assay for the pathogenicity classification of MEFV variants

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Conflict of interest: None

[Objective] Pyrin-associated autoinflammatory diseases (PAADs) including Familial Mediterranean fever (FMF) and pyrin-associated autoinflammation with neutrophilic dermatosis (PAAND) is autoinflammatory diseases caused by pathogenic *MEFV* variants. Although genetic analysis is an important tool for diagnosing PAADs, many of *MEFV* variants remain to be 'variants of unknown significance (VUS)' due to the lack of reliable functional assay. Thus, in this study, we aimed to establish a rapid in vitro functional assay for evaluating the pathogenicity of *MEFV* variants. [Methods] Thirty-three *MEFV* variants were transfected in the cell lines and the response to various pyrin agonists of each variant was assessed. [Results] Disease-associated *MEFV* variants showed hyper-responsiveness to pyrin agonists compared to the wild type. The pathogenicity of each MEFV variant was evaluated and classified based on this reactivity. [Conclusions] The novel functional test enabled us to rapidly assess the pathogenicity of *MEFV* variants, and this assay may contribute to the prompt and accurate diagnosis of PAADs by predicting the impact of *MEFV* mutations on the pathogenesis of the disease in patients.

W72-3

Cold-inducible RNA-binding protein (CIRP) and autoinflammatory disease: new inflammatory biomarker in adult Still's disease

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Conflict of interest: None

[Objective] Cold-inducible RNA-binding protein (CIRP) belongs to a family of cold-shock proteins which is upregulated in various stress condition. Recently, CIRP has been identified as danger-associated proteins (DAMPs). Adult Still's disease (ASD) is a systemic autoinflammatory disease, in which DAMPs-mediated inflammasome activation seems to be involved in the disease pathogenesis. The aim of this study is to clarify the role of CIRP in ASD. [Methods] 43 ASD patients were included. Serum levels of CIRP was measured by ELISA. CD14-positive monocytes were isolated by magnetic cell sorting system and CIRP expression was confirmed by western blotting. [Results] In ASD patients, serum CIRP levels was significantly higher compared with healthy controls and rheumatoid arthritis patients. Serum CIRP wes significantly correlated with serum levels of ferritin (r=0.47, p=0.002), IL-18 (r=0.32, p=0.03) and disease activity score (Pouchot's score) (r=0.45, p=0.0025). However, the serum CIRP levels was not significantly different among 3 disease phenotypes. The expression of CIRP in monocyte was promoted. [Conclusions] We identified CIRP as a novel biomarker reflecting the activity of ASD. These results suggest that CIRP may play a significant role in the pathophysiology of ASD

W72-4

The report of patients with novel autoinflammatory disease VEXAS and relapsing polychondritis with UBA1 mutation

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Conflict of interest: None

[Objective] Recently, it is proposed a novel adult-onset autoinflammatory disease VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, characterized by relapsing polychondritis (RP), myelodysplastic syndrome (MDS). In this study, we conducted genetic screening of *UBA1* somatic mutations for patients clinically diagnosed with RP. [Methods] Patients with RP who met the Damiani criteria at Yokohama City University Hospital and Yokohama Minami Kyousai Hospital between 2010 and 2020 were included. Sanger sequencing was used for screening. Patients' clinical findings were retrospectively evaluated. [Results] Twelve RP patients (10 males, 2 females) (72.3 ± 12.7 years old) were included. Of the 11 cases whose genomic DNA were available, 6 males (54.5%) were positive for *UBA1* mosaicisms at p. Met41. Patients with *UBA1* mutations manifested skin rush, MDS, serositis and characteristic vacuoles in myeloid and erythroid precursor cells from bone marrow aspirates. These findings were consistent with the clinical features of VEXAS syndrome. [Conclusions] In our study, more than half of elderly male patients were found to have *UBA1* p. Met41 mosaic mutations. VEXAS is a novel disease comprising RP, and it is required the accumulation of cases and the elucidation of the treatment.

W72-5

PAB syndrome: a new subtype of PAPA syndrome

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Conflict of interest: None

PAPA syndrome with pyogenic arthritis (PA), pyoderma gangrenosum (PG), and acne as three signs and many similar PAPA syndrome subtypes have been reported. The case was a 22-year-old Japanese man. Arthritis of the knee and ankle joints, PG, acne and *PSTPIP1* gene variant (E101G) were observed, and PAPA syndrome was suspected. During the course, melena appeared and inflammatory bowel disease was complicated. Arthritis was different in age and pathology from PA reported in PAPA syn-

drome. In addition, regarding inflammatory bowel disease, endoscopy and pathological images were different from ulcerative colitis and Crohn's disease, and it was an unclassifiable inflammatory bowel disease. Examination of the *PSTPIP1* gene in a family survey revealed an E101G heterozygous variant in healthy fathers, suggesting that this variant may not be involved in this condition. This case is a new subtype of PAPA syndrome that is different from PAPA, PASH, PAPASH, PASS, PsAPASH, and PAC syndrome, because he did not have any complications of PA, hidradenitis suppurativa, spondyloarthritis, and psoriatic arthritis. We diagnosed him with PG, acne, and unclassified inflammatory bowel disease (PAB) syndrome, which we propose to be a new subtype of PAPA syndrome.

W72-6

Genetic testing with a next-generation sequencer was useful in diagnosing 9 cases of adult-onset autoinflammatory syndrome

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Conflict of interest: None

[Background] We examined the usefulness of genome analysis by the next-generation sequencer (NGS) for diagnosis of adult-onset autoinflammatory syndrome. [Methods] We obtained Informed consent from 9 patients treated with colchicine from 2005 to 2020. Subjects were 52.0 ± 8.8 y.o., M:F = 6:3, 166.4 ± 6.8 cm, BMI 22.8 ± 2.8, treatment history 74.7 ± 66.3 months, maximum colchicine dose 1.2 ± 0.3 mg, PSL 4.9 ± 4.1 mg. Peak CRP showed 6.5 ± 4.8 mg / dl. All cases showed fever of 38 °C higher repeated more than 3 times. Concomitant symptoms showed arthritis in 8 cases, abdominal pain in 3 cases, and no pericarditis, pleuritis or meningitis. Clinical symptoms improved with colchicine administration in all cases. NGS were performed by Kazusa DNA Laboratory. [Results] Mutations of 8/9 cases were found based on the presence of low-frequency variants compared with the internationally used human genome reference. FMF MEFV mutations without exon10 were observed in 6/9 cases (L110P-E148Q and G304R 1 case, R202Q 1 case, P369S-R408Q 1 case, c.1759 + 8C> T 1 case, S503C 1 case, E148Q 1 case). Other Mutations were found at NLRC4, NLRP12, and NOD2 in 2 cases. [Conclusion] Six FMF atypical patients were identified. Genetic diagnosis by NGS is useful and considered for diagnosis.

W73-1

A Japanese family case with cryopyrin-associated periodic syndrome: clinical and treatment characteristics

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Conflict of interest: None

[Background] CAPS is an inherited autoinflammatory disease caused by gain-of-function mutations in *NLRP3* gene, with a genotype-phenotype correlation. The clinical picture for each mutation have been previously reported, but there are few reports on pre- and post-treatment clinical characteristics among generations within families carrying the same mutation. [Patients] A 2-year-old boy (proband), his father and grandmother had several symptoms such as urticarial-like rash, persistently positive inflammatory reaction, and hearing impairment. All 3 patients had a same pathogenic mutation in *NLRP3* gene, a c.1043C>T (p. Thr348Met) heterozygous mutation, and were diagnosed with CAPS. With Canakinumab treatment for proband and his father, their skin rash disappeared and abnormal laboratory data improved. The hearing of the proband showed slight improvement, but not his father. [Clinical Significance] All patients had hearing problem, while fever, skin rash, conjunctivitis, and arthritis were varied among patients. Treatment response to anti-IL-1 therapy varied in relation to the age of initiation of treatment. "Close collaboration between pediatricians and internists" is important to make a prompt diagnosis and provide appropriate treatment for inherited autoinflammatory diseases.

W73-2

Galectin-9 regulates serum amyloid A-induced inflammasome activation in human neutrophils

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Conflict of interest: None

[Objective] The aim of this study is to investigate the effects of Gal-9 on inflammasome activation in neutrophils [Methods] Human neutrophils isolated form healthy subjects were stimulated with serum amyloid A (SAA). The cellular supernatants were analyzed by IL-1β or caspase-1 specific ELISA and immunoblot using anti-IL-1β antibodies. We investigate the role of Gal-9 on SAA-induced inflammasome activation and IL-1b processing by human neutrophils. [Results] SAA stimulation induced the release of cleavage of IL-1b (p17) from neutrophils. ELISA data demonstrated that SAA stimulation also induced cleaved caspase-1 (p20) secretion from human neutrophils, and this release was suppressed by Gal-9 pretreatment. Gal-9 pretreatment diminished the SAA-induced cleaved IL-1b secretion, however, did not affect SAA-induced pro-IL-1b secretion from neutrophils. [Conclusions] Our data showed that SAA promoted the inflammasome-mediated processing and secretion of IL-1b and pretreatment with Gal-9 suppressed these responses in human neutrophils. These findings suggest that Gal-9 functions as a negative regulator of SAA-induced inflammasome activation and may be a potential therapeutic target for the treatment of autoinflammatory disorders.

W73-3

Calcium pyrophosphate crystal deposition may modify or complicate the diagnosis and course of polymyalgia rheumatica: case series

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Conflict of interest: None

Polymyalgia rheumatica (PMR) is known as an inflammatory condition frequently occurs in the elderly, whereas calcium pyrophosphate crystal deposition (CPPD) is also common in the elderly and occasionally develops in similar clinical course named "pseudo-PMR." Case 1: 83 year-old woman referred to as "PMR." US guided aspiration of subdeltoid bursitis confirmed CPP crystal which resulted in the diagnosis of pseudo-PMR. Case 2: 72 year-old man previously diagnosed and treated as PMR was presented as recurrence, there newly showed obvious crystal deposition in conventional radiography. Case 3: 70 year-old woman on the course of treatment for PMR presented with newly occurred arthritis in bilateral sternoclavicular joints, there US confirmed subradiological crystal deposition. Physicians should recognize that CPPD may mimic PMR and complicate the diagnosis and course of PMR.

W73-4

Three cases of calcific tendinitis of the flexor carpi ulnaris tendon diagnosed by ultrasonography in rheumatology outpatients

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Conflict of interest: None

Calcific tendinitis is often unrecognized and poorly managed. In some cases, it is misdiagnosed as one of the complications of rheumatic disease. On the other hands, pisiform attachment of flexor carpi ulnaris tendon is the common site of calcific tendinitis. This report supported usefulness of ultrasonography to detect calcific tendinitis in outpatient examination. Case 1; A 43-year-old-female with a history of dermatomyositis, presented with sudden onset right wrist pain. Ultrasonography showed hyperechoic calcification and increase blood flow signal at the attachment of the flexor

carpi ulnaris tendon to the pisiform bone. Treatment with acetaminophen improved her tendinitis. Case 2; A 78-year-old-female with a history of intestinal Behçet disease, presented with sudden onset left wrist edema. Ultrasonography showed characteristic findings of basic calcium phosphate (BCP) crystals deposits, same as case 1. Having taken celecoxib for 10 days improved her tendinitis. Case 3; A82-year-old-female presented with sudden onset right wrist pain and edema. Only anticentromere antibody was positive in laboratory exam. Ultrasonography revealed BCP crystals at the attachment of the flexor carpi ulnaris tendon to the pisiform bone. Low dose predonisolone and loxoprofen improved her symptom.

W73-5

Examination of ankle joint change in gout and hyperuricemia patients using HR-pQCT

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Conflict of interest: None

[Objective] More than 20% of gout is found in the ankle joint (I. Tanaka, ACR 2017) and bone formation and calcification are observed in the large joint gout. The gouty ankle joints were imaged with HR-pQCT to examine joint lesions. [Methods] The subjects were 14 male patients with ankle gout, and 5 patients had tophus. Ankle joints were imaged by HR-pQCT, and 2D / 3D images were created. [Results] Excessive bone formation with cortical bone and cavernous bone structure was observed in 4 cases of the anterior tibial muscle tendon enthesis, 1 case in the lower end of the tibia. Calcification was observed in 2 cases of the anterior inferior tibial ligament enthesis and in one case each of the tibialis posterior tendon, Achilles tendon, the talar joint, and the subtalar joint. Bone spur was observed in 11 cases of Achilles tendon enthesis, 5 cases of the planter fascia enthesis, 4 cases of Chopart joint. Bone erosions were found in 13 cases of the talus, 6 cases of the fibula, 6 cases of the tibia, 3 cases of the calcaneus. [Conclusions] Bone formation and calcification were observed at the enthesis. Bone formation was often observed by X-ray and US in the elbow and knee joints of gout patients, and it was considered necessary to investigate the relationship between gout and enthesitis.

W73-6

Examination of finger and wrist joint lesions in gout cases using HR-pQCT

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Conflict of interest: None

[Objective] We experienced a Pencil in Cup deformity similar to spondyloarthritis (SpA) in a gout case with finger and wrist arthritis. We examined the finger and wrist joints of gout cases using HR-pQCT. [Methods] In 32 gout cases, the finger and wrist joints were imaged with HR-pQCT and bone formation, calcification, and bone erosion were examined. [Results] In the finger joints, the bone erosion was observed 12% in 320 DIP / IP joints, 11% in 256 PIP joints, 13% in 320 MCP joints. The bone formation was observed 16% in DIP / IP joints, 13% in PIP joints, 10% in MCP joints. Pencil in Cup deformity was observed in 6 joints in 3 cases. In the 64 wrist joints, the bone erosion was observed 52% (88 places), the bone formation was observed 33% (41 places) and the bone formation or calcification between carpal bones was observed 19% (22 places). [Conclusions] Unlike osteoarthritis, bone formation was observed in the many PIP and MCP joints of the finger. Bone erosion and Pencil in Cup deformity was also observed. In addition, bone formation and calcification between the carpal bones were observed. In recent years, the role of IL-17 in gout has been reported, and the possibility of bone metabolism similar to SpA was considered in gouty joint lesions observed by HR-pQCT.

W74-1

Next-generation online telemedicine system utilizing mixed reality for rheumatoid arthritis

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Conflict of interest: None

Telemedicine can be performed using a conventional videophone or web conferencing system. Then, joint lesions can only be observed and inferred from 2D images, and it is difficult to perform accurate joint assessments, which is essential for the management of rheumatoid arthritis. Therefore, we have developed a system that can assess joints accurately in 3D images in real-time, using Azure Kinect DK/HoloLens 2, which are mixed reality technologies, and Teams provided by Microsoft. Furthermore, by applying AI, we plan to implement additionally to this system a function to evaluate automatically the changes in patient's facial expressions and a function to record dialogue with the patient in chronological order. It is expected that this system will enable remote medical care specializing in rheumatology, which is standardized at a high level even in areas without rheumatologists such as remote islands and remote areas. This system remotely connects Nagasaki University Hospital and Goto Chuoh Hospital, but it is not limited to these areas and it is possible to connect rheumatologists to any area that can be connected to the network. It is also effective for the purpose of avoiding the risk of infection during long-distance hospital visits under the epidemic of COVID-19 infection.

W74-2

Immune checkpoint inhibitor induced muscular diseases

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Conflict of interest: None

[Background] Immune checkpoint inhibitors (ICIs) have improved the survival of advanced malignancies, while ICIs also potentially activate immune responses against non-tumor self-cells, called immune-related adverse events (irAE). Muscular involvements are also reported as irAE (muscular irAE), but its detailed characteristics are still unknown. [Methods] We retrospectively analyzed patients diagnosed with muscular irAE from October 2017 to September 2020. [Results] Of the 203 patients received ICI, 3 patients developed muscular irAE; myocarditis, myasthenia gravis, and dermatomyositis, respectively. 2 patients were treated with nivolumab, and another one with pembrolizumab. Time of onset from ICI initiation was 1-6 (mean 4) months. Anti-acetylcholine receptor antibody was detected in myasthenia gravis case, while no auto-antibody was detected in other cases. All patients were withdrawn ICI and received corticosteroid, intravenous immunoglobulin therapy was added in dermatomyositis case, and led to clinical improvement. ICI was restarted in one case, but discontinued due to cancer progression. 2 patients died by the progression of cancer. [Conclusions] Muscular irAE could be managed with corticosteroid and withdrawal of ICI, but the progression of cancer was observed in some cases.

W74-3

Romosozumab (ROMO) dose not affect the disease activity of rheumatoid arthritis (RA) patient after 6 months osteoporosis treatment

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Conflict of interest: None

[Objective] It has been reported that inhibition of sclerostin promotes

TNF-dependent inflammatory joint destruction in basic research. In this study, we investigated the disease activity of RA patients combined with osteoporosis treated by ROMO [Methods] Of the 40 RA patients who were followed up for 6 months after administration of ROMO at our hospital, 38 patients were included and 2 patients who changed their biologics were excluded. Disease activity (DAS28-CRP, DAS28-ESR, CDAI) were investigated before and 6 months after ROMO administration. [Results] Of the 38 cases (1 male, 37 female, average age 75 years), 7 were in the TNF group (ADA: 1, ETN: 1, GLM: 4, IFX: 1), and 19 in the non-TNF group (ABT: 8, TCZ: 10, and TOF: 1), 12 were in non-bio group. The mean values of DAS28-CRP, DAS28-ESR, and CDAI in the TNF group (n=7) were 1.70, 3.32, and 4.00 before administration and 1.57, 3.12, and 2.66 after administration. Those in the non-TNF group (n=19) were 1.95, 2.76, and 5.87 before administration and 1.91, 2.59, and 5.13 after administration. Those in the non-bio group (n=12) were 2.70, 2.97, and 5.17 before administration and 2.21, 2.95, and 5.04 after administration. [Conclusions] In this study, no effect of ROMO on RA disease activity was observed 6 months after administration.

W74-4

Clinical course of progressive physical dysfunction due to hypermobility of joints in two cases of Ehlers-Danlos syndrome

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Conflict of interest: None

Few doctors have experience of diagnosing and treating Ehlers-Danlos syndromes (EDS), owing to their extreme rarity. Therefore, most patients were suffering from misunderstood their complaints without accurate diagnosis. International EDS criteria revised in 2017, however, provides us with the chance of facilitating accurate and timely diagnosis. I hope that following two cases report will serve as beginning to relieve the suffering in patients with EDS. [Case 1] Fifties. She had symptom of joint laxity and some episodes of falls and fractures in her childhood, and severe general joint laxity and laceration of skin in adulthood. Knee and foot orthosis against painful knee joints instability and flat foot failed to avoid progressing gait disturbance and she started using wheelchair at fifty. [Case 2] Forties. She had right shoulder pain after fall at age of 14. Bilateral shoulder surgeries with diagnosis of loose shoulder resulted in severe contracture and dysfunction of left shoulder. Knee, wrist and finger joints pain and instability also occurred. She was diagnosed as psychogenic reaction and treated with antidepressant. She was away from medical care, and subsequent 20-year lasting polyarthralgia, joint instability and fatigue resulted in gait disturbance limited to 20 m walking.

W74-5

A case of pulmonary hypertrophic osteoarthritis preceded by polyarthritis initially suspected to be caused by an autoimmune disease

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Conflict of interest: None

[Case] The patient was a 61 year old man with polyarthritis. At the first visit, there was a markedly clubbed fingers and toes. There was no symptoms in the small joints, but swelling, redness, and pain were present only in the large joints. On suspicion of hypertrophic osteoarthritis (HO) associated with a pulmonary tumor, CT scan was performed. It showed a mass of approximately 80 mm in long diameter in the right upper lobe. The tumor was pathologically diagnosed as non-small cell lung cancer. Therefore, we concluded that the patient had pulmonary HO (PHO). [Discussion] PHO is one of the paraneoplastic syndrome, which is characterized by a trifecta of clubbed fingers, arthritis and periosteal neoplasia. The underlying diseases of clubbed fingers include bronchiectasis, hyperthyroidism, and congenital cyanotic disease, of which lung cancer is the most important. [Clinical significance] We experienced a case of lung cancer, which was preceded by polyarthritis initially suspected to be caused by an autoimmune disease. The discovery of the clubbed fingers led to the diagnosis of lung cancer. It is important to keep in mind that the patients who present both polyarthritis and clubbed fingers may possibly suffer from respiratory diseases including lung cancer.

W74-6

A retrospective study of cases of collagen disease requiring palliative care team intervention

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Conflict of interest: None

[Objective] The World Health Organization Definition of Palliative Care (2014) listed rheumatic disease as a target disease for palliative care and there is a potential demand for palliative care. However, there are only few reports about interventions in a real clinical setting. [Methods] We retrospectively reviewed in-hospital collagen disease cases which required palliative care interventions between September 2010 and August 2020. [Results] There were 3,001 total admissions and 118 deaths. There were 26 cases of palliative care team interventions. The purpose of the interventions are physical symptom relief in all cases, psychiatric symptom relief in 4 cases, family care in 4 cases, and decision support in 2 cases. Outcomes were in-hospital deaths in 13 cases, transfers to palliative care hospital in 2 cases, discharges home in 9 cases. The causes of death were collagen disease in 5 cases, infection or complications in 3 cases and malignancy in 5 cases. [Conclusions] Patients who required palliative care team intervention had diverse causes and outcomes and received a wide range of support. However, the percentage of intervention reached only about 10% even in patients who died in hospital. Further intervention of palliative care might be required.

W75-1

Two cases of rheumatoid arthritis who learned the self-injection technique in the wake of the new coronavirus epidemic

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Conflict of interest: None

[Purpose] We report 2 cases of rheumatoid arthritis (RA) who refused self-injection learned the self-injection technique in the wake of a new coronavirus (COVID-19) epidemic. [Case 1] A 47-year-old woman developed the disease at the age of 32. Adalimumab (ADA) was introduced 11 years ago, and MTX (6 mg / week) was used in combination. Bony ankylosis of both wrist joints is observed, but grip strength is preserved and there is no problem with the self-injection procedure. [Case 2] An 18-year-old woman developed arthritis at the age of 13, and ADA was introduced. There is no limitation on the range of motion of the fingers and there is no problem with the self-injection procedure. [Course] It has been reported that patients using immunosuppressive drugs are more likely to get sick with COVID-19, and if they get sick once, they are more likely to get seriously ill, and they are afraid of frequent visits to hospitals. There was an offer to train in self-injection techniques. They practiced with a pen-type syringe and learned the procedure without any problems. [Clinical significance] Learning self-injection is also beneficial for patients. This time, we felt that the "fear" of COVID-19 was far greater than that of self-injection for RA patients using immunosuppressants.

W75-2

Practice on the care of RA patients with unfounded fears and anxieties in the COVID-19 pandemic

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Hikarichuo Clinic

Conflict of interest: None

[Objective] In the first wave of the COVID-19 pandemic, RA patients have been feeling anxiety without opportunity to get any adequate consultations for the management of reducing healthcare encounters. We have tried to allay their unfounded fears and anxieties by shared decision-making process. There is the most important thing that the risk of poor outcomes would be related to general risk factors such as aging and comorbidity. We have practiced on the care of them. Some patients who had chronic obstructive pulmonary disease (COPD) and high D-dimer titer for intravascular hyper-coagulation have been especially selected. [Methods] At the beginning of second wave, we asked RA patients to answer few questions for a survey about our management at the first wave. Comorbidities of the patients (n=345, Females 85.8%, 70y≦ 47.2%) in a survey were smoker 9.0%, pneumonitis 5.5%, D-dimer2.0≦8/30 26.7%. They were treated with MTX (59.0%), Biologics (33.9%), Steroids (22.9%). [Results] In this survey, 56.5% of the cases answered that their anxiety were allayed by our trials in the first wave. [Conclusions] It's most important for RA teams to try to improve their abilities of self-prevention for maintaining better lives and keeping lower risks of poor outcomes in the era with COVID-19.

W75-3

Study on the safety of JAK inhibitors under our multidisciplinary rheumatology care team

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Conflict of interest: None

[Objective] The present study aimed to reveal the safety issue on JAK inhibitors (JAKinibs) in our multidisciplinary rheumatology clinic. [Methods] Retrospectively reviewed the medical records of all the patients with RA treated with JAKinibs by the end of February, 2020. [Results] Total 22 patients with mean age of 65 were treated with either tofacitinib (n=10) or balicitinib (n=12). MTX and prednisolone (PSL) was co-administered in one (5%) and 6 (27%), respectively. Ten patients (45%) were complicated with 2 or more risk factors of infection. Mean duration of JAKinibs treatment was 14 months. Kaplan-Meyer survival analysis showed the treatment success rate of 82% at 1 year and 74% at 2 years. Cumulative rates of the JAKinibs withdrawal at 1 year was 5% for adverse events and 14% for insufficiency, respectively. One 72 years old male with COPD experienced recurrent pneumonia twice (4 and 22 after the start of tofacitinib 10 mg/day). There was no herpes zoster, malignancy or death. Overall incidence of serious infection was 8.03/100 person-year. [Conclusions] Our multidisciplinary care team failed to avoid serious infection in elderly patients under JAKinibs therapy. Indication of JAKinibs in elderly patients with multiple risk factors should be carefully assessed individually.

W75-4

Significance of Foot-care on Patients with Rheumatoid Arthritis (RA)

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Conflict of interest: None

[Objective] We evaluated continuous foot-care on RA patients for several years. [Methods] 135 RA patients with foot-care data between February 2019 to May 2020 are included. We analyzed association of the number and duration of foot-care with disease activity and foot care symptoms based on records of the foot-care check sheet and foot care VAS originally created at our hospital. [Results] Overall score of foot-care check sheet pre- and post- foot-care significantly improved ($p < 0.0001$). Correlation between the number of foot-care and disease activity was observed. In terms of symptoms, there was a significant difference only in the open leg ($P = 0.04$), which was significantly higher in the group with high disease activity. Regardless of no correlation between foot-care and disease activity, there were significant differences in open foot ($P < 0.001$), double toes ($P = 0.001$), and hallux valgus ($P = 0.02$). Abnormal skin color, callus, open foot, hallux valgus and tinea unguium were observed even during regular foot-care. [Conclusions] Based on the observation of foot-care in high disease activity patients, nursing is required. Continuous foot-care had not only subjective effects such as patient satisfaction and patient evaluation including quality of life but were objectively significant.

W75-5

Survey on patients' needs for treatment of rheumatoid arthritis

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Conflict of interest: None

[Objective] As shared decision making is important in rheumatoid arthritis (RA) treatment, understanding patients' needs for RA treatment is important for healthcare providers. The purpose of this study was to clarify the demand of RA patients. [Methods] A questionnaire survey was conducted among 206 RA patients attending our hospital between January 1, 2018 and March 31, 2018. [Results] Regarding RA symptoms, 66%, 33%, and 49% of patients were suffered from pain, malaise, and stiffness, and 91%, 68%, and 79% of them consulted about the symptoms with their doctors. Patients' desire for treatment were "improvement of pain" (15%), "remission" (8.3%), and "satisfied with the current treatment" (7.8%). Patient' future hope were "normal life", "travel" and "hobbies". Important factors in drug selection were "pain relief," "suppression of joint destruction," and "price,". 45% of RA patients wish to spend less than 20,000 yen per month for the treatment, however only 5% of the patients were satisfied with the current treatment cost. [Conclusions] RA patients did not enough discuss their symptoms with physicians. It is important for health care providers to understand RA patients' needs. Team medicine and good communication skill are inevitable for conducting SDM in limited time.

W75-6

Patient VAS in rheumatoid patient

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Conflict of interest: None

[Objective] To examine whether there is a difference between the VAS heard by physicians from patients and the VAS heard by nurses from patients [Methods] Patients with RA who were attending our hospital. Sixty-four patients whose VAS could be heard by physicians and nurses on the same day were included. [Results] Patients were divided into three groups: those whose values were within ±10% of the physician and nurse (hereafter referred to as the "no error" group), those who told the physician that their V A S was more than 10 higher than the nurse (hereafter referred to as "group A"), and those who told the physician that their V A S was more than 10 lower than the nurse (hereafter referred to as "group B"). Results] There were 48 patients (75%) in the error-free group, 6 patients (9%) in group A, and 10 patients (15%) in group B. Group A had a lower B M I than the error-free group (18.4 VS 21.6 kg/m2 $P<0.05$) and the items related to Hand 20 pain (No.19: 5 points V S 2 points $P<0.05$) and confidence (No.20: 5 points V S 2 points $P<0.05$) scored higher in the item on confidence (No.20: 5 points V S 2 points $P<0.05$). [Conclusions] The survey suggested the characteristics of a group of patients who reported higher scores to the doctor than to the nurses.

W76-1

Establishment of independence evaluation index for patients with childhood-onset rheumatic diseases

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Conflict of interest: None

[Objective] Outcome measures for transition care do not yet exist in Japan across all disease areas. This study aims to establish an independent evaluation index for patients with pediatric rheumatic diseases in reference to the "Rotterdam Transition Profile (RTP)" used overseas for cerebral palsy patients. [Methods] Pediatric rheumatologists, adult rheumatologists, transition care nurses, a patient's guardian, and an adult patient examined the contents of "activity and participation" of the International Classification of Functioning, Disability, and Health that was the basis of the RTP and discussed social independence that should be achieved in patients with rheumatic diseases in adulthood. [Results] The social independence that should be achieved in patients with rheumatic diseases was considered comparable to that of healthy adults if provided that appropriate support was available. [Conclusions] Through experts' consensus from different perspectives, we were able to draft a new independence evaluation index for patients with childhood-onset rheumatic diseases. We will plan to add and aggregate opinions from many experts and complete the project.

W76-2

The current status of transition for patients with pediatric rheumatic diseases in our department

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Conflict of interest: None

[Objective] To assess the current status of the transition of patients with pediatric rheumatic diseases and consider future measures. [Methods] Questionnaires were mailed to patients admitted to our department or seen multiple times and who were 20 years of age or older as of 2019. The data were compared with the Pediatric Chronic Specific Disease Study data published in 2007. [Results] 114 patients responded to the survey (response rate 45.8%). There was a significant decrease in the number of patients attending pediatric services. Use of medical support of designated incurable diseases increased. Of the items in "Transition Checklist" developed by the PRAJ, fewer than 90% of patients were able to see their doctor early or consult with a healthcare provider. Problems with transition included explanation of medical conditions at the onset of the disease and documents such as designated intractable diseases. [Discussion] Compared to 2007 survey, the transition from our department to the adult department was increased. The revision of the designated incurable disease system benefited many patients. We would like to promote the use of "Mirai note" from now on because it contains important information and continuous medical data from the onset of the disease and a transition checklist.

W76-3

A Prospective cohort study on the short and long-term prognosis including pregnancy outcomes of young patients with systemic lupus erythematosus in Japan. (PLEASURE-J study): Progress report of pregnancy subcohort

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Conflict of interest: None

[Objective] To clarify the pregnancy outcomes of young systemic lupus erythematosus patients in Japan. [Methods] The PLEASURE-J cohort is prospective nationwide longitudinal cohort. Newly diagnosed young patients who are aged 6 to 40 and meet the 1997 update of the ACR modification criteria for SLE are recruited. The pregnancy exposure registry has been also developed by collecting data about pregnancy outcomes and their disease activity and treatment during pregnancy. [Results] Among 145 women of childbearing age, 9 cases with 10 pregnancies were reported to become pregnant. Six cases (7 pregnancies) got pregnant after they were diagnosed with SLE. Three were planned while 4 were unintended. Six patients delivered healthy babies. Three patients were diagnosed with SLE during pregnancy. One had improved her symptom with prednosolone and delivered a healthy baby at 37 weeks while 2 developed lupus nephritis at 7 and 26 weeks respectively and they had delivered very low birth weight babies before 30 weeks. [Conclusions] The PLEASURE-J cohort is the first Japanese nationwide prospective cohort focus on reproductive issues among young SLE patients. This cohort would be expected to be a unique data resource for future clinical research including young patient's reproductive problems.

W76-4

Pregnancy Outcomes and Risk Factor in Women with Systemic Lupus Erythematosus

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Conflict of interest: None

Objective: To examine the maternal and fetal outcomes in SLE women and investigate the risk factor of pregnancy outcomes in SLE. **Methods:** Of 111 pregnancies in 70 SLE women who were treated in our department from January 1996 to March 2018, we retrospectively examined 98 pregnancies in 57 women previously diagnosed with SLE at conception. **Results:** Median age at conception was 30.0 years (IQR 26.0-33.0), median SLEDAI-2K was 2 (IQR 0-4), and median glucocorticoid dose (prednisolone equivalent) was 9.0 mg/day (IQR 5.0-10.0). Pregnancy outcomes were natural abortion 13 (13.3%), induced abortion 11 (11.2%), stillbirth 1 (1.0%), and delivery 73 (74.5%). Preterm birth was observed in 20

(27.4%), and low birth weight was observed in 29 (39.7%). Preeclampsia and SLE flare were observed in 12 (12.2%) and 6 (6.1%), respectively. The median duration of gestation was 38.0 weeks (IQR 36.5-39.0), and median birth weight was 2582 g (IQR 2287-2888). Multivariate analysis revealed that glucocorticoid dose at conception is the independent risk factor for preterm delivery and low birth weight. **Conclusion:** In SLE women, frequencies of preterm birth and low birth weight were high. A higher dose of glucocorticoid at conception was associated with preterm delivery and low birth weight.

W76-5

Descriptive analysis of pregnancy plan, infertility treatment and its outcome in female patients with rheumatoid arthritis in daily practice

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Conflict of interest: None

[Objective] To investigate pregnancy plan and infertility treatment and its outcome in female patients with rheumatoid arthritis (RA). [Methods] We identified RA patients aged 20-50 years who answered 'pregnant' or 'delivered' in the IORRA survey in 2010-16 and whose pregnancy and delivery were confirmed in the medical records. We conducted additional questionnaire survey about their pregnancy plan, infertility treatment, and its outcome. [Results] Eighty patients were asked to investigate and 42 patients (69 pregnancy cases) answered. RA influenced their pregnancy planning in 85.1% of the patients. In the delivered cases (n=57), the age at pregnancy (median [IQR]) was younger (34.0 years [31.5-36.0] vs 38.0 years [37.3-39.0], $p<0.01$) and the disease duration was shorter (6.0 years [4.0-10.0] vs 12.5 years [7.0-18.8], $p=0.03$) than in the spontaneous abortion cases (n=9). In the delivered cases, 71.9% of patients had spontaneous pregnancy and 17.5% became pregnant by assisted reproductive technology. Self-reported disease activity improved in 54.4% of cases in the late pregnancy, and worsened in 40.4% within 6 months after delivery. [Conclusions] The influence of RA on pregnancy planning, fertility, pregnancy course, and outcome were revealed.

W76-6

Behçet's disease and pregnancy: a retrospective study from two facilities in Yokohama

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Conflict of interest: None

[Objective] Behçet's disease (BD) often occurs at childbearing age, but there is little research on pregnancy associated with BD. [Methods] We retrospectively examined BD patients' medical records who had been attended to Yokohama City University Hospitals from 2000 to 2020. We investigated pregnancy outcomes, disease phenotypes according to the diagnostic criteria of Behçet's Disease Research Committee in Japan, disease activity, and medications during pregnancy. [Results] 31 pregnancies from 25 patients were identified. BD types were as follows; complete-type (n=4), incomplete-type (n=26), probable-type (n=1), gastrointestinal (n=8), vascular (n=3), and neuro (n=2) BD. Exacerbations of BD disease activity were seen in 6 cases, all of which required additional treatment. Medications were prednisolone, colchicine, and biologics. Pregnancy outcomes were as follows; 27 livebirths (4 preterm births), 3 spontaneous abortions, and 1 artificial abortion. The odds ratio for the risk of preterm birth compared to the Japanese general population was 2.64. [Conclusions] There were exacerbations of BD disease activity during pregnancy, and more preterm births than the general population, suggesting that intensive care is required in pregnant BD female.

International Concurrent Workshop

ICW1-1

Serological trends of rheumatoid arthritis over the last three decades

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Conflict of interest: None

Objective: The aim of this study is to investigate the serological trends of patients with rheumatoid arthritis (RA) over the last three decades. Methods: We reviewed all consecutive patients with RA in Keio University Hospital between 2016 and 2017. We divided the patients according to the year of diagnosis of RA; before 1984, 1985 to 1994, 1995 to 2004, 2005 to 2014 and after 2015. We investigated the clinical characteristics of those patients by those decades. Trends was tested by Cochrane Armitage test or Jonkheere-Terpstra test. Results: A total of 1693 patients with RA were enrolled. The mean age at diagnosis was 51.9 years old, and 83.2% were women. The number of patients with RA was 43 (2.5%) in before 1984, 129 (7.6%) in 1985-1994, 342 (20.2%) in 1995-2004, 946 (55.9%) in 2005-2014 and 233 (13.8%) in after 2015. The proportion of female was decreased (90.7%, 86.8%, 81.7%, 77.3%, respectively, $p<0.001$), and the mean age at diagnosis was increased (42.9 years, 48.1 years, 54.0 years, 58.0 years, respectively, $p<0.001$). The proportion of patients with smoking history was increased (14.0%, 20.8%, 25.7%, 32.5%, respectively, $p<0.001$), and the mean body weight was increased (50.0 kg, 53.1 kg, 54.6 kg, 56.0 kg, respectively, $p<0.001$) by the decades. Anti-cyclic citrullinated peptide antibody (anti-CCP) and rheumatoid factor positivity was significantly decreased by the decades (anti-CCP, 90.3, 81.7, 73.2, 63.4%, $p<0.001$; rheumatoid factor, 86.8%, 85.1%, 74.4%, 70.0%, $p<0.001$, respectively]. Conclusion: Incidence of seronegative RA has been increasing over the recent decades along with changes in gender ratio, the age of diagnosis and body weight.

ICW1-2

RF recognizes specific domains of IgG heavy chain complexed with HLA class II molecules

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Conflict of interest: None

[Objective] Rheumatoid factor (RF) is an autoantibody that binds to IgG Fc fragments (CH2 and CH3 domains) and is detected in patients with rheumatoid arthritis (RA). We previously reported that IgG heavy chain (IgGH) is transported to the cell surface as it is by HLA class II molecule via association with the peptide-binding groove and that IgGH/HLA class II complex is specifically recognized by RF. However, its mechanisms have not been fully understood. Here we tried to identify the binding sites of IgGH to HLA class II and recognition sites of IgGH by RF. [Methods] Each domain (VH, CH1, CH2, and CH3) or two to three contiguous domains of human IgGH were sub-cloned and transfected with HLA-DR into HEK293T cells. The flag-tagged IgGH domains presented by the HLA-DR molecules on the cell surface were detected by anti-flag antibodies using flow cytometry (FCM). Next, binding of RF to IgGH domains/HLA-DR complex was evaluated by RA patients' sera and anti-IgM antibody using FCM. [Results] IgGH domains containing VH, CH1, or CH2 were able to bind to HLA-DR molecules. The IgGH domains were efficiently presented by HLA-DR4, a risk allele of RA. On the contrary, CH3 domain alone hardly bound to HLA-DR molecules. Next, RF recognized a structure containing the IgGH CH-CH2-CH3 domains (CH1-CH2-CH3 or VH-CH1-CH2-CH3) complexed with HLA-DR molecules. Each domain alone or two contiguous domains was not recognized by RF. [Conclusions] It was found that at least three contiguous IgGH domains, including CH1-CH2-CH3, are required for both the presentation by HLA class II molecules and recognition by RF. These results imply that specific IgGH structures presented by HLA class II molecules may be involved in RF recognition.

ICW1-3

Fluctuation in anti-cyclic citrullinated protein antibody level predicts relapse from remission in rheumatoid arthritis: KURAMA Cohort

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Conflict of interest: Yes

[Objective] The positivity of anti-citrullinated protein/peptide antibodies (ACPAs) is a clinically useful diagnostic and prognostic marker in rheumatoid arthritis (RA). However, the significance of ACPA titer and its fluctuation remain unclear. This study aimed to assess the role of ACPA titer and its fluctuation on disease activity and the prognosis of RA. [Methods] Data obtained from the Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) cohort was analyzed. Patients whose ACPA was measured at least twice between 2011 and 2019 and whose ACPA was positive at least once were included in this study. The association between the clinical variable and ACPA titer or its change was investigated. [Results] ACPA titer was measured in a total of 3286 patients, 1806 of whom were ACPA-positive at least once. Among them, the ACPA titer level was measured more than once in 1355 patients. Weak correlation was observed between the ACPA titer level and disease activity. Additionally, there was no trend in the fluctuation of ACPA titer level in each patient; ACPA titer level fluctuated in some patients, but not in others. Patients with high variable levels of ACPA titer were more likely to relapse from remission. In the analysis of two consecutive ACPA measurements, the titer changes predicted the relapse from remission within a year of the second measurement. [Conclusions] The ACPA titer level fluctuated in some patients. Weak correlation was observed between the ACPA titer level and disease activity. Fluctuation in ACPA titer level predicted relapse from remission in patients with RA.

ICW1-4

Diagnostic accuracy of anti-nuclear matrix protein 2 antibody in various immunological assays

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Conflict of interest: None

[Objective] Myositis-specific autoantibodies detected in the sera from patients with dermatomyositis (DM) are known to reveal clinical subsets, thus it has been one of important clinical issues to detect them. An immunoblotting assay (IB), Euroline® by EUROIMMUN, has been globally used to detect myositis-specific autoantibodies because of its simplicity. We evaluate the accuracy of the IB kit for anti-nuclear matrix protein 2 (NXP2) antibody, one of the myositis-specific autoantibodies. [Methods] We have established a western blotting-immunoprecipitation (WB-IP) using a human cell line, K562 cells, to detect anti-NXP2 antibody, which completely corresponds to the results by a radioisotope-immunoprecipitation (RI-IP) using K562 cells as a standard assay. Seventy-three serum samples from cases with DM, in which anti-NXP2 antibody were detected by these assays, WB-IP and RI-IP, in our laboratory from April 2016 to September 2020, were enrolled. All samples were assessed by the IB kit using a recombinant human NXP2 protein that was produced in *Escherichia coli*, and another WB-IP using a recombinant human NXP2 whole protein that was produced through a baculovirus-insect cell system. [Results] Only 40 samples (54.8%) showed anti-NXP2 antibody positivity by the IB kit, all of which were confirmed by WB-IP using the NXP2 protein. Among 33 samples with the false-negative anti-NXP2 antibody, define and weak bands were observed in 15 and 8 samples, respectively by WB-

IP using the NXP2 protein. However, even WB-IP using the NXP2 protein could not detect the antibody in the rest 10 sample. [Conclusions] The IB kit showed appreciably low sensitivity to detect anti-NXP2 antibody, moreover, the sensitivity of WB-IP using the NXP2 protein was also lower than WB-IP/RI-IP using K562 cells. These inferiorities may be due to post transcriptional modification and/or difference of 3-dimmentional structure of recombinant protein compared to nature protein in human cells.

ICW1-5

Anti-gAChR antibody as a novel biomarker for lupus enteritis in systemic lupus erythematosus

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Conflict of interest: None

[Objective] Anti-ganglionic nicotinic acetylcholine receptor (gAChR) antibody (Ab) is associated with widespread autonomic dysfunction in autoimmune autonomic ganglionopathy. Although it is also detected in several autoimmune diseases, including systemic lupus erythematosus (SLE), the clinical significance of anti-gAChR Ab remains unclear. The aim of this study was to identify the clinical manifestation of lupus patients with anti-gAChR Ab. [Methods] This retrospective study comprised adult patients with SLE who visited Hokkaido University Hospital from 2007 through 2019 and whose sera were collected. A luciferase immunoprecipitation system assay was performed to measure anti-gAChRα3 and β4 subunits Ab in the sera of these patients. The Mann-Whitney U test was used for comparison of continuous data, while the Fisher's exact test was used for comparison of categorical variables. Predictors affecting clinical manifestations were assessed by Logistic regression analysis. The cumulative recurrence rate was estimated by Kaplan-Meier analysis. [Results] Overall, 99 patients with SLE were enrolled in this study. The main clinical manifestations of these patients were lupus nephritis (48.4%), neuropsychiatric SLE (44.4%), and lupus enteritis (LE, 19.1%). Among these patients, anti-gAChRα3 and β4 subunit Ab were positive for 22 (22.2%) and 6 (6.0%), respectively. The patients with anti-gAChRα3 Ab had more frequently LE than the others (45.4 vs. 11.6%, $p<0.001$). Logistic regression analysis revealed that anti-gAChRα3 Ab (odds ratio [OR] 17.4, $p<0.001$) and lupus cystitis (OR 34.0, $p=0.017$) were independent predictors for having LE. The ten-year cumulative LE relapse rate from the sera collection was significantly high in the patients with anti-gAChRα3 Ab compared to those without (35.7% vs. 4.9%, $p<0.001$). [Conclusions] Anti-gAChRα3 Ab would be a new biomarker for development and recurrence of LE in patients with SLE.

ICW1-6

Anti-centromere antibodies target centromere-kinetochore macrocomplex

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Conflict of interest: None

[Objective] Anti-centromere antibodies (ACAs) are detected in patients with various autoimmune diseases, such as Sjögren's syndrome (SS), systemic sclerosis (SSc), and primary biliary cholangitis (PBC). However, the targeted antigens of ACAs are not fully elucidated despite the accumulating understanding of the molecular structure of the centromere and the kinetochore, which is assembled on the centromere. The aim of this study was to comprehensively reveal the autoantigenicity of centromere proteins. [Methods] A centromere antigen library including 16 principal subcomplexes composed of 41 centromere/kinetochore proteins was constructed. Centromere protein/complex binding beads were used to detect serum ACAs in patients with SS, SSc, and PBC. The clinical significance of ACAs was statistically analyzed. [Results] A total of 241 individuals with SS, SSc, or PBC and healthy controls were recruited for serum ACA profiling. A broad spectrum of serum autoantibodies against centromere/kinetochore proteins was observed, and some of them had comparative frequency as anti-CENP-B antibody, which is the known major ACA. The prevalence of each antibody was shared across the three diseases. Using the combination of centromere proteins could detect ACAs with higher sensitivity than conventional methods. [Conclusions] We demonstrated that serum autoantibodies target the centromere-kinetochore macrocomplex in patients with SS, SSc, and PBC. Autoantibody detection assay with multiple centromere antigens may be potentially applicable in clinical situation.

ICW2-1

Aortic calcification correlates with bone mineral density loss in the femoral neck

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Conflict of interest: None

[Objective] Correlation of factors including arterio-sclerosis with bone mineral density in the femoral neck was investigated. [Methods] A total of 774 subjects who are drug naïve for osteoporotic drugs included in the study. Bone mineral density (BMD) in the femoral neck of each of them was measured using dual-energy X-ray absorptiometry. Calcification of the aortic wall was evaluated with X-ray picture of lumbar lateral view. Calcification of aortic wall (AS) was classified into three numerical groups; 0: no calcification, 1: calcification demonstrated but not continuous over two vertebral bodies length, 2: continuous calcification over two vertebral bodies length. Correlation of factors such as sex, age, rheumatoid arthritis history, past bone fragility fracture history, serum creatinine (Cr), cystatin C (CysC), serum Cr-to-CysC ratio (Cr/CysC), tartrate-resistant acid phosphatase-5b (TRACP-5b), type-1 procollagen N-terminal propeptide, parathyroid hormone, aminoterminal form pro-brain natriuretic peptide-32, homocysteine level, body mass index (BMI), with the BMD were evaluated using linear regression analysis. The analyses were performed using univariate model (UM) first, and then using multivariate model (MLR) with factors that demonstrated significant correlation with BMD with the UM. Significant factors using UM were then evaluated with binary logistic regression analysis (BLR) in according to T score less than -2.5. [Results] Significant factors with MLR were being female, Cr/CysC, AS, and BMI. However, using BLR, significant factors were age, AS, and BMI. In these, most significant factor was AS. [Conclusions] Aortic calcification demonstrated significant correlation with BMD loss. These results suggested that AS would be a strong candidate of the index that may screen osteoporosis.

ICW2-2

The impact of roentgenographic calcification of aortic wall on bone metabolism

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Conflict of interest: None

[Objective] The impact of roentgenographic calcification of aortic wall on bone metabolism was investigated. [Methods] A total of 774 subjects included in the study. Each of them was evaluated with X-ray picture of lumbar lateral view. Calcification of aortic wall was classified into three groups; None: no calcification, Partial: calcification demonstrated but not continuous over two vertebral bodies length, Continuous: continuous calcification over two vertebral bodies length. Sex, age, rheumatoid arthritis history (RA), past bone fragility fracture history (BFF), serum creatinine (Cr), cystatin C (CysC), tartrate-resistant acid phosphatase-5b (TRACP-5b), type-1 procollagen N-terminal propeptide (P1NP), parathyroid hormone (PTH), aminoterminal form pro-brain natriuretic peptide-32 (NT-proBNP), homocysteine (Hc) level, body mass index (BMI), and bone mineral density of the femoral head (BMD) were compared in regard with the calcification criteria. [Results] The Partial and the Continuous groups demonstrated significantly more female ratio, BFF ratio, higher level of Hc, and lower level of BMD than that of the None group, whereas the Continuous group demonstrated significant more female and BFF ratio, higher serum Cr, CysC, TRACP-5b, P1NP, PTH, NT-proBNP level, and BMI than those of the other two groups. Hc and BMD demonstrated

no significant difference between the Partial and the Continuous groups. [Conclusions] Calcification of aortic wall is a convenient and worthful screening index for osteoporosis. The continuous type of calcification had more risk of bone fragility fracture than the partial type.

ICW2-3

Underlying diseases could affect the incidence of localized periosteal thickening preceding atypical femoral fractures in patients with autoimmune rheumatic disease

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Conflict of interest: None

[Objectives] Femoral localized periosteal thickening (LPT, also called beaking) of the lateral cortex often precedes atypical femoral fracture (AFF). In two cohorts, the incidence of LPT was 1) 8~10% in patients with autoimmune rheumatic diseases [56% had systemic lupus erythematosus (SLE)] taking prednisolone (PSL) and bisphosphonate (BP) and 2) 2.4% in those with rheumatoid arthritis (RA). To determine the influence of underlying diseases on the development of LPT, a *post-hoc* analysis of data from those two cohorts was performed. [Methods] The study enrolled 379 patients (mean age 63.3 ± 13.8 years; 74.2% female; 73.6% with RA, 19.8% with SLE). [Results] LPT was evident in 12 patients at enrollment. The prevalence of SLE (50% *vs*. 19%, $p = 0.017$), connective tissue diseases or vasculitis (CTD) (75% *vs*. 34%, $p = 0.005$), comorbid diseases requiring glucocorticoid treatment other than RA (non-RA) (83% *vs*. 37%, $p = 0.002$), and diabetes mellitus (DM) (33% *vs*. 11%, $p = 0.037$) were higher, and the prevalence of RA (33% *vs*. 75%, $p = 0.003$) was lower, in patients with LPT than without. The patients with LPT had longer durations of BP and PSL use and a higher daily PSL dose. SLE (OR 4.3, 95%CI 1.4-13.8; $p = 0.014$), CTD (OR 5.9, 95%CI 1.6-22.1; $p = 0.009$), non-RA (OR 8.7, 95%CI 1.9-40.3; $p = 0.006$), and DM (OR 4.2, 95%CI 1.2-14.6; $p = 0.024$) were significant risk factors for LPT, while RA reduced the risk (OR 0.17, 95%CI 0.05-0.57; $p = 0.004$). After adjusting for age, DM, duration of BP use, calcium preparation use, and durations of PSL, CTD and non-RA were significant risk factors, while RA reduced the risk of LPT. The significance disappeared after adjusting for the daily PSL instead of the duration of PSL use. [Conclusions] Among patients with autoimmune rheumatic diseases, a comorbid disease requiring glucocorticoid treatment rather than RA was a risk factor and RA reduced the risk for LPT, which might be related to the difference in the daily PSL dose.

ICW2-4

Characterization of Bone Turnover Markers in the Early Stage of Rapidly Destructive Coxopathy

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Conflict of interest: None

[Objective] Serum bone turnover markers are higher in the end stage of rapidly destructive coxopathy (RDC) than hip osteoarthritis (OA). However, the characteristics of makers in the early stage of RDC remain unclear. In RDC with bone destruction, delayed treatment may result in poor outcome with difficulties in total hip arthroplasty because of severe loss of bone stock with increased blood loss during surgery. Therefore, there is a need for early diagnosis of RDC before the occurrence of significant bone destruction. This study aimed to characterize bone turnover markers that are associated with femoral head destruction in the early stage of RDC. [Methods] This study included 29 female patients with RDC diagnosed with radiographs and computed tomography, which demonstrated chondrolysis >2 mm during 12 months from the disease onset. This study also included 9 postmenopausal female patients with OA secondary to developmental dysplasia showing femoral head destruction. Serum levels of tartrate-resistant acid phosphatase 5b (TRACP-5b) and bone alkaline phosphatase (BAP) were assayed within 12 months from the disease onset. Cortical thickness index (CTI) correlated with bone mineral density of the hip was measured on the radiograph at the onset of hip pain. [Results] RDC were classified into two types based on the absence (type 1, n=13) and presence (type 2, n=16) of subsequent femoral head destruction within 12 months after the onset. TRACP-5b and BAP significantly increased in RDC type 2 compared with type 1 and OA. Receiver operating characteristic curve analyses indicated that TRACP-5b and BAP could differentiate RDC type 2 from type 1 within 12 months after the onset. No difference in CTI, age at onset, body mass index, or duration between the onset of hip pain and blood test was found among RDC types 1 and 2 and OA. [Conclusions] High serum levels of bone turnover markers may be associated with femoral head destruction in the early stage of RDC.

ICW2-5

Combined effect of teriparatide and an anti-RANKL monoclonal antibody on bone defect regeneration in mice with glucocorticoid-induced osteoporosis

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Conflict of interest: None

[Objective] Glucocorticoids are used for the treatment of various diseases, including rheumatoid arthritis. However, it is often accompanied by glucocorticoid-induced osteoporosis (GIOP). The purpose of this study was to examine the effect of single or combination therapy of teriparatide (TPTD) and a monoclonal antibody against the murine receptor activator of nuclear factor κB ligand (anti-RANKL Ab) on bone regeneration in a mouse model of GIOP. [Methods] C57BL/6J mice (24 weeks of age) were divided into five groups: (1) the SHAM group: sham operation + saline; (2) the prednisolone (PSL) group: PSL + saline; (3) the TPTD group: PSL + TPTD; (4) the Ab group: PSL + anti-RANKL Ab; and (5) the COMB group: PSL + TPTD + anti-RANKL Ab (n = 8 per group). With the exception of the SHAM group, 7.5 mg of PSL was inserted subcutaneously. Four weeks after insertion, bone defects with a diameter of 0.9 mm were created on both femurs to assess bone regeneration. After surgery, therapeutic intervention was continued for 4 weeks. Saline or TPTD was injected five times per week, whereas the anti-RANKL Ab was injected once on the day after surgery. Subsequently, the following analyses were performed: micro-computed tomography analysis of bone regeneration and bone mineral density (BMD), and histological, histomorphometrical, and biomechanical analyses with nanoindentation. [Results] The volume of regenerated cancellous bone at the bone defect site was higher in the COMB group compared with the other groups. As for regenerated cortical bone, the COMB group showed the highest BMD and higher hardness (vs. the PSL and TPTD groups). And the COMB group showed the highest lumbar spine BMD increase (vs. the PSL, TPTD, and Ab groups). [Conclusions] In a GIOP mouse, the combination therapy of TPTD plus the anti-RANKL Ab increased BMD in the regenerated cancellous bone and the lumbar spine compared with single administration of each agent, and also increased regenerated cortical bone strength.

ICW2-6

New Mechanistic Insights into the Roles of the Osteoblastic/Cartilage Transcription Factor for Production of Matrix Metalloproteases

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Conflict of interest: None

[Objective] Dysregulation of matrix metalloproteinases (MMPs) causes tissue damage in rheumatoid arthritis (RA). MMP-13 produced by chondrocytes degrades the proteoglycan molecule, aggrecan, leading to destruction of cartilage and joint space narrowing. RUNX2, a master transcription factor required for osteoblast and cartilage differentiation, regulates expression of a number of its target genes including MMP-13. It is well-established that RUNX2 activity is regulated through the interaction with transcription factors, chromatin remodeling proteins and transcriptional co-activators. However, the regulatory mechanism of RUNX2-mediated MMP-13 production has yet to be elucidated. The purpose of the present study is to clarify the mechanism by which RUNX2 controls MMP-13 expression during the development of RA. [Methods] Co-IP, ChIP, promoter assay, phosphorylation assay, immunofluorescence and knockdown experiments were performed to investigate the molecular mechanism in this study. [Results] In distinction to the well-established regulatory mechanisms of RUNX2 activation, we have uncovered a previously undescribed model in the present study showing that a non-receptor tyrosine kinase ABL directly binds to, phosphorylates and activates RUNX2 through its SH2-domain which is required for MMP-13 expression. We show that the ABL-RUNX2 complex formation is required for expression of MMP-13. Additionally, we identified several tyrosine residues of RUNX2 as a minimum phospho-switch which is phosphorylated by ABL and required for its transcriptional activity. We show that depletion of ABL attenuates RUNX2-mediated MMP-13 expression. [Conclusions] Our study provides new mechanistic insights into the roles of ABL for RUNX2 activation and expands the concept that the ABL-RUNX2-MMP-13 axis may be associated with the process of cartilage degradation, followed by joint narrowing and destruction in RA.

ICW3-1

Bcl-6 regulates natural TPH-like cell differentiation

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Conflict of interest: None

Objective PD-1^{hi}CXCR5^{-} peripheral T helper (T_{PH}) cells were recently reported to promote B cells to produce autoantibodies in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). On the other hand, previously we showed that autoreactive CD4^{+} T cells can differentiate into naturally occurring peripheral T helper-like (natural T_{PH}-like) cells, which are rendered anergic in vivo, in the thymus of gene-manipulated and wild-type mice. Natural T_{PH}-like cells have similar characteristics to human T_{PH} cells, as they produce IL-21 and promote B cells to produce immunoglobulin. However, differential pathways for helper T cells which drive autoantibody production have not been fully clarified yet. Methods To investigate whether natural TPH-like cells also exist in the absence of transgenics of self-antigen, we sorted Foxp3^{+}CD4^{+} T cells, Foxp3^{-}PD-1^{-}CD4^{+} T cells, and Foxp3^{-}PD-1^{+}CD4^{+} T cells from the spleen and thymus of Foxp3-GFP mice by flow cytometry, and quantified expression of Bcl6. We also generated Bcl6$^{-/-}$ DBL (DO11.10 x Ldn-OVA) mice, and compared the differentiation of T_{PH}-like cells in Bcl6$^{+/+}$, Bcl6$^{-/-}$, Bcl6$^{+/+}$ DBL, and Bcl6$^{-/-}$ DBL mice. Results Bcl6 expression was higher in Foxp3^{-}PD-1^{+}CD4^{+} T cells than in Foxp3^{+}CD4^{+} T cells or Foxp3^{-}PD-1^{-}CD4^{+} T cells of spleen and thymus. Bcl6$^{+/+}$ mice have more splenic natural T_{PH}-like cell population than Bcl6$^{-/-}$ mice. Similarly, Bcl6$^{+/+}$ mice have more thymic T_{PH}-like cells than Bcl6$^{-/-}$ mice. Furthermore, T_{PH}-like cells and Fas^{+}GL7^{+}CD19^{+}B cells disappeared in Bcl6$^{-/-}$ DBL mice as compared with DBL mice. CXCR5 was not expressed in T_{PH}-like cells in splenocytes of Bcl6$^{+/+}$ mice, which is consistent with natural T_{PH}-like cells in RDBLSf mice. These results highlight the significance of Bcl-6 in the generation of natural T_{PH}-like cells. Conclusions Bcl-6 is required for generation of natural T_{PH}-like cells.

ICW3-2

Reciprocal repression of STAT3 and SMAD3/4 regulates Th17 differentiation, which predicts therapeutic response to IL-6 antagonism in rheumatoid arthritis

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Conflict of interest: None

[Objective] IL-6 and TGF-β cooperatively induce differentiation of Th17. By contrast with the effectiveness of targeting IL-6 and JAK-STAT signaling in rheumatoid arthritis (RA), IL-17 antagonism is not therapeutically effective and the roles of canonical TGF-β signaling via SMAD in arthritogenic T cells remain largely unknown. Here, we sought to investigate whether and how canonical SMAD-mediated TGF-β signaling affects STAT3-mediated signaling in arthritogenic Th17 and the therapeutic sensitivity to biologic disease-modifying anti-rheumatic drugs. [Methods] We investigated the interactions between STAT3-mediated IL-6 and SMAD-mediated TGF-β signaling pathways in Th17 differentiation in vitro and murine collagen-induced arthritis (CIA) model using T cell-specific SMAD4 conditional knockout mice (*Cd4Cre; Smad4*$^{+/+,\ fl/fl}$) and SMAD3 knockout mice. Expression of mRNA of Th17 signature genes, STAT3 and SMAD3/4 in peripheral blood mononuclear cells (PBMCs) from RA patients before and after the treatment with infliximab (IFX), tocilizumab (TCZ) or abatacept (ABT) for six months were analyzed with quantitative RT-PCR. [Results] T cell-specific SMAD4 deletion and SMAD3 deficiency significantly exacerbated CIA with significantly increased STAT3-induced Th17. C-terminally phosphorylated SMAD3 with SMAD4 repressed the transcription of STAT3, whereas phosphorylated STAT3 (Y705 and S727) repressed the transcription of SMAD3 and SMAD4, reciprocally. Th17 signature gene expression in PBMCs were significantly correlated with the therapeutic sensitivity to TCZ. Low SMAD3/STAT3 and SMAD4/STAT3 ratios showed high correlation with the effectiveness of TCZ and the refractoriness to IFX and ABT in RA. [Conclusions] Canonical TGF-β signaling rather suppresses STAT3-induced arthritogenic Th17 differentiation via reciprocal repression between SMAD3/4 and STAT3. Ratios between SMAD3/4 and STAT3 in PBMCs could be predictive biomarkers for IL-6 antagonism in RA.

ICW3-3

ADAM9 Drives Th17 cell differentiation and Autoimmunity by Activating TGF-beta1

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Conflict of interest: None

[Objective] A disintegrin and metalloproteinases (ADAMs) have important roles in the regulation of T cells function by cleaving enzymatically key factors in various immune responses. The role of ADAM family members in Th17 cell differentiation is unknown. [Methods] We assessed the expression of ADAM family members in murine Th17 polarizing cells and the role of ADAM9 for Th17 cell differentiation in vitro. Mechanistically, the enzymatic activity of ADAM9 for latency-associated peptide (LAP), a component of latent transforming growth factor β1 (TGF-β1), was examined. To assess the role of ADAM9 for Th17-dependent autoimmune diseases, we used experimental autoimmune encephalomyelitis (EAE). We also assessed ADAM9 expression in CD4^{+} T cells from patients with systemic lupus erythematosus (SLE) and healthy controls. We deleted *ADAM9* in CD4^{+} T cells from patients with SLE using the CRISPR/Cas9 gene-editing system and assessed Th17 cell differentiation. [Results] We identified ADAM9 to be specifically expressed in Th17 cells. The silencing of ADAM9 reduced in vitro differentiation to Th17 cells, while ADAM9 overexpression restored Th17 differentiation. We found that ADAM9 cleaved the LAP to produce bioactive TGF-β1 which promoted SMAD2/3 phosphorylation and activation. A transcription factor inducible cAMP early repressor (ICER) was found to bind directly to the *ADAM9* promoter and promote its transcription. ADAM9-deficient mice

displayed mitigated EAE and transfer of ADAM9-deficient myelin oligodendrocyte globulin-specific T cells into *Rag1-/-* mice failed to induce disease. At the translational level, ADAM9 was enriched in $CD4^+$ T cells from patients with SLE and *ADAM9* gene deletion in lupus primary $CD4^+$ T cells clearly attenuated their ability to differentiate into Th17 cells. [Conclusions] These findings revealed that ADAM9 as a protease provides Th17 cells with an ability to activate TGF-β1 and accelerates its differentiation, resulting in aberrant autoimmunity.

ICW3-4

Tissue resident GATA3+ regulatory T cells regulated by the IL-33-ST2 axis and amphiregulin play roles in the convalescence stage of crescentic glomerulonephritis

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Conflict of interest: Yes

[Objective] Tregs that reside or accumulate in nonlymphoid tissues, called tissue Tregs, contribute to the maintenance of tissue homeostasis and peripheral immune tolerance. To clarify the function and characteristics of tissue Tregs in a crescentic glomerulonephritis (cGN) model. [Methods] cGN was induced in an experimental mouse model using an anti-glomerular basement membrane antibody. Tregs among the $CD4^+$ T cells that accumulated in the kidney during the chronic phase of cGN were examined by microarray analysis, flow cytometry analysis, and immunohistochemical analysis to examine expressed genes and surface markers. Conventional T cells (Tconv) and Tregs were co-transferred into T cell-deficient $Cd3\varepsilon^{-/-}$ mice to evaluate renal function and crescent formation, and to investigate the functions of the genes and surface markers expressed on the Tregs. [Results] In microarray analysis, intrarenal Tregs showed a tissue Treg phenotype, including high expression of ST2 (IL-33 receptor subunit), amphiregulin (Areg), and PPARγ. In renal Tregs, $T\text{-}bet^+$Tregs and $ROR\gamma t^+$Tregs were also present, but $GATA3^+$Tregs were predominant in convalescent kidneys, comprising 40%-50% of all Tregs. In the co-transplantation into $Cd3\varepsilon^{-/-}$ mice, GATA3 knockdown in Treg cells using the CRISPR/Cas9 system exacerbated crescent formation. Tconv alone and $Tbx21^{-/-}$Tregs also caused deterioration in renal function, but $Rorc^{-/-}$Tregs and wild-type Tregs improved renal function. IL-33 was expressed on fibroblasts and endothelial cells in the tubulointerstitial lesion, and in *Il-33*$^{-/-}$ mice, proteinuria was exacerbated and $GATA3^+$ Tregs were decreased. Co-transfer of Tconv and *St2*$^{-/-}$Treg or *Areg*$^{-/-}$Treg caused deterioration in renal function and decreased $GATA3^+$Tregs. A PPARγ agonist enhanced $GATA3^+$Treg accumulation in the kidneys, and ameliorated renal injury. [Conclusion] $GATA3^+$ tissue Tregs regulated by the IL-33-ST2 axis and amphiregulin contribute to improved renal function in the convalescence stage of cGN.

ICW3-5

Antigen specific suppression made on DC by Foxp3 Treg is not irreversible

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Conflict of interest: None

[Objective] Chemotactic recruitment of Treg to a target inflammation site is critical for Treg to exert suppression to maintain immune homeostasis. Effective recruitment and proliferation in the target tissue/organ would also be an important factor for the development of Treg cell therapy. However, after Tregs are recruited, effector specificity and irreversibility of suppressive property of dendritic cells (DCs) mediated by Treg remained unresolved. [Methods] (1): Recruitment-Ag specific Tregs (Recruitable-Tregs) were injected into recipient mice together with Target-Ag specific CD4 T cells (Teff) and DC presenting both target-Ag and recruitment-Ag (DC-2Ag) intravenously and effector specificity was analyzed on day 3. (2): DC-2Ag and Recruitable-Tregs were co-cultured and DC-2Ag were sorted out and analyzed for their ability to stimulate target-Ag specific CD4T cells or recruitment-Ag specific CD4 T cells. [Results] (1): Recruitable-Treg did not suppress Teff response but suppressed recruitment-Ag specific T cell response. (2): Suppression made on DC-2Ag was antigen specific, though the suppression was broken by re-expression of antigens on the suppressed DCs. [Conclusions] Just recruiting Tregs to the target DCs is not enough to suppress T cell response to the target-antigen. The recruitable-Tregs suppress recruitment-Ag specific response, but the suppression made on DCs was not irreversible. These results suggest that Treg suppression was not achieved by cell death or irreversible functional change of DCs.

ICW3-6

TNFR2 signaling enhances suppressive function of Follicular regulatory T cells

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Conflict of interest: None

[Objective] Tumor Necrosis Factor (TNF) α is a multifunctional cytokine with pro-inflammatory and anti-inflammatory characteristics. TNFα modulates the proliferation and function of Treg via TNFR2. Recently, a subset of CD4+ Treg termed follicular regulatory T (Tfr) cells has been found. Function of human Tfr in vivo is not well understood, however it has been shown that Tfr cells limit the function of Tfh cells and repress immunoglobulin secretion from B cells in vitro. Tfr cells might contribute the immunological abnormality in autoimmune diseases. TNFR2 signaling enhances suppressive activities in Treg cells, on the other hand it is still unclear whether Tfr cells response to TNFα via TNFR2. We examine the role of TNFR2 signaling in this new regulatory cell subset. [Methods] We sorted Tfr (CD3+ CD4+ CXCR5+ CD25+ CD127low or CD14-CD4+ CXCR5+ CD25+ CD127low) cells from mononuclear cells of healthy donor using FACS Aria. We examined the gene expression, proliferation, and suppressive ability of these cells stimulated with an anti- TNFR2 agonistic antibody in vitro. [Results] RNA-seq revealed altered transcriptome of these TNFR2-stimulated cells in co-stilmulatory/inhibitory molecules and known Treg associated genes (i.e. Foxp3, CTLA-4, LAG3, etc.). Foxp3 expression was upregulated after stimulation with TNFR2 agonists. TNFR2 agonists greatly enhanced proliferation of Tfr cells. Although unstimulated Tfr cells did not suppress expansion of Tfh (CD14- CD4+ CXCR5+ CD25- CD127high) cells, Tfr cells stimulated with the TNFR2 agonist suppressed expansion of these cells. TNFR2-stimulated Tfr cells suppressed differentiation of naïve B cells into antibody-producing cells and production of immunogloblin from B cells. [Conclusions] TNFR2 agonist enhanced proliferation and suppressive function in Tfr cells in vitro assays. These findings suggest that TNF receptor 1 specific inhibition might be a better strategy than pan-TNF inhibitors.

ICW4-1

Angiotensin-converting enzyme 2, a SARS-CoV-2 receptor, is upregulated by IL-6 via STAT3 signaling in synovial fibroblasts and lymphocytes

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Conflict of interest: None

[Objective] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading rapidly worldwide since early 2020, resulting in a pandemic of a new respiratory disease called coronavirus disease 2019 (COVID-19). IL-6 levels in patients with complicated COVID-19 have been reported to be approximately threefold higher than those in non-complicated cases. Coronaviruses possess envelope-anchored spike proteins that bind host cell surface receptors to initiate viral entry into target cells. The spike protein of SARS-CoV-2 mediates binding to the host receptor angiotensin-converting enzyme 2 (ACE2). However, the regulatory mechanism of ACE2 has seldom been reported. [Methods] ACE2 expression levels in synovial specimens from rheumatoid arthritis (RA) and osteoarthritis (OA) patients who underwent joint replacement surgery were analyzed using immunohistochemistry and real-time RT-qPCR. Cultured primary fibroblast-like synoviocytes (FLS) and Jurkat cells (human T cell line) were treated with IL-6, TNF, and siRNA against STAT3; ACE2 levels were then evaluated using real-time RT-qPCR and western blot analyses. [Results] In both RA and OA synovial tissues, ACE2 was expressed in the synovial lining, sublining regions, and mononuclear cells. ACE2 expression levels in active RA synovial tissues were higher than in inactive RA specimens. Cultures of RA-FLS and Jurkat cells revealed that ACE2 expression was increased by IL-6 but not by TNF. The use of siRNA against STAT3 reduced IL-6-dependent ACE2 expression in RA-FLS. [Conclusions] ACE2 was upregulated in the active synovial tissues of RA and OA patients and maintained by STAT3-mediated activation through the IL-6 pathway. Further analyses of IL-6-induced ACE2 transcription in other cells and tissues, besides synovial fibroblasts and lymphocytes, may help elucidate the mechanisms of SARS-CoV-2 entry into target cells. Further, these insights may lead to the development of the novel therapeutic targets against COVID-19.

ICW4-3

Analysis of heterogeneity of IL-6 secretion from synovial fibroblasts by cell-to-cell interaction

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is an autoimmune disease characterized by destructive synovitis. Synovial fibroblasts (SFs) are stromal cells in synovium, and they produce pathogenic mediators represented by IL-6 in the inflammatory network with immune cells. The objective of this study is to investigate the effect of cell-to-cell interaction on IL-6 production of SFs using live cell imaging for secretion activity (LCI-S). [Methods] Synovial tissues were obtained from RA patients undergoing joint replacement surgery at the University of Tokyo Hospital. RA patients fulfilled the 2010 ACR/EULAR criteria for the classification of RA. IL-6 secretion from synovial cells was detected with LCI-S. First, single cell suspensions of synovial tissue were used to evaluate the difference in IL-6 secretion pattern depending on cell-to-cell interaction. Second, immune cell populations (T cells and B cells) were sorted by flow cytometry, and co-cultured with freshly isolated SFs to examine the effect of interaction partner on IL-6 secretion. [Results] When IL-6 secretion from spindle-shaped synovial cells was observed using LCI-S for 48 hours, it was classified into cell-to-cell interaction-dependent secretion and independent secretion. The analysis of IL-6 secretion pattern (peak and duration) showed that interaction with immune cells affected the length of secretion rather than the height of the secretion peaks, that is, IL-6 was secreted for a longer period of time by cell-to-cell interaction. Furthermore, this IL-6 secretion pattern was also subdivided by interaction partners. [Conclusions] Our study suggests that cell-to-cell interaction between SFs and specific immune cell population results in prolonged IL-6 secretion from SFs. This mechanism could play an important role in the amplification of synovial inflammation in RA joints.

ICW4-4

CD34+ synovial fibroblast subset has high osteogenic and chondrogenic potentials in vitro

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Conflict of interest: None

[Objective] Synovial fibroblasts (SFs) play crucial roles in the pathogenesis of rheumatoid arthritis (RA). We have reported that $CD34^-THY1^+$ and $CD34^+$ SF subsets, which are responsible for tissue injury and inflammation, are pathologically expanded in RA. SFs also play a role as mesenchymal stem cells (MSCs). In RA, the repairing activities of SFs as MSCs are impaired, leading to the persistent joint damage. Suppressing the pathogenic functions of the pathologically expanded SF subsets and, at the same time, restoring the repairing activity of SFs as MSCs could be an effective therapeutic strategy for RA. However, the differences of SF subsets as MSCs has not been clarified yet. The objective of this study is to clarify the differences in osteogenic and chondrogenic potentials among SF subsets. [Methods] SFs were obtained from synovial tissues by enzymatic digestion. Three SF subsets were isolated using cell sorter based on the expression of CD34 and THY1. The SF subsets were expanded, and then cultured in osteogenic or chondrogenic condition. The osteogenic potential was evaluated with alizarin red staining and qPCR for the expression of alkaline phosphatase (*ALPL*). The chondrogenic potential was evaluated with the diameter of the formed chondrocyte pellets. The proportion of positive cells for CD73, a MSC markers, in the freshly isolated SF subsets was evaluated using flow cytometry. [Results] The calcified area formed under the osteogenic condition in $CD34^+$ subset was 4- and 2.5-fold higher than $CD34^-THY1^-$ and $CD34^-THY1^+$ subsets, respectively. The expression level of *ALPL* in $CD34^+$ subset was 2- and 1.5-fold higher than $CD34^-THY1^-$ and $CD34^-THY1^+$ subsets, respectively. The size of chondrocyte pellets was larger in $CD34^+$ subsets than other subsets by about 30%. The average percentage of $CD73^+$ cells in $CD34^-THY1^-$, $CD34^-THY1^+$, and $CD34^+$ subsets was 68, 77, and 90%, respectively. [Conclusions] $CD34^+$ SF subset has high osteogenic and chondrogenic potentials in vitro.

ICW4-5

Impact of JAK inhibitors on epigenome and transcriptome landscapes of synovial fibroblasts

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Conflict of interest: Yes

[Objective] Rheumatoid arthritis (RA) is an autoimmune disease characterized by destructive synovitis. Synovial fibroblasts (SFs) play a crucial role in synovial inflammation through expressing a variety of pathogenic molecules represented by IL-6. Recent progress in RA treatment has been achieved with janus kinase (JAK) inhibitors (e.g., Tofacitinib [TOFA], Baricitinib [BARI]). However, functional mechanisms of these compounds on SFs are still unveiled. The objective of this study is to investigate epigenomic and transcriptomic effects of BARI on RASFs, and to compare immunological characteristics with TOFA or with other classes of disease modified anti-rheumatic-drugs (DMARDs). [Methods] RASFs (n = 6) were incubated with representative inflammatory cytokines in RA joints (TNF-α+IL-1β+IFN-γ) for 12 hours. Following the stimulation, cells were treated with DMARDs (Methotrexate, Iguratimod, Adalimumab [ADA], TOFA and BARI) for additional 24 hours. RNA sequencing and ATAC-sequencing were carried out with these samples. Differentially expressed genes (DEGs) and differential transcriptional factor activity were analyzed with the R package edgeR and HINT-ATAC software, respectively. [Results] Principal component analysis (PCA) showed that BARI induce a distinct transcriptomic signature compared to TOFA as well as DMARDs of other classes. Focusing on the differences between JAK inhibitors, gene expression of some inflammatory mediators (e.g., *STAT1, IL7R*) was significantly suppressed in BARI, but not in TOFA, accompanied by changes in chromatin accessibility of its regulatory site. Furthermore, the transcriptional activity of B lymphocyte-induced maturation protein1 (Blimp1) and

STAT1 was predicted to be lower in BARI compared to TOFA. [Conclusions] Blimp1 and STAT1 are reported to bind to each other's regulatory regions. In BARI, Blimp1 and STAT1 could form a feedback loop, and the expression of some STAT1 target genes is deeply suppressed even at epigenomic level.

ICW5-1

Immunomics analysis of rheumatoid arthritis identified pre-dendritic cells as a key cell subset of treatment resistance

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Conflict of interest: Yes

[Objective] No biomarker exists to predict difficult to treat rheumatoid arthritis (RA) patients and little is known about the biology of treatment resistance. Previously, we have shown that specific gene module of flow cytometrically sorted plasmacytoid dendritic cells (pDCs) subset were associated with treatment resistance in RA by RNA-seq profiling of 18 immune cell subsets from 55 pre-treatment RA patients. [Methods] To identify the responsible sub-population of pDCs that are associated with treatment resistance, CIBERSORTx deconvolution of pDCs were performed with multiple public single cell RNA sequencing data. The flow-cytometric data were also re-analyzed. In addition, as part of the PREDICTABA study, we performed mass cytometric analysis of 23 RA patients starting abatacept (ABA) to identify immune cell population that predict treatment resistance. Achievement of CDAI50 at 6 months was used as treatment response criteria. [Results] The treatment resistance associated pDCs gene module was consistent with pre dendritic cells (pre-DCs) signature genes and was correlated to the statistically deconvoluted proportion of pre-DCs ($r = 0.70$, $p = 9.00E-08$). Rare pre-DCs contaminated within the pDCs with the standard flow-cytometic gating strategy. Deconvoluted and flow-cytometric proportions of pre-DCs were elevated in treatment resistant patients ($p = 0.06$ and $p = 0.10$). Furthermore, mass cytometry analysis of an independent cohort validated that pre-DCs are increased in the ABA non- responsive group than responsive group ($p = 0.006$). [Conclusions] The increase of pre-DCs predicted the treatment resistance of RA. Pre-DCs could have pathophysiological relevance to difficult to treat RA patients.

ICW5-2

Functional analysis of Rheumatoid arthritis-related gene NFAG1 in inflammation development in joint

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Conflict of interest: None

[Background] Rheumatoid arthritis is characterized by chronic inflammation, immune abnormality, and bone destruction. We have identified a molecular mechanism of chronic inflammation, called the inflammation amplifier, which is a hyper NFκB activation machinery driven by co-activation of NFκB and STAT3 in non-immune cells such as endothelial cells, fibroblasts. Previous reports showed that rs13277113, an intergenic single nucleotide polymorphism (SNP) on chromosome 8, is genetically associated with autoimmune diseases including rheumatoid arthritis and other autoimmune diseases and the risk allele of the SNP correlates with elevated expression of an adjacent gene, NFAG1. However, the biological function of NFAG1 remains unknown. [Objective] To clarify the function of NFAG1 and its molecular mechanism [Methods] [Results] In the present work, we show that NFAG1 is positively involved in the development of inflammatory diseases. Deficiency of NFAG1 in fibroblast-like synoviocytes and vascular endothelial cells suppresses IL-6 and chemokine expression in vitro. Forced expression of NFAG1 enhanced NFκB and IL-6 promotor activities. Mechanistic analysis showed that NFAG1 suppressed RIPK1 cleavage by Caspase8, while forced expression of NFAG1 enhanced NFκB activation via NFAG1-RIPK1 binding with coiled coil element and 57-129 amino acids region of NFAG1 dependent manner. NFAG1 deficiency also suppressed a cytokine-mediated arthritis in vivo. Furthermore, NFAG1 expression of RA patients in joint was significantly higher than that of control patients dependent on risk alleles on rs13277113. [Conclusions] These results suggest that NFAG1 acts as a NFκB activator and we clarified the role of this genetic risk factor.

ICW5-3

Functional Differences Between RANKL-Induced Osteoclasts and Tumor Necrosis Factor alpha and Interleukin-6-Induced Osteoclasts Differentiated From Peripheral Blood Mononuclear Cells in Patients With Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We previously reported that stimulation of mouse bone marrow-derived macrophages with TNFα and IL-6 induced differentiation of osteoclast-like cells. The present study aimed to clarify the characteristics and function of human TNFα and IL-6-induced osteoclasts (T6iOCs) using peripheral blood cells from patients with rheumatoid arthritis (RA) and healthy donors. We also analyzed the differences of the molecular expression patterns and functions between the novel T6iOCs and conventional osteoclasts. [Methods] Peripheral blood monocytes were cultured in the presence of both TNFα and IL-6 or RANKL, and their bone resorption ability were evaluated. The expression levels of nuclear factor of activated T cell (NFAT) c1, proinflammatory cytokines, and MMP-3 were analyzed. The effects of osteoprotegerin (OPG), NFAT inhibitor, and JAK inhibitor were examined. Furthermore, the relationship between the number of T6iOCs or osteoclasts differentiated from peripheral blood mononuclear cells (PBMCs) in patients with RA and the modified total Sharp score (mTSS) or the whole-body bone mineral density (BMD) were examined. [Results] Stimulating peripheral blood monocytes with both TNFα and IL-6 induced T6iOCs with an ability to absorb bone matrix. The cell differentiation was not inhibited by the addition of OPG; TNFα and IL-6 stimulation promoted NFATc1 expression, while the NFAT and JAK inhibitors prevented T6iOC formation. Expression of IL-1β, TNFα, IL-12p40, and MMP-3 was significantly increased in T6iOCs, but not in osteoclasts. IL-1β up-regulates the differentiation of T6iOCs. The number of T6iOCs differentiated from PBMCs in patients with RA positively correlated with mTSS, whereas osteoclast number negatively correlated with the whole-body BMD of the same patients. [Conclusions] Our results demonstrate thatT6iOCs differentiate via RANKL-independent pathways and may contribute to the joint destruction in the inflammatory arthritis, such as RA.

ICW5-4

Role of T cell immunoglobulin and mucin domain-3 (TIM-3) in determining clinical phenotype of RA

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Conflict of interest: None

[Background] T cell immunoglobulin and mucin domein-3 (TIM-3) is a surface molecule expressed on immune cells. Galectin-9-mediated ligation of TIM-3 induces the amelioration of autoimmune diseases. The relationship between disease activity of rheumatoid arthritis (RA) and TIM-3 was unknown. [Objective] This study is conducted to determine whether soluble TIM-3 (sTIM-3) is elevated in RA patients, and to investigate the relationship between sTIM-3 and clinical features of RA. [Methods] Our study included 116 RA patients and 27 healthy control subjects. Serum levels of sTIM-3 were measured by ELISA. Correlations between sTIM-3 and RA parameters including ACPA titer, erythrocyte sedimentation rate (ESR) and matrix metalloproteinase-3 (MMP-3) were assessed. [Result] Serum levels of sTIM-3 were significantly elevated in RA patients compared with those in healthy subjects, and it was positively correlated with ACPA titer ($r = 0.27$, $p = 0.005$), ESR ($r = 0.27$, $p = 0.004$) and MMP-3 ($r = 0.35$, $p < 0.001$), respectively. In RA patients with higher ACPA titers (≧200 U/mL), sTIM-3 was not correlated with ESR or MMP-3. However, there was a modest correlation between serum levels of sTIM-3 and higher ACPA titers ($r = 0.52$, $p = 0.001$). On the other hand, sTIM-3 was correlated with ESR ($r = 0.36$, $p = 0.001$) and MMP-3 ($r = 0.38$, $p < 0.001$) in RA patients with lower ACPA titers (<200 U/mL). There was no correlation between serum levels of sTIM-3 and lower ACPA titers ($r = 0.086$, $p = 0.45$). [Discussion] Serum levels of sTIM-3 was increased in RA patients, and was associated with proinflammatory markers in RA patients under a ACPA status. Our data suggest that sTIM-3 can be a novel biomarker for the determination of disease activity. The positive correlation between sTIM-3 and higher ACPA titers suggests that RA group with high sTIM-3 titers may be in an acquired immune condition, which may be indicator of drug selection.

ICW5-5

Significant association of TIGIT expression on T cell subsets with disease activity in rheumatoid arthritis patients

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Conflict of interest: None

[Bachground] T cell immunoreceptor with immunoglobulin (Ig) and immunoreceptor tyrosine-based inhibitory motif (ITIM) domains (TIGIT) is a newly identified inhibitory immune checkpoint molecule. It has already been reported that the expression levels of TIGIT on whole CD4+ T cells and CD8+ T cells was elevated and that on CD4+ T cells were positive correlation with disease activity in patients of RA. On the other hand, their detailed subsets have not been fully elucidated. [Objective] We aimed to analyze the expression levels of TIGIT in peripheral blood T cell subsets of RA patients. Their correlation RA disease activity was also analyzed. [Methods] Untreated patients with RA diagnosed with 2010 ACR/EULAR classification criteria in our department from 2019 to 2020 were included. We separated CD4+T cells into 5 subsets (naïve, central memory (CM), effector memory (EM), T follicular helper (Tfh) and T peripheral helper (Tph)), and CD8+T cells into 4 subsets (naïve, CM, EM and effector memory re-expresses CD45RA (TEMRA)) using FACS. We then analyzed the levels of TIGIT expression on those subsets. Patient clinical information was collected from medical records. [Results] Ten RA patients and fifteen healthy controls (HC) were enrolled. In the peripheral blood of RA patients, the expression levels of TIGIT in EM, Tfh and Tph was significantly higher in CD4+ T cells compared with that of HC ($p<0.0001$, $p=0.004$ and $p=0.003$). Further analyses showed a positive correlation between CDAI score in RA and TIGIT expression in those ($p=0.038$, $p=0.048$ and $p=0.029$). On the other hand, there was no remarkable findings in TIGIT expression on CD8+ T cells. [Conclusions] TIGIT expression on EM, Tfh and Tph in CD4+ T cells were positive correlation with disease activity in RA. T cell suppression by TIGIT may be a candidate of treatment option for RA.

ICW5-6

Localization of Toll-like receptors expressing immune-cells and immune-regulatory cells in synovial tissues of the patients with rheumatoid arthritis treated by abatacept

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Conflict of interest: None

[Objective] Abatacept (ABT) is one of biologics agents for rheumatoid arthritis (RA) which has improved the clinical results drastically and move a paradigm shift. ABT is a soluble fusion protein, which links the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA4) and bind to CD80/86. The aim of this study is to examine the effect of ABT for evaluating immune-reactive cells which express Toll-like receptors (TLR) in the synovial tissue samples of RA patients with ABT therapy (ABT groups) compared to them with conventional synthetic DMARDs therapy (csDMARD groups). [Methods] Synovial tissue samples of 42 RA (21 ABT and 21 csDMARD samples) were obtained from each patient with RA at the total knee or hip arthroplasty. They were immunohistochemically stained with TLR+ and immune-reactive cells including T cells, B cells, macrophage, conventional dendritic cells, regulatory T cells (FoxP3) and indoleamine 2, 3-dioxygenase+ cells (IDO) with inflammatory grading (0-3). TLR positive cells were analyzed by double Immunofluorescent methods. [Results] ABT and csDMARD group was shown the similar grading scores (2.2 vs 2.1), DAS28CRP4 (4.7 vs 4.4) and CRP (1.2 vs 1.0). IDO+ and FoxP3+ cells, not T cells, B cells and macrophages, were correlated significant with DAS28CRP (4) in lymphoid aggregation in ABT groups ($p< 0.01$). TLR immunoreactivity was also confirmed in plasmacytoid DCs and IDO+ cells by immunofluorescent staining. [Conclusions] TLR+ cells and immuno-inflammatory cells were remained with related local synovial tissue inflammatory grading, however, FoxP3, IDO, TLR7, TLR9+ cells in lymphoid aggregation were correlated with DAS28 in ABT group in this study. ABT might have potency of regulation joint inflammation and destruction due to CTLA4 and IDO pathway with anti-inflammatory effects.

ICW6-1

Identification of differentially expressed genes of microglia in lupus-prone mice

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Conflict of interest: Yes

[Objective] Neuropsychiatric systemic lupus erythematosus (NPSLE) is one of the most severe manifestations of SLE. Recently activated microglia have gained attention in the pathogenesis of NPSLE. The objectives of this study were to clarify the role of microglia and proinflammatory cytokines in NPSLE. [Methods] Microglia were isolated from 16-week-old (adult) MRL/MpJ-Fas^{lpr} (MRL/*lpr*) mice and MRL/MpJ mice. The activation of microglia was examined by gene expression levels of proinflammatory cytokines (*Tnfa, Il6, Il1b*) using real-time PCR. In order to assess the effects of different cytokines for microglial activation, microglia were isolated from 0-3-day-old MRL/*lpr* mice and cultured with or without the cytokines (IFNα, IFNγ, IL-6, and TNFα). Furthermore, we performed RNA sequencing to evaluate changes in their gene expression profiles of these cells. [Results] Gene expression levels of the proinflammatory cytokines in microglia of adult MRL/*lpr* mice were increased compared with the counterparts. The comprehensive gene expression analysis via RNA sequencing revealed a total of 901 differentially expressed genes (DEGs) with the upregulation in adult MRL/*lpr*. Gene ontology analysis indicated that the biological functions related to response to virus and cytokine-mediated signaling pathway, suggesting that microglia of MRL/*lpr* was activated by a series of proinflammatory cytokine stimulations. Indeed, the microglia turned into their activated phenotype by cytokine stimulation in vitro. Among 97 genes identified as the upregulated genes in

both microglia treated with cytokines and those from adult MRL/*lpr,* we focused on IkB epsilon (*Ikbke*) gene. The inhibitor of IKBKE ameliorated activated phenotype of microglia. [Conclusions] Microglia in MRL/*lpr* exhibit an activated phenotype associated with proinflammatory cytokines. IKBKE is a potential therapeutic target for NPSLE.

ICW6-2

Soluble Triggering Receptor Expressed on Myeloid Cells 2 (sTREM2) in Cerebrospinal Fluid as a Microglial Activation Surrogate for Development of Diffuse Psychiatric/Neuropsychological Syndromes in Patients with Systemic Lupus Erythematosus (dNPSLE)

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Conflict of interest: None

[Objective] sTREM2 is an activation marker for microglia related to behavioral abnormalities in mouse model of dNPSLE following anti-glutamate receptor subunit GluN2 antibody (anti-GluN2) exposure to neurons. The aim of this study is to investigate the potential role of sTREM2 as a factor surrogating microglial activation contributing to complication of dNPSLE in patients with SLE. [Methods] Lupus patients with NPSLE admitted to our hospital were collected. sTREM2 in serum and cerebrospinal fluid (CSF) were measured by ELISA, compared between dNPSLE and focal neurological manifestations of NPSLE (fNPSLE). Anti-GluN2, a previously known pathogenic and diagnostic factor for dNPSLE was also measured by ELISA. [Results] dNPSLE (N=25) and fNPSLE (N=13) were recruited. There was no significant difference in serum sTREM2 between dNPSLE (217.5, 0-3322.18 [median, range] pg/ml) and fNPSLE (438.0, 0-1571.84 pg/ml) (p=0.9208). In contrast, the CSF sTREM2 in dNPSLE patients were significantly higher (72.48, 0-173.9 pg/ml) than those in fNPSLE (0, 0-86.46 pg/ml) (p=0.0240). There was no correlation between the sTREM2 levels in serum and in CSF (r^2=0.0047, p=0.7611). Interestingly, the CSF sTREM2 significantly correlated with CSF anti-GluN2 (r^2=0.2516, p=0.0339) in patients with dNPSLE. [Conclusions] sTREM was specifically upregulated in CSF dNPSLE and corelated with anti-GluN2, a known pathogenic antibody in animal models. Our results indicate that sTREM2 is a potential surrogate for microglia activation induced by anti-GluN2-mediating neuronal damage in human with dNPSLE.

ICW6-3

Anti-TRIM21 antibody is associated with type I interferon and B-cell abnormalities in systemic lupus erythematosus

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Conflict of interest: None

[Objective] TRIM21 is an autoantigen that reacts with anti-SS-A antibody (Ab) present in sera of patients with systemic lupus erythematosus (SLE) and Sjögren's syndrome. Previous studies have shown that TRIM21 dysfunction promotes aberrant B-cell differentiation and Ab production, and anti- TRIM21 Ab may associate with the TRIM21 dysfunction in human SLE pathogenesis. Here we examined the effect of anti-TRIM21 Ab seropositivity on B-cell functions in SLE pathogenesis. [Methods] Twenty-seven patients with SLE before receiving immunosuppressive therapy and 4 healthy controls were enrolled in the study. The levels of cytokines and immunoglobulins were measured using a cytometer bead array. The expression level of TRIM21 protein in peripheral blood mononuclear cells (PBMCs) was evaluated by western blotting. [Results] Eight patients were seropositive for anti-TRIM21 Ab while 19 were seronegative. There were no significant differences in the background parameters between the seropositive and seronegative groups. The levels of interferon (IFN)-α and IFN-β were significantly higher in sera of SLE patients with anti-TRIM21 Ab as compared with those of healthy controls (5.0 ± 2.0 vs 18.9 ± 12.9 pg/ml, p = 0.04, and 19.9 ± 19.0 vs 163.1 ± 110.5 pg/ml, p = 0.02, respectively). The serum levels of IgG1, IgG3, and IgA were significantly higher in SLE patients with anti-TRIM21 Ab as compared with those without anti-TRIM21 Ab (1914 ± 864 vs 2547 ± 532 μg/ml, p = 0.005, 77.9 ± 33.3 vs 111.9 ± 25.5 μg/ml, p = 0.04, and 649.4 ± 252.8 vs 976.7 ± 512.9 μg/ml, p = 0.01, respectively) and healthy controls. SLE patients with anti-TRIM21 Ab showed a significantly lower expression level of TRIM21 protein in PBMCs as compared with those without anti-TRIM21 Ab (p = 0.03). [Conclusions] Anti-TRIM21 Ab may affect the TRIM21 functions in SLE pathogenesis and be a candidate for a novel biomarker for the contribution of type I IFN and B-cell abnormalities to the pathogenesis.

ICW6-4

CD38 modulates lipid raft formation in CD4 T cells from patients with SLE

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Conflict of interest: None

[Objective] Lipid rafts, membrane structure enriched with gangliosides, are increased and involved in abnormal T cell signaling in SLE. The mechanisms involved in lipid raft formation is not known. CD38-deficient mice are resistant to high-fat diet, suggesting CD38 may affect lipid metabolism. CD38 in CD4 T cells in SLE is increased and, thus, we hypothesized that CD38 is responsible for the increased lipid raft formation by altering the lipid profile in SLE. [Methods] CD38 knocked-out Jurkat cells was generated by Crispr/Cas9. CD4 T cells were isolated from healthy and patients with SLE. Lipidomics was performed by LC-MS/MS. Gangliosides, b4galnt1, orai1 level and calcium flux were measured by flow cytometry. Acetylation was measured by immunoprecipitation. Electroporation was performed by Amaxa nucleofector system. [Results] Choleratoxin-B, a raft marker, binding to the surface of CD4CD38+ cells from healthy subjects and patients with SLE was increased in amounts parallel to the levels of CD38. Lipidomics studies of CD38 deficient and sufficient Jurkat cells revealed clear differences in the profile of alpha-series of monosialogangliosides, showing a shift from GM3 to GM2 and GD1a. The expression of b4galnt1, which generates GM3 to GM2, was increased in CD4CD38+ cells in a CD38-dependent manner. Both acetylation and expression levels of b4galnt1 was dependent on SIRT1 activity regulated by CD38. Finally, CD4CD38+ cells from SLE subjects showed higher calcium flux compared to healthy subjects in b4galnt1-dependent manner. CD4CD38+ cells showed higher calcium entry with higher expression of Orai1, a major store-operated calcium entry channel. This suggests that CD38 recruits more orai1 by altering lipid raft composition and transduce increased amounts of calcium. [Conclusions] CD38 alters lipid raft formation by increasing b4galnt1. Altered lipid raft composition leads to increased Ora1 and increased calcium fluxes.

ICW6-5

GLUT1-dependent glycolysis in T-bet+CD11c+ B cell differentiation and its role in systemic Lupus erythematosus (SLE)

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Conflict of interest: None

[Objective] To clarify the cellular metabolism in differentiation of T-bet$^+$CD11c$^+$ B cells and their relevance to SLE. [Methods] For the *in vitro* exam, peripheral human B cells were sorted and divided into subsets, which were cultured under various stimuli. We assessed the generation of T-bet$^+$CD11c$^+$ B cells and their metabolic changes by flux analyzer. Further, the expression of T-bet and metabolic markers in B cells from SLE patients were examined by flow cytometry. [Results] ***In vitro*** **examination** 1) T-bet$^+$CD11c$^+$ B cells were maximally induced when IgD$^+$CD27$^-$ naïve B cells were stimulated with B cell receptor+CD40 ligand+IL-21+IFN-

γ+TLR9 ligand. In contrast, $IgD^{-}CD27^{+}$ class-switched memory B cells (CMs) differentiated into plasmablasts under the same stimuli. 2) Proinflammatory cytokines were predominantly produced when naïve B differentiated into $T\text{-}bet^{+}CD11c^{+}$ B cells, whereas IgG production was produced when CMs differentiated into plasmablasts. 3) The differentiation of naive B cells into $T\text{-}bet^{+}$ B cells relied mainly on glycolysis accompanied with GLUT1 upregulation whereas the differentiation of CMs into plasmablasts was accompanied with oxidative phosphorylation (OXPHOS)-dominant metabolic changes. 4) 2-Deoxy-D-glucose (glycolytic inhibitor) markedly suppressed proliferation of $T\text{-}bet^{+}$ B cells and cytokines production, while Metformin, which inhibits OXPHOS but not glycolysis, did not affect to them. **Analysis of patient samples** 5) The proportion of $T\text{-}bet^{+}$ B cells was higher in SLE patients compared with healthy controls. This proportion was also strongly associated with active nephritis. Additionally, expressions of p-S6 (reflecting mTORC1 activation) and GLUT1 were upregulated in $CD27^{-}$ B cells (included $T\text{-}bet^{+}$ B cells) compared to those in $CD27^{+}$ B cells. [Conclusions] We found that naïve B cells differentiated into $T\text{-}bet^{+}$ B cells via shifting to GLUT1-dependent glycolysis and may be involved in SLE pathogenesis. Metabolic regulation might be a novel therapeutic target for SLE.

ICW6-6

Identification of IFN-g-producing effector B cells in humans: Relevance to the pathogenesis of systemic lupus erythematosus

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Conflict of interest: None

[Objective] Clinical efficacy of B cell-targeting therapy underscores a crucial role of antibody (Ab)-independent functions such as cytokine production of B cells in the pathogenesis of autoimmune diseases. The type 2 interferon IFN-g is a key cytokine involved in systemic lupus erythematosus (SLE) and produced by a variety of immune cells. It, however, remains somewhat elusive whether human B cells have potential to produce IFN-g. Here, we have sought to identify IFN-g-producing effector B cells (IFN-g-Beffs) in humans and investigate their role in the pathogenesis of SLE. [Methods] Sorted B cell subsets from peripheral blood (PB) from healthy controls (HC) and patients with SLE were stimulated with $CD4^{+}$ T cell-related cytokines and Toll-like receptor (TLR) ligands, and subjected to the analysis of IFN-g expression at both mRNA and protein levels. We also analyzed the surface markers of IFN-g-Beffs in HCPB and investigated whether this subset exists in PB of patients with SLE. [Results] Among $CD4^{+}$ T cell-derived cytokines, IFN-g and IL-21 significantly induced the generation of IFN-g-Beffs from switched-memory (Sm) B cells. In the presence of anti-BCR/CD40L with IFN-g and IL-21 mimicking stimulation of Sm B cells by follicular helper $CD4^{+}$ type 1 cells (Tfh1 cells), IFN-g-Beffs were significantly induced in the $CXCR3^{+}$ fraction. In addition, CpG, a TLR9 ligand, facilitated the generation of IFN-g-Beffs, a characteristic marker of which was CD11c. The frequency of $CXCR3^{+}$ Sm B cells was higher in patients with SLE than in HC. Moreover, IFN-g-Beffs were detected in inflammatory lesions as well as PB and they were again enriched within the $CD11c^{+}$ subpopulations. Jak inhibitors inhibited the expression of IFN-g mRNA and protein in $CXCR3^{+}$ Sm B cells from patients with SLE. [Conclusions] Taken together, these findings suggest the existence of a novel human IFN-g-producing effector B cell subset that plays a role in the pathogenesis of SLE by closely interacting with $CD4^{+}$ T cells.

ICW7-1

A global atlas of genetic associations of 220 deep phenotypes enabled genetic-driven categorization of autoimmune diseases

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Conflict of interest: None

[Objective] The current genome-wide association studies (GWASs) do not yet capture sufficient diversity in terms of (i) population, in that the vast majority of GWASs have been predominated by European populations, (ii) scope of phenotypes, which have been limited to target diseases of a sampling cohort, and (iii) a systematic method to interpret a plethora of summary results for understanding disease pathogenesis and epidemiology. [Methods] To expand the atlas of genetic associations, here we conducted 220 deep-phenotype GWASs in BioBank Japan (BBJ), including 108 novel phenotypes ever conducted in East Asian populations. We then performed GWASs for corresponding harmonized phenotypes in UK Biobank (UKB) and FinnGen, and finally performed trans-ethnic meta-analyses (n = 628,000). We performed truncated singular-value decomposition (TSVD) on the matrix of GWAS summary statistics of 159 diseases, and derived latent components shared across the diseases. [Results] Through trans-ethnic meta-analyses, we identified over 4,000 novel loci, which substantially deepened the resolution of the genomic map of human traits, benefited from East Asian endemic diseases and East Asian specific variants. Further, TSVD of summary statistics identified latent genetic components, which pinpointed the responsible variants and shared biological mechanisms underlying current disease classifications across populations. We found a convergent component between rheumatoid arthritis and SLE, which implicated interleukin pathway and lymphoid-tissue specificity. The decomposed components also enabled genetically informed subtyping of similar diseases (e.g., type I vs IV allergic diseases). [Conclusions] Our study suggests a potential avenue for hypothesis-free re-investigation of human disease classifications through genetics.

ICW7-2

Polygenic risk scores predict radiographic progression in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To investigate polygenic risk scores (PRS) using Genome Wide Association Study (GWAS) data for rheumatoid arthritis (RA) susceptibility can be a predictor of radiographic progression. [Methods] We constructed the PRS using summary data from Asian GWAS meta-analysis and the genotyping data of RA patients in Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort. We analyzed difference of PRS between top quartile of patients (severe progression: SP) with Sharp/ van der Heijde score (SHS) progression in 5 years and rest of the patients (non-severe progression: non SP) by welch-t test. Next, we divided the subjects into five groups based on PRS and analyzed risk of SP in each group by referring to the lowest group. Finally, we performed logistic regression analysis for the SP using PRS and other factors. [Results] Nine-hundred and sixty-five RA patients who had SHS were analyzed. The mean (standard deviation) age was 56 (12.4) years old and 85.8% were female. The proportions of patients with anti- cyclic citrullinated peptide (CCP) antibody, methotrexate (MTX) user, and biological disease-modifying anti-rheumatic drugs (bDMARD) user were 84.8%, 49.0%, 9.0%, respectively. The median SHS in SP group was 49 (interquartile range (IQR) 41 to 66) and that of non-SP group was 11 (IQR 4 to 21). There was a significant difference between PRS of the two groups (-0.000484 vs -0.000530, p=0.006). Patients with top quintile of PRS had a higher risk for SP compared to those with bottom quintile of PRS (odds ratio (OR) = 1.98 (95% confidence interval (CI) 1.24-3.15). Multivariate logistic regression analysis showed that sex (female) (p = 0.0006, OR 2.53, 95%CI 1.49-4.28), Human Leukocyte Antigen (HLA)-DRB1 shared-epitope alleles (p = 0.008, OR 1.36, 95%CI 1.08-1.71), PRS (p =

0.0015, OR, 95%CI 1.27 1.09-1.48) were independent risk factors for SP. [Conclusion] PRS using GWAS data for RA susceptibility can be a predictor of radiographic progression.

ICW7-3

Autoimmunity associated HLAs regulate T cell receptor repertoire in vivo

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Conflict of interest: Yes

[Objective] Human Leukocyte Antigen (HLA) alleles strongly regulate the susceptibility to autoimmune diseases. This study aims to elucidate the immunological function of autoimmune-associated HLA alleles *in vivo*. [Methods] 407 Japanese individuals were included from the ImmuNexUT cohort of ten autoimmune disesease patients and healthy controls. Whole genome sequencing (WGS) and 28 purified immune cell RNA-sequencing were performed. HLA alleles were estimated from WGS. HLA alleles, that were associated with immune mediated diseases in Japanese cohorts, were considered to be "autoimmune-associated". MiXCR pipeline identified T cell receptor (TCR) in each T cell subsets and public clones shared between individuals. We tested associations between major HLA alleles and transcriptome, *TRBV* gene usage of TCR repertoire, and public clones. [Results] In the association tests between HLA alleles and immune cell transcriptome, significant associations at FDR < 0.05 were accumulated in extended MHC region and TCR gene expression. Associations between HLA class 2 alleles and TCR repertoire of CD4 T cell subsets were more eminent than class 1 HLA alleles. Autoimmune associated HLAs, such as HLA-DRB1*04:05 for rheumatoid arthritis, regulated *TRBV* gene usage of naïve and specific effector CD4 T cell subsets, but to a lesser extent in regulatory CD4 T cells or CD8 T cells. In addition, autoimmune associated HLAs regulated publicity of CD4 T cell clones. [Conclusions] This study revealed an *in vivo* evidence that HLA alleles regulate effector CD4 TCR repertoire in autoimmune patients. Identified immune cell subsets, genes, and TCR clones could serve as candidate diagnostic and therapeutic targets in the near future.

ICW7-5

Transcription factor T-bet represses collagen-induced arthritis by suppressing the activation of the gene encoding IL-17A through inhibition of expression and function of RORgt

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Conflict of interest: None

[Objective] To clarify the role of T-bet in the pathogenesis of collagen-induced arthritis (CIA). [Methods] 1) C57BL/6 wild-type (WT) mice and T-bet knockout (T-bet KO) mice were immunized with type II collagen (CII), and the incidence and severity of CIA were assessed. 2) After CII immunization, CD4+ T cells from draining lymph nodes (LNs) were stimulated with phorbol myristate acetate and ionomycin, and the percentage of IL-17A or RORγt-positive cells were measured by flow cytometry. 3) After CII immunization, CD4+ T cells and CD11c+ dendritic cells (DCs) isolated from draining LNs were cultured with CII, and the levels of IL-17A and IFNγ in culture supernatant were measured by enzyme-linked immunosorbent assay. 4) The expression levels of Th17 related-genes in CD4+ T cells after CII immunization were measured by qRT-PCR. 5) T-bet$^{flox/flox}$ mice and CD4-Cre T-bet$^{flox/flox}$ (conditional KO; cKO) mice were immunized with CII, and the incidence and severity of CIA were assessed. [Results] 1) The arthritis score and the incidence were significantly more severe in T-bet KO mice. 2) Percentage of RORγt-positive CD4+ T cells was significantly higher in T-bet KO mice. In RORγt-positive fraction, percentage of IL-17A+ CD4+ T cells was significantly higher in T-bet KO mice, but in RORγt-negative fraction, percentage of IL-17A+ CD4+ T cells was scarce and comparable. 3) CII-reactive IL-17 production was significantly higher but that of IFNγ was significantly lower in T-bet-deficient CD4+ T cells. The CII-reactive cytokine production was irrelevant to T-bet in DCs. 4) The expression levels of *rorc* and its downstream genes including *il17a* were significantly higher in T-bet-deficient CD4+ T cells. 5) The arthritis score and the incidence were more severe in cKO mice compared with T-bet$^{flox/flox}$ mice. [Conclusions] T-bet in CD4+ T cells repressed the pathogenesis of CIA, which might be due to suppression of both expression and function of RORγt, resulting in down-regulation of IL-17A production.

ICW7-6

Excessive Angiotensin II exacerbates bone erosion in a murine tumor necrosis factor-mediated arthritis model

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Conflict of interest: Yes

[Objective] Angiotensin II (Ang II) is the main effector peptide of the renin-angiotensin system (RAS), which regulates the cardiovascular system. The RAS is reportedly involved in bone metabolism. The upregulation of RAS components has been shown in arthritic synovial tissues, suggesting the potential involvement of Ang II in arthritis. Accordingly, in the present study, we aimed to investigate the role of Ang II in bone erosion and systemic bone loss using a murine arthritis model. [Methods] Ang II was infused by osmotic pumps in tumor necrosis factor-transgenic (TNFtg) mice. Arthritis, joint destruction, and systemic bone loss were examined by clinical observation of paw swelling or erythema, histology, and micro-computed tomography. To suppress endogenous Ang II, Ang II type 1 receptor (AT1R)-deficient mice were crossed with TNFtg mice. Inflammation and bone properties were evaluated as mentioned above. [Results] Ang II infusion did not significantly affect the severity of clinical and histological inflammation, whereas bone erosion in the inflamed joints was significantly augmented in association with increased osteoclast formation. Ang II administration did not affect the bone mass of the tibia or vertebra. Genetic deletion of AT1R did not significantly affect inflammation, bone erosion, or systemic bone loss. [Conclusions] Exogenous Ang II administration significantly exacerbated joint destruction without affecting inflammation. These results suggest that excessive systemic activation of the RAS can be a risk factor for progressive joint destruction. Our findings indicate an important implication for the clinical use of RAS inhibitors in patients with rheumatoid arthritis.

ICW8-1

Accuracy of the physical examination of the foot and ankle through socks or stockings in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Foot and ankle joint disorders are serious issues for patients with rheumatoid arthritis (RA). Rheumatoid foot is also reported as the first symptom of the disease in 43% of patients with RA in Japan. However, physicians tend to omit examinations of the foot and ankle in routine practice. One of the reasons is that it consumes a lot of time within tight time constraints. The aim of this study was to evaluate the accuracy of the physical examination of the foot and ankle through socks and stocking in patients with RA. [Methods] From November 2019 to September 2020, 48 patients with RA were enrolled in this study. Patients who underwent previous foot surgeries were excluded. Standard socks and stockings were prepared for this study. A rheumatologist and a senior resident performed physical examination of the foot and ankle to assess swelling and tenderness in the order of wearing socks, wearing stockings, and bare feet.

Concordance rates between barefoot examinations by the rheumatologist and examinations through socks and stockings were investigated. [Results] The rheumatologist had a concordance rate of 95.7% through socks, and 99.2% through stockings. The senior resident had a concordance rate of 90.2% through socks, and 89.2% through stockings. The concordance rate of bare foot examinations between the rheumatologist and the senior resident was 89.9%. [Conclusions] Examinations through socks and stockings by both the rheumatologist and the senior resident had high concordance rates with the bare foot examinations by the rheumatologist. This study showed that physical examination of the foot and ankle through socks or stockings may be an option to decrease the examination time of the foot and ankle in RA patients.

ICW8-2

The influence of escalated PGA score on daily activity and quality of life for patient with rheumatoid arthritis

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Conflict of interest: None

[Objective] The influence of escalated patient's global assessment (PGA) score on disease activity, daily activity, and quality of life for patient with rheumatoid arthritis (RA) was investigated. [Methods] A total of 24,075 times of monitoring for RA was performed. Contents of monitoring included TJC, SJC, PGA, EGA, CRP, and calculated values of DAS28, CDAI, SDAI, composite index of Boolean evaluation (Boolean), pain score with visual analog scale (PS-VAS), Health Assessment Questionnaire Disability Index (HAQ-DI), and quality of life score (QOLS) calculated from Euro-QOL questionnaire with 5th dimensions. Each measurement was classified with the PGA score divided by one increment from zero to ten. Mean values of DAS28, CDAI, SDAI, remission rate of these indices and Boolean remission rate, and mean values of PS-VAS, HAQ-DI, and QOLS were statistically evaluated. [Results] Number of measures counted 10428, 3099, 3110, 2346, 998, 1773, 751, 703, 655, 139, and 73 for each level of PGA. PGA level from 3 to 5, and 5 to 10 were put together for number adjusting. Mean DAS28, CDAI, and SDAI demonstrated significant increase as PGA level increased, and remission rate of the all indices including Boolean demonstrated significant decrease as PGA level increases ($p<0.01\%$). Boolean remission rate demonstrated zero percent from two, and CDAI and SDAI remission rate demonstrated zero from five, whereas DAS remission rate showed gradual decrease then zero percent was not shown in any level. Mean value of PS-VAS and HAQ-DI score demonstrated also significant decrease as PGA level increases, and QOLS demonstrated significant decrease as PGA level increases ($p<0.01\%$). Increase of HAQ-DI score and decline of QOLS demonstrated more steep from PGA level 3, whereas no significant difference demonstrated from zero to one. [Conclusions] Increase of PGA affects daily activities and quality of life. However, evident level that increases deterioration risk was supposed to be from three of PGA.

ICW8-3

Optimal level of patient's global assessment that deserves clinical remission in patient with rheumatoid arthritis

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Conflict of interest: None

[Objective] Patient's global assessment (PGA) is one most difficult component in part of disease activity index for treatment of rheumatoid arthritis (RA), that often causes an obstacle to attaining clinical remission. Moreover, PGA level influences daily activities. The optimal level of PGA score for both disease activity and daily activities was investigated from real world data. [Methods] A total of 24,038 times of monitoring for RA was performed. Contents of monitoring included TJC, SJC, PGA, EGA, CRP, and calculated values of DAS28, CDAI, SDAI, composite index of Boolean evaluation (Boolean), pain score with visual analog scale (PS-VAS), and Health Assessment Questionnaire Disability Index (HAQ-DI). Each measurement was classified with the PGA score divided by one increment from zero to ten. HAQ-DI below 0.5 was determined as remission (HAQ remission). Sensitivity and specificity regarding attaining HAQ remission according to each level of PGA score were calculated, and cutoff index (COI) was determined with receiver operating characteristic (ROC) curve. For PS-VAS, sensitivity and specificity of Boolean remission regarding each level of PS-VAS after classification divided by one increment was calculated, and comparable level (PS-VAS remission) was determined with reference of the curve. ROC was performed according to PGA level, and COI was determined with a same manner. [Results] HAQ remission counted 15,703, whereas no HAQ remission counted 8,335. Using ROC, COI of the PGA level was 2.0, whereas sensitivity and specificity were 63.4% and 66.3%, respectively. PS-VAS remission level was 10 mm. Optimal PGA level was 1.0, and sensitivity and specificity regarding PS-VAS remission were 87.1% and 71.3%, respectively. [Conclusions] Optimal level of PGA score for attaining both PS-VAS and HAQ-DI is 1.0.

ICW8-4

Impact of achieving zero in patient's global assessment for patient with rheumatoid arthritis

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Conflict of interest: None

[Objective] Impact of achieving zero in patient's global assessment (PGA) in treating rheumatoid arthritis (RA) was investigated from one institute's real world data. [Methods] A total of 24,075 times of monitoring for patient with RA was performed. Contents of monitoring included TJC, SJC, PGA, EGA, CRP, and calculated values of DAS28, CDAI, SDAI, composite index of Boolean evaluation (Boolean), pain score with visual analog scale (PS-VAS), Health Assessment Questionnaire Disability Index (HAQ-DI), and quality of life score (QOLS) calculated from Euro-QOL questionnaire with 5thdimensions. Each measurement was classified with the PGA score; PGA=0 (G=0), PGA>0 and PGA<=1 (G≦1), and PGA>1 (G>1). Statistical significances between the two groups of these were determined for each of parameters and Boolean remission rate, DAS28 remission rate, CDAI remission rate, and SDAI remission rate. [Results] Number of measurement for the groups counted 10,428, 3,099, and 10,528 for G=0, G≦1, and G>1, respectively. Mean values of DAS28, CDAI, SDAI, DAS28 remission rate, CDAI remission rate, SDAI remission rate, and Boolean remission rate were 2.09, 1.67, and 1.59, 8.19, 2.65, and 1.21, 8.87, 3.01, and 1.63, 66.2%, 86.4%, and 89.4%, 17.7%, 70.4%, and 84.8%, 22.6%, 71.2%, and 83.6%, and 0.0%, 70.2%, and 77.0%, for G=0, G≦1, and G>1, respectively. All parameters demonstrated significant difference between the two groups within 0.01%. Mean values of PS-VAS, HAQ-DI, and QOLS were 39.1, 12.5, and 13.1, 0.598, 0.307, and 0.331, and 0.789, 0.868, and 0.865, for G=0, G≦1, and G>1, respectively. There were significant difference within 0.01% between those of the G=0 and the G>1, and G≦1 and the G>1, however, no significant difference between those of the G=0 and G<=1 demonstrated. [Conclusion] The impact of achieving zero in PGA is evident for the disease activity indices, however, it is not so much for the other parameters. In the other parameters PGA within 1 is more meaningful.

ICW8-5

Evaluator's global assessment reflects disease activity but not linearly correlates with daily activity or quality of life compared to patient' global assessment

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Conflict of interest: None

[Objective] Influence of evaluator's global assessment (EGA) on disease activity and daily activity, and quality of life were investigated. [Methods] A total of 24,075 times of monitoring for RA was performed. Contents of monitoring included TJC, SJC, PGA, EGA, CRP, and calculated values of DAS28, CDAI, SDAI, composite index of Boolean evaluation (Boolean), pain score with visual analog scale (PS-VAS), Health Assessment Questionnaire Disability Index (HAQ-DI), and quality of life

score (QOLS) calculated from Euro-QOL questionnaire with 5th dimensions. Each measurement was classified with the EGA score divided by one increment from zero to ten. Mean values of DAS28, CDAI, SDAI, remission rate of these indices and Boolean remission rate, and mean values of PS-VAS, HAQ-DI, and QOLS were statistically evaluated. Results were compared to the results that was analyzed in according to the PGA score substituted with the EGA score. [Results] Number of measures counted 15424, 2001, 3688, 1731, 664, 293, 144, 88, 29, 2, and 11 for each level of EGA. The EGA score tended to concentrate more in zero to two in comparing to the PGA score. Mean DAS28, CDAI, and SDAI demonstrated significant increase as the EGA level increased, and remission rate of the all indices including Boolean demonstrated significant decrease as the EGA level increases ($p<0.01\%$). CDAI, SDAI, and Boolean remission rate demonstrated zero percent from two. Mean value of PS-VAS and HAQ-DI score demonstrated also significant decrease as the EGA level increases, and QOLS demonstrated significant decrease as the EGA level increases ($p<0.01\%$). However, these tendency showed more irregular compared to that analyzed with the PGA score. Correlation coefficients with regarding to the EGA score was always less than that with regarding to the PGA score. [Conclusions] It is more reliable to estimate daily activity and quality of life from the PGA score than to estimate from the EGA score.

ICW8-6

The impact of time to achieve Boolean remission on maintaining disease activity after achievement in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the association of time span from treatment initiation to first Boolean remission with maintaining disease activity, daily activity and quality of life (QOL) after attaining Boolean remission based on data in real-world settings. [Methods] Data of 465 patients treated for more than three consecutive years and achieved Boolean remission more than once were evaluated. The relationship of time span from treatment initiation to first remission (TS) and baseline patient data at RA diagnosis were evaluated. Statistical analyses included evaluating the relationship of TS with simplified disease activity index (SDAI) score, modified health assessment questionnaire-disability index (HAQ-DI) score, pain score with visual analog scale (PS-VAS), Sharp/van der Heijde score (SHS), and QOL score (QOLS) calculated from the EuroQol-5th dimension-5L at first remission and thereafter. The patients were divided into those with TSs of ≦6 months (G ≦ 6) and >6 months (G > 6) to compare changes in study parameters and Boolean remission rate (BRR) after the first remission between the two groups. [Results] PS-VAS, SHS and QOLS at first remission and thereafter were significantly correlated with TS; these parameters at baseline were also significantly correlated with TS. TS was significantly correlated with SDAI score, HAQ score, PS-VAS, SHS and QOLS after the remission. The SDAI score and BRR after first remission were significantly better in the G ≦ 6 group than in the G > 6 group. [Conclusion] TS is an important key to maintain SDAI score, HAQ score, PS-VAS, SHS and QOLS.

ICW9-1

Altered cellular phenotypes in bronchoalveolar lavage fluid of connective tissue disease-associated interstitial lung disease with single-cell RNA sequencing

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Conflict of interest: Yes

[Objective] Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a severe complication of autoimmune disease, e.g. rheumatoid arthritis (RA), dermatomyositis (DM), systemic sclerosis (SSc), Sjogren's syndrome (SjS) and so on. CTD-ILD is a heterogeneous syndrome by driven by different diseases and cell types. This complexity provides a challenging field for elucidating the mechanism of the disease. We try to clarify the pathological difference of CTD-ILD complicated by different autoimmune diseases. [Methods] We collected bronchoalveolar lavage fluid (BALF) through bronchoscopy from 4 RA, 5 DM, 2 SSc, 4 SjS patients who complicated interstitial pneumonia, and 6 idiopathic interstitial pneumonia (IIP) patients as controls. Multi-color flowcytometry (MCFC) was applied to BALF samples from CTD-ILD patients of different connective tissue diseases and IIP patients. We estimated cytokine/chemokine levels in BALF from each patient with multiple ELISA. We applied Seq-Well, a robust, portable, and cost-efficient platform for massively parallel single-cell RNA sequencing (scRNA-seq) to analyze immune cells in BALF of CTD-ILD patients. [Results] We found neutrophils increased in BALF of RA patients, while lymphocytes increased in BALF of DM and SjS patients calculated with MCFC. The concentrations of IL-12p40 and CXCL10, both are associated with lymphocyte chemotaxis, were increased in BALF of DM patients. By using scRNA-seq, we found 13 different phenotypes of alveolar macrophages in CTD-ILD patients and the strong connection between alveolar macrophages and $CD16^+$ blood monocytes. [Conclusions] Neutrophils increase in BALF of RA patients while lymphocytes increase in those of DM and SjS patients, possibly because of altered chemokine levels in BALF. Alveolar macrophages showed different phenotypes in CTD-ILD patients from those in IIP patients, indicating altered functions of these cells in CTD-ILD. Further analysis is ongoing.

ICW9-2

Transcriptome analysis of alveolar macrophages identifies involvement of PD-1/PD-Ls in pathogenesis of rheumatoid arthritis-associated interstitial lung disease

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Conflict of interest: None

Objective: As we have presented, PD-1 were highly expressed on alveolar T cells in patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD) and most of PD-1++CD4+ T cells in bronchoalveolar lavage fluid were considered peripheral helper T cells, and PD-1 expression on alveolar CD4+ T cells could be affected by alveolar macrophages (AMs). To clarify it, we examined the transcriptional differences of AMs by disease. Methods: Transcriptome analysis of AMs from 5 patients with RA-ILD and 5 patients with drug-induced interstitial lung disease (DI-ILD) were performed. Differentially expressed genes were extracted by setting the criterion for statistical significance as a P value < 0.05 and an absolute log fold change > 1.2. Results: By gene ontology enrichment analysis, macrophages chemotaxis related pathways were upregulated in RA-ILD compared with DI-ILD. In RA-ILD, toll-like receptor 4 signaling pathway was upregulated and regulation of activated T cell proliferation and positive regulation of adaptive immune response were downregulated compared with DI-ILD. To examine how to interact between AMs and PD-1+ T cells, *CD274* and *PDCD1LG2*, the gene names of PD-ligand (PD-L) 1/2, were significantly downregulated in RA-ILD compared with DI-ILD (P = 0.0496 and 0.0002, respectively). Conclusions: The result of gene ontology enrichment analysis was suggestive of a proinflammatory status in AMs of RA-ILD. Insufficient regulation of PD-1 on alveolar T cells by PD-Ls on AMs might be important in pathogenesis of RA-ILD.

ICW9-3

Treatment of Interstitial Pneumonia with Autoimmune Features Refractory to Conventional Therapy: A Single-center Observational Cohort Study

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Conflict of interest: None

[Objective] Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue disease (CTD), a condition recently

termed interstitial pneumonia with autoimmune features (IPAF). To date, however, few studies have comprehensively described treatment choices for these patients in real-world practice. The aim of this study was to investigate therapeutic strategies in patients with refractory IPAF. [Methods] We enrolled 68 patients who were diagnosed with IPAF at our department between April 2009 and March 2019. Of these, 30 patients were treated with glucocorticoid (GC) and/or immunosuppressants (IS) and were divided into two groups, a monotherapy (GC) and a combination therapy (GC and IS) group. The other 38 patients were untreated. Clinical, laboratory and imaging data were collected from medical records and statistically analyzed. [Results] Among the treated and untreated patients, exacerbation rate was 46.7% (n=14) and 7.9% (n=3) (P=0.0002), respectively. Among the treated patients, smoking history and high titer of KL-6 were significant risk factors for exacerbation (P=0.008 and 0.019, respectively). The number of risk factors was positively and significantly associated with the rate of exacerbation (P=0.0007). There was no significant difference in treatment method between patients with and without risk factors. On comparison of long-term outcomes between the monotherapy and combination therapy groups, 3-year non-exacerbation rate was 68.6% and 32.7% (P=0.14), respectively. The rate of severe adverse events requiring hospitalization due to infections such as pneumonia was 21.4% and 6.7% (P=0.24), respectively. [Conclusions] IPAF patients with risk factors had a high exacerbation rate regardless of treatment. New interventions aimed at preventing exacerbation in these patients are required.

ICW9-4

Quantitative evaluation of chest CT differentiates the dominance of pulmonary vascular disease or interstitial lung disease on hemodynamic abnormalities in systemic sclerosis

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Conflict of interest: None

[Objective] Group 1 and 3 pulmonary hypertension (PH) develop through different pathological mechanisms but have similar hemodynamic abnormalities. Systemic sclerosis (SSc) is associated with both pulmonary vascular disease (PVD) and interstitial lung disease (ILD), making it challenging to differentiate group 1 and 3 PH in those patients. We aimed to assess the dominance of PVD or ILD in SSc patients by quantitative evaluation of chest computed tomography (CT). [Methods] A total of 76 SSc patients were included. Chest CT was evaluated by artificial intelligence (AI) and using a software (Synapse Vincent Ver.3.0, Fujifilm). Patients were divided into four groups according to PFT (forced vital capacity (FVC) of <60%, 60-70%, 70-100% and >100%). After training by transfer learning with representative images, attempted to predict the patient grouping. The dominance of PVD or ILD was defined as divergent or parallel change between the first and last CT, respectively, in mean pulmonary arterial pressure (mPAP) and abnormal area in the lung (%) calculated using a software. P values were calculated by Mann-Whitney U test. [Results] The median [range] values of mPAP and FVC were 23 [9-65] mmHg and 85.7 [24.6-136.5] %. AI only moderately predicted the PFT-based patient grouping from chest CT with accuracy of 52.4%. Further, normal lung volume calculated using a software only moderately correlated with FVC (r=-0.475). Of 37 SSc and PH patients, 18 were defined as PVD dominance while 19 as ILD dominance. Abnormal area in the lung at baseline was greater (p=0.002), whereas PFT parameters, including FVC (p=0.38), at baseline were not different, in patients with ILD dominance compared to those with PVD dominance. [Conclusions] Given that even AI insufficiently estimated FVC from chest CT, chest CT findings and PFT would be independent parameters. Quantitative evaluation of chest CT may be superior to PFT in terms of the differentiation of PVD or ILD dominance in SSc and PH patients.

ICW9-5

The evaluation of relationship between occurrence of spontaneous pneumomediastinum and mortality in dermatomyositis or polymyositis patients with interstitial lung disease: A retrospective cohort study

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Conflict of interest: None

[Objective] Spontaneous pneumomediastinum (SPNM) has been considered as a poor prognostic factor in dermatomyositis (DM)/polymyositis (PM) patients with interstitial lung disease (ILD). It was reported that anti-melanoma differentiation associated gene 5 (MDA5) antibody-positive patients, known as a new subgroup with a poor prognosis, frequently had SPNM. Thus, we hypothesized that SPNM is not a true risk factor for death but a confounding factor of anti-MDA5 antibody positivity. We aimed to evaluate the relationship between the occurrence of SPMN and mortality in DM/PM patients with ILD adjusting the anti-MDA5 antibody status. [Methods] We retrospectively identified PM/DM/clinically amyopathic DM (CADM) patients with ILD who were admitted to our hospital for treating PM/DM/CADM from 2013 to 2019. The diagnosis of SPNM was based on computed tomography images. The outcome was time to death within one year from therapy initiation or strengthening. We collected baseline characteristics and treatments by chart review. We performed cox-regression analysis adjusting anti-MDA5 antibody status to investigate SPNM mortality risk. [Results] Forty-six patients were included in this study. Anti-MDA5 antibody was positive in 17 patients (37%). SPMN occurred in 11 of 46 patients (24%), while it occurred in eight of 17 anti-MDA5 antibody-positive patients (47%). Four deaths were observed in the SPNM group, while two were observed in the non-SPNM group. All decedents in the SPMN group was anti-MDA5 antibody-positive. Although the mortality rate in the SPNM group was significantly higher than in the non-SPMN group in univariate analysis, the mortality rate was not significantly different between the groups when adjusting anti-MDA5 antibody status in the multivariate analysis. [Conclusions] Our study suggests that SPNM occurred in PM/DM/CADM patients is not a poor prognosis factor but a confounding factor of anti-MDA5 antibody-positive patients with ILD.

ICW9-6

Predictive factors of pneumomediastinum during management of connective tissue disease-related interstitial lung disease: A retrospective study

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Conflict of interest: None

[Objective] To identify factors associated with pneumomediastinum (PNM) during management of connective tissue disease (CTD)-related interstitial lung disease (ILD). [Methods] The subjects were patients with CTD-ILD who admitted to our department between Dec 2014 and Nov 2019, and initiated corticosteroid therapy for ILD. We retrospectively examined 1) comparison of baseline characteristics between patients who developed PNM after the initiation of corticosteroid therapy (PNM group, n=13) and those who did not develop PNM (control group, n=49), 2) clinical course of patients with PNM, and 3) identification of factors associated with development of PNM. [Results] 1) The age and gender were comparable between PNM and control (CTL) groups, while body mass index (BMI) was significantly lower in PNM group than in CTL group. The proportion of CADM and serum LDH was significantly higher, and PaO2 and %DLCO were significantly lower in PNM group than in CTL group. The proportion of methyl PSL pulse therapy and cyclosporine use was significantly higher in PNM group than in CTL group. 2) All PNM (n=13) occurred less than 120 days after the initiation of corticosteroid therapy. At a mean follow-up time of 748±709 days after the initiation of therapy, 9 patients were alive and 4 patients died. All 4 patients died because of respiratory failure associated with ILD. 3) BMI (OR [95%CI]: 0.482 [0.272-0.853]) and serum LDH (1.013 [1-1.025]) at baseline were identified as independent factors associated with development of PNM after the initiation of corticosteroid therapy by multiple logistic regression analysis. The

optimal cutoff point of BMI and LDH for predicting PNM based on ROC analysis were 20.2 kg/m² and 378 U/l, respectively. LDH provided the highest specificity of 87.8%, while BMI and/or LDH provided the highest sensitivity of 100%. [Conclusions] Low BMI and high serum LDH at baseline might be useful predictive factors for the development of PNM in patients with CTD-ILD.

ICW10-1

IL-6 signal inhibition by SAR s. c q2w demonstrated significantly higher level than that of TCZ s. c q2w but lower than TCZ s. c q1w

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Conflict of interest: None

[Objective] Interleukin-6 (IL-6) plays an important role in the pathophysiology of rheumatoid arthritis (RA). Tocilizumab (TCZ) and Sarilumab (SAR) are monoclonal antibodies which binds to membrane and soluble forms of human IL-6 receptor and inhibits IL-6/STAT3 signaling. We had previously reported the bioassay for measuring the strength of IL-6/STAT3 signal inhibition by TCZ. In this study, we measured phosphorylated STAT3 (pSTAT3) in RA patients treated with subcutaneous (s. c) administration of TCZ and SAR, in order to assess the difference in strength of IL-6/STAT3 signal inhibition among both medications. [Methods] RA patients who achieved low disease activity (CDAI<=10) by treatment with weekly or biweekly administration of 162 mg s. c of TCZ (TCZ q1w, n = 8, and TCZ q2w group, n = 8), and those with 200 mg s. c of SAR biweekly (SAR q2w group, n = 7) were collected. Clinical characteristics of each groups were studied, the concentration of serum IL-6 and soluble IL-6 receptor (sIL-6R) were measured by ELISA. Whole blood samples from each group were stimulated with 100 ng/ml of IL-6. The proportion of pSTAT3 positive CD4+ T cells was measured by phosflow cytometric analysis. [Results] The clinical characteristics, concentration of serum IL-6 and sIL-6R of each group were not significantly different between each group. Proportion of pSTAT3 positive CD4+ T cells stimulated by 100 ng/ml of rhIL-6 showed significant difference in each group (median 1.8 [0.9-3.0] % vs 7.7 [2.9-8.0] % vs 12.5 [11.4-16.6] % in TCZ q1w, SAR q2w, TCZ q2w group, respectively, $p<0.05$ for all comparisons). [Conclusions] The strength of IL-6/STAT3 signal inhibition by SAR 200 mg q2w showed significantly higher level than that of TCZ s. c q2w but lower than TCZ s. c q1w. The result of this study might be useful in considering the adjustment of the strength of IL-6 blockade treatment in each RA patient.

ICW10-2

Difficult-to-treat RA with respect to responsiveness to b/tsDMARDs - from the FIRST registry

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Conflict of interest: Yes

[Objective] Difficult-to-treat rheumatoid arthritis (dt-RA) is an emerging concept defined as persistency of signs and/or symptoms despite prior treatment. However, it has not been elucidated whether number of biologic and targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs) treatment failures affect status of refractoriness to another treatment. Therefore, this study aimed to find cut-off values for dt-RA with respect to responsiveness to newly used b/tsDMARDs. [Methods] A retrospective cohort study was conducted using the FIRST registry of University of Occupational and Environmental Health, Japan. An inadequate response to current b/tsDMARDs was defined as clinical disease activity index >10 at week 22 or termination of treatment within 22 weeks due to insufficient efficacy. Cut-off values were defined according to the number of past failures to DMARDs and current dose of glucocorticoid. Responsiveness to newly used b/tsDMARDs were compared with respect to above- versus below- cut-off values. Hazards of treatment cessation due to adverse events were compared using the same thresholds. [Results] Failures to more than one conventional synthetic DMARDs (csDMARDs) and more than three b/tsDMARDs were independent cut-off values associated with poor responsiveness to newly used b/tsDMARD treatment. Failures to more than two csDMARDs and concomitant use of glucocorticoid were significantly correlated with an increased hazard of infection. Failures to more than one csDMARDs was weakly associated with less improvement in titre of erythrocyte sedimentation rate, while that to more than three b/tsDMARDs was associated with less improvement in health assessment questionnaire. [Conclusions] We propose cut-off values of two or more failures to csDMARDs and/or four or more b/tsDMARDs as a definition of dt-RA with respect to responsiveness to use of b/tsDMARDs.

ICW10-3

Effectiveness of biological DMARD/JAK inhibitor monotherapy in patients with rheumatoid arthritis - ANSWER longitudinal cohort study -

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Conflict of interest: None

[Objective] To examine the drug tolerability, discontinuation reasons, and effectiveness of biological DMARD/JAK inhibitor (bDMARD/JAKi) in rheumatoid arthritis (RA) patients in a longitudinal multicentor cohort study. [Methods] All RA patients treated with bDMARD/JAKi monotherapy without any conventional synthetic DMARDs (csDMARDs) were included. The drug retention was compared among bDMARD/JAKi monotherapy using Cox proportional hazards models adjusted with inverse probability of weights (IPW) estimated by generalized propensity score and using a random effect to account for multiple treatment courses (TCs) per patient after multiple imputation by chained equations. CDAI change over time was graphically displayed with a generalized additive mixed-effect model and analyzed using a bi-linear mixed-effect model adjusted with IPW for longitudinal data. [Results] A total of 833 TCs from 647 patients was included (CTLA4-Ig: 194TCs, IL-6i: 215, JAKi: 66, TNFi: 358). Drug discontinuation was significantly higher in TNFi monotherapy than IL-6i (HR: 1.37, 95%CI: 1.04-1.80, P=0.02) but similar among CTLA4-Ig, IL-6i, and JAKi. The low retention rate of TNFi monotherapy was mainly attributable to lack of effectiveness (HR: 1.36, 95%CI: 1.01-1.84, P=0.04). JAKi monotherapy was more likely to discontinue due to remission (P=0.004) while csDMARDs were more likely to be added during monotherapy in CTLA4-Ig (P=0.04). In terms of CDAI change over time, all the monotherapies were similar in the initial 4 months, but TNFi monotherapy had worse slope as of 4 months (0.94/month, P=0.03), suggesting lack of effectiveness in TNFi monotherapy may be due to secondary failure. [Conclusion] CTLA4-Ig, IL-6i, and JAKi monotherapy were superior to TNFi in terms of drug retention and effectiveness. The discontinuation reasons, however, differ based on type of bDMARD/JAKi-IR. Because the number of patients with JAKi monotherapy was relatively smaller than that of the others, larger studies are needed.

ICW10-4

Drug with different vs same mode of action in patients with rheumatoid arthritis and an inadequate response to bDMARD/JAKi - ANSWER longitudinal cohort study -

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Conflict of interest: None

[Objective] To examine the drug tolerability, discontinuation reasons, and effectiveness of drugs with different and same modes of action (MOA) in RA patients with inadequate response to biological DMARD/JAK inhibitor (bDMARD/JAKi-IR) in a longitudinal multicentor cohort study. [Methods] All RA patients treated with an alternative bDMARD/JAKi after a prior bDMARD/JAKi-IR were included. The drug retention of different MOA was compared with same MOA using Cox proportional hazards models adjusted with inverse probability of weights (IPW) and using a random effect to account for multiple treatment courses (TCs) per patient after multiple imputation by chained equations. CDAI change over time was graphically displayed with a generalized additive mixed-effect model and analyzed using a bi-linear mixed-effect model adjusted with IPW for longitudinal data. Subgroup analyses based on type of bDMARD/JAKi-IR were conducted. [Results] A total of 829 TCs from 564 patients was included, of which 644 (77%) TCs were initiated as different MOA. Drug discontinuation was significantly lower in different MOA than in same MOA (HR: 0.70, 95%CI: 0.53-0.93, P=0.02). The low retention rate of same MOA was mainly attributable to lack of effectiveness (HR: 0.67, 95%CI: 0.49-0.93, P=0.02). In terms of CDAI change over time, different MOA was similar to same MOA in the initial 3 months (P=0.49), but had better slope than same MOA as of 3 months (-0.68/month, P=0.007), suggesting difference in lack of effectiveness may be due to secondary failure. In subgroup analyses, different MOA had better retention rate than same MOA among TNFi-IR (P<0.001), but similar rate among IL-6i-IR (P=0.17) and JAKi-IR (P=0.09). [Conclusion] Overall, MOA should be changed in RA patients with bDMARDs/JAKi-IR. The effectiveness may, however, differ based on type of bDMARD/JAKi-IR. Because the number of patients with IL-6i-IR and JAKi-IR were relatively smaller than that of TNFi-IR, larger studies are needed.

ICW10-5

The possibility of drug free remission after sustained remission in patients with RA - The three-year results of the FREE-J study, a real world prospective observational cohort study

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Conflict of interest: None

Objective: To investigate the possibility of drug free remission in patients with RA who achieved sustained remission. Methods: 427 patients who were treated with combination of MTX (≧8 mg) and bDMARDs (TNFi: 324, TCZ: 70, ABT: 33) and sustained remission were assigned to five groups according to the following treatment strategies by shared decision making; 1) continue all DMARDs (n=80), 2) reduce MTX (n=184), 3) discontinue MTX (n=24), 4) reduce bDMARDs (n=68), and 5) discontinue bDMARDs (n=71). After 1 year, the patients who maintained remission (DAS28ESR <2.6) discontinued either MTX or bDMARDs step by step, otherwise continued the same treatment. The remission rate and associated factors at year 3 were assessed. Results: The remission rate at year 1 was 1) 86%, 2) 82%, 3) 79%, 4) 75%, and 5) 55%, and the discontinuation of bDMARDs (group 5) was significantly lower remission than the continuation of all DMARDs (group 1) (p=<0.001). Immediate discontinuation (n=43) vs step-down discontinuation (n=19) of bDMARDs for achievement remission at year 2 was higher in immediate discontinuation (72% vs 21%, p=<0.001). Among the 259 patients who were not flaring at year 3, the remission rate of patients who continued bDMARDs (n=125) was 74%, reduced bDMARDs (n=44): 61%, and discontinued bDMARDs (n=90): 56%. The remission of bDMARDs discontinuation was significantly low (p=0.005). It was difficult to sustained remission after discontinuing bDMARDs. The number of drug free patients was 41, with 54% remission, 71% LDA and 29% flare (the median duration from drug free to flaring was 21 weeks). The remission rate for MTX discontinuation dropped from 67% in year 2 to 58% in year 3, depending on the usage of bDMARDs. Conclusions: Reduction of MTX, discontinuation of MTX, and reduction of bDMARDs may be an acceptable therapeutic option after sustained remission in RA patients. The usage of bDMARDs was the most important factor associated with sustained remission for clinical practice.

ICW10-6

Potential of anti-TIM-3 antibodies as novel biologics for the treatment of rheumatoid arthritis

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Conflict of interest: Yes

[Objective] TIM-3 was originally identified through a screen for TH1-specific markers, but since then it has also been found on cytotoxic CD8+ T cells, TH17, Treg, monocytes, dendritic cells, mast cells and microglia. Moreover, recent data show that Gal-9 suppresses the generation of Th17 and promotes the induction of regulatory T cells in a collagen-induced arthritis model. In preliminary study, we demonstrated that arthritis score correlated with the number of CD11b+TIM-3+ cells in splenocytes and administered anti-TIM-3 antibody to spontaneous arthritis mice. [Methods] SKG mice were treated with anti-TIM-3 antibodies three times a week to determine the effect on arthritis scores. [Results] ZyA was administered and anti-TIM-3 antibody treatment was started after inducing arthritis and evaluated after 9 weeks. The arthritis score in the anti-TIM-3 group was 5.3 compared to the mean of 3.2 in the control group, showing a marked improvement. [Conclusions] Anti-TIM-3 antibodies have attracted attention as checkpoint inhibitors, but they also show promise as novel biologics, and we plan to conduct more detailed experiments on autoimmune responses such as cytokine chemokines and Treg cells.

ICW11-1

Examination of efficacy and safety of JAK inhibitors for rheumatoid arthritis in clinical practice and prognosis of cases in which JAK inhibitors are ineffective

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Conflict of interest: None

[Objective] Evaluate JAKi's efficacy and safety in real-world clinical practice and examine the next treatment option in patients of JAKi failure. [Methods] Patients with RA who attended our hospital and used JAKi between February 2014 and October 2020 were included in the study. Patient background and clinical findings, including gender, age at onset and starting JAKi, disease activity of RA, and laboratory data, were collected from the clinical charts retrospectively. Disease activity was evaluated at the time of starting JAKi, at 3, 6, and 12 months after starting JAKi, and every year thereafter. The log-rank test was used to compare the continuation rates between tofacitinib (TOF) and baricitinib (BAR). [Results] Among 234 patients were enrolled, 144, 80, and 10 were used TOF, BAR, and peficitinib (PEF), respectively. The age at starting JAKi was 71.6 ± 12.0 years for TOF, 70.5 ± 11.8 years for BAR, and 61.0 ± 13.8 years for PEF. The rates of biologic and JAKi naïve patients was 42.4% for TOF, 46.3% for BAR, 50.0% for PEF. There was no significant difference in 1-year continuation rates between TOF and BAR (77.3% vs. 67.5%, respectively, $p = 0.15$). The mean duration of treatment for TOF and BAR was 2.2 ± 2.0 years and 1.1 ± 1.1 years, respectively. The discontinued rates due to ineffectiveness, malignancy, infections, and herpes zoster incidence in patients using TOF and BAR were 8.3% and 13.8%, 2.8% and 5.0%, 5.6% and 1.3%, 10.4% and 8.8%, respectively. Among 22 of the 23 patients who discontinued JAKi due to non-response were switched to a biologic agent or JAKi, including one with a TNF inhibitor, 10 with IL-6 receptor antibodies, two with abatacept, and nine with other JAKi. [Conclusions] Our results demonstrate the efficacy and safety of JAKi in older RA patients compared with clinical trials. Further studies are needed to determine the next-line treatment of the patients of JAKi failure.

ICW11-2

Efficacy and Safety of Filgotinib for Patients with Rheumatoid Arthritis with Inadequate Response to Methotrexate: 52-Week Results

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Conflict of interest: Yes

[Objective] Filgotinib (FIL) is an oral, potent, selective Janus kinase 1 inhibitor. The Phase III FINCH 1 study (NCT02889796) assessed the efficacy/safety of FIL in patients (pts) with moderately to severely active rheumatoid arthritis (RA) and an inadequate response to methotrexate (MTX-IR). FINCH 1 primary outcomes at Week (W) 12 and W24 have been reported; we present study results through W52. [Methods] FINCH 1 pts were randomized (3:3:2:3) to oral FIL 200 mg or FIL 100 mg QD, subcutaneous adalimumab (ADA) 40 mg every 2W or placebo (PBO) up to week 52 on a background of stable MTX; pts randomized to PBO were re-randomized to FIL 100 or 200 mg at W24. Efficacy was assessed via clinical, radiographic and pt-reported outcomes (PROs). Comparison with W52 data were not adjusted for multiplicity. [Results] Of the 1755 pts randomized (81.8% female; mean [SD] disease duration, 7.8 [7.6] years; mean [SD] baseline DAS28 (CRP), 5.7 [0.9]) 1417 pts received treatment through W52. Efficacy measures (e.g. proportion of pts with ACR20 / DAS28 (CRP)<2.6) were sustained from W24 through W52 for both the FIL 200 mg (W24: 78%/48%; W52: 78%/54%) and 100 mg arms (W24: 78%/35%; W52: 76%/43%). Rates of ACR20 / DAS28 (CRP)<2.6 in ADA recipients at W24 and 52 were 75%/36% and 74%/46%, respectively; DAS28 (CRP)<2.6 nominal p for FIL 200 mg vs ADA=0.024 at W52. Remission as defined by SDAI, CDAI and Boolean-based definition was stable through W52 for both doses. Further efficacy data will be presented. The safety profile of FIL through W52 was consistent with W24 data; rates of adverse events (AEs), serious AEs, AEs of specific interest, and infections (including H. Zoster) were infrequent and balanced between treatment arms and analyses epochs (data to be presented). [Conclusions] Through W52, both FIL 200 and 100 mg showed sustained efficacy based on clinical and PROs and radiographic progression and were well tolerated in MTX-IR pts with RA.

ICW11-3

Filgotinib Provided Rapid and Sustained Improvements in Functional Status, Pain, Health-related Quality of Life, and Fatigue in Patients with Rheumatoid Arthritis and Inadequate Response to Methotrexate

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Conflict of interest: Yes

[Objective] To present patient (pt)-reported outcomes (PROs) from the Phase III FINCH 1 study (NCT02889796) of the efficacy/safety of filgotinib (FIL)-an oral, potent, selective JAK1 inhibitor-in pts with moderately to severely active rheumatoid arthritis (RA) who have an inadequate response to methotrexate (MTX). [Methods] Patients (n=1755) were randomized 3:3:2:3 to FIL 200 mg (n=475) + MTX, FIL 100 mg + MTX (n=480), placebo (PBO) + MTX (n=475) or s.c. adalimumab (ADA) 40 mg + MTX (n=325) for up to 52 weeks (W); PBO pts were rerandomized 1:1 to FIL 100 or 200 mg at W24. PROs included HAQ-DI and VAS pain scale, SF-36, and FACIT-Fatigue. Change from baseline (Δ) through W24 for FIL vs. PBO comparisons used a mixed-effect model; the proportion of pts with a minimum clinically important difference (MCID; ≧0.22 reduction) in Δ HAQ-DI through W24 used logistic regression. [Results] 1417/1755 patients received study drug through W52. Δ in HAQ-DI and VAS pain scale (mm) vs PBO reached nominal significance ($p < 0.001$) at W2 for both FIL 200 mg (HAQ-DI, -0.30; VAS, -16) and FIL 100 mg (HAQ-DI, -0.22; VAS, -12); the Δ at W24 (FIL 200 mg: HAQ-DI, -0.82; VAS, -38 / FIL 100 mg: HAQ-DI, -0.75; VAS, -37) and was maintained through W52 (FIL 200 mg: HAQ-DI, -0.93; VAS, -43 / FIL 100 mg: HAQ-DI, -0.85; VAS, -41). At W2, vs. PBO (40.2%), a nominally significantly greater proportion of pts achieved the HAQ-DI MCID in FIL 200 (52.5%; $p<0.001$) and 100 mg (46.7%; $p=0.043$) arms; benefit vs PBO was maintained up to W24 and the proportion of pts who achieved an HAQ-DI MCID remained ≧75.8% in FIL 200 mg and ≧71.5% in the FIL 100 mg groups from W12-52. FIL provided nominally significant improvements vs PBO in SF-36 and FACIT-Fatigue scores from W2-24 with benefit maintaining to W52. PRO outcomes with FIL were generally comparable vs ADA. [Conclusions] Both doses of FIL provided rapid and sustained improvements in functional status, pain, HRQoL, and fatigue vs PBO for pts with RA and inadequate response to MTX.

ICW11-4

Efficacy and Safety of Filgotinib in Methotrexate-Naïve Patients with Rheumatoid Arthritis: 52-Week Results

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Conflict of interest: Yes

[Objective] Filgotinib (FIL) is an oral, potent, selective Janus Kinase 1 inhibitor. The phase III FINCH 3 study (NCT02886728) assessed the efficacy and safety of FIL in methotrexate (MTX)-naïve patients (pts) with moderately to severely active rheumatoid arthritis (RA). Week (W) 24 primary outcomes were presented previously; we report FINCH 3 results through W52. [Methods] FINCH 3 randomized pts (2:1:1:2) to oral FIL 200 mg QD + MTX ≤20 mg weekly, FIL 100 mg + MTX, FIL 200 mg monotherapy (mono) + placebo (PBO), or PBO + MTX, up to W52. Comparisons at W52 were not adjusted for multiplicity. Safety was assessed from adverse events and laboratory abnormalities. [Results] 975/1249 treated pts received the study drug through W52. Efficacy measures (proportion of pts with ACR20 / DAS28 (CRP)<2.6) were sustained from W24 through W52 for both the FIL 200 mg + MTX (W24: 81.0%/54.1%; W52: 75.0%/53.4%; n=416) and FIL 100 mg + MTX (W24: 80.2%/42.5%; W52: 73.4%/43.0%; n=207) arms. Rates of ACR20 / DAS28 (CRP)<2.6 for pts on FIL mono treatment (n=210) were 78.1%/42.4% and 74.8%/46.2%, at W24 and W52 respectively; rates in pts receiving MTX (n=416) were 71.4%/29.1% and 61.8%/31.5% at W24 and W52, respectively. P values for comparison of ACR20 and DAS28 (CRP)<2.6 were ≦0.05 and ≦0.01, respectively. Remission as defined by SDAI, CDAI and Boolean-based definition was stable through W52. The safety profile of FIL through W52 was consistent with W24 data; rates of serious adverse events were 6.3% for both doses of FIL + MTX, 8.1% for FIL mono, and 6.7% for MTX. Incidences of H. zoster were 1.4% for both doses of FIL in combination with MTX, 1.9% for FIL mono, and 1.0% for MTX. Further measures of efficacy and safety will be presented. [Conclusions] Efficacy of FIL 200 mg + MTX, FIL 100 mg + MTX, and FIL 200 mg mono was sustained through W52, with faster onset and consistently numerically greater efficacy for FIL 200 vs 100 mg. No new safety signals were observed.

ICW11-5

Effect of filgotinib on pain in patients with rheumatoid arthritis: Results from phase 3 clinical trials

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Conflict of interest: Yes

[Objective] Filgotinib (FIL), an oral, JAK1 selective inhibitor, was efficacious and generally well tolerated in the FINCH (F) 1-3 rheumatoid arthritis (RA) clinical trial program; we report post hoc analyses of the impact of FIL on pain from these studies. [Methods] Pts (with active RA and inadequate response [IR] to methotrexate [MTX-IR]) in F1 (NCT 02889796) received FIL 200 mg, FIL 100 mg, adalimumab (ADA) 40 mg, or placebo (PBO) on background MTX up to 52W; at W24, PBO pts were rerandomized to FIL 200 or 100 mg. In F2 (NCT02873936), pts with a prior IR to biologic DMARDs) received FIL 200 or 100 mg, or PBO on background csDMARD (s) for 24W. MTX-naïve pts in F3 (NCT02886728) received FIL 200 mg+MTX, FIL 100 mg+MTX, or monotherapy with FIL 200 mg or MTX up to 52W. Pain was assessed by the visual analog scale (VAS). Comparisons were not adjusted for multiplicity. P values are nominal. [Results] Baseline pain was high among all arms across studies (mean VAS scores, 64-68 mm). At W2, significantly (p≦0.05) more patients on FIL vs PBO had reductions in VAS scores rated as moderate (≧30%) or severe (≧50%) in F1 (≧30/≧50%: FIL 200 mg, 36.2/20.0%; FIL 100 mg, 30.1/12.9%; PBO, 18.7/8.2%) and F2 (≧30/≧50%: FIL 200 mg, 44.2/24.5%; FIL 100 mg, 36.6/17.0%; PBO, 21.6/8.8%) and vs MTX in F3 (≧30%/≧50%: FIL 200 mg+MTX, 44.4/24.6%; FIL 200 mg monotherapy, 36.2/21.4%; FIL 100 mg+MTX, 34.5/20.4%; MTX, 19.2/10.1%). Pain was reduced by ≧90% by W52 in 25.1% and 22.8% of pts on FIL 200 or 100 mg, respectively, in F1 (ADA, 21.8%) and 31.6, 24.8 and 26.2% of pts receiving FIL 200/100 mg+MTX or FIL 200 mg alone, respectively, in F3 (MTX, 15.9%). Improvements in VAS score ≧70/90% and the proportion of pts with a residual score of ≦10, 20 and 40 mm will be shown. [Conclusions] FIL 200 and 100 mg provided rapid, clinically meaningful pain relief over a range of pts. The degree of improvement was substantial for many pts; ≧40% of pts had a ≧50% reduction in pain and nearly 25% had a 90% reduction in F1/F3.

ICW11-6

Filgotinib Provided Rapid and Sustained Relief of Pain and Fatigue and Improved Health-Related Quality of Life in Patients with Rheumatoid Arthritis and Inadequate Response to Biologic DMARDs

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Conflict of interest: Yes

[Objective] To present patient (pt)-reported outcomes (PROs) from the Phase III FINCH 2 study (NCT02873936) of the efficacy/safety of filgotinib (FIL)-an oral, selective JAK1 inhibitor-in pts with moderately to severely active rheumatoid arthritis (RA) and an inadequate response to biologic DMARD (s). [Methods] Patients were randomized 1:1:1 to FIL 200 mg, FIL 100 mg, or placebo (PBO) while continuing conventional synthetic (cs) DMARD therapy. PROs, collected at serial time points to week (W) 24, included the VAS pain scale, FACIT-Fatigue, and SF-36 physical (PCS) and mental component scores (MCS); changes from baseline vs. PBO were compared via a mixed-effects model. [Results] A total of 448 pts were treated with FIL 200 mg (n=147), FIL 100 mg (n=153) or PBO (n=148); 381 pts completed the study and Baseline [BL] mean [SD] VAS 67, [21.0]; SF-36 PCS, 31.1 [7.89]; SF-36 MCS, 44.3 [11.6]; FACIT-Fatigue, 24.4 [11.6]; values did not vary between treatment arms. Significant (P<0.01) changes from BL in LS-mean VAS pain scores (mm) occurred by W2 and maintain through W24 with FIL 200 mg (W2, -19; W24, -34) and FIL100 mg (W2, -17; W24, -30) vs. PBO (W2, -5; W24, -18). For both FIL arms, a significant (p<0.01) improvement from BL in fatigue was seen at W4 (FIL 200 mg, 6.9; FIL 100 mg, 6.6) that maintained to W24 for FIL 200 mg, 11.5 [p<0.001]) vs PBO (W4, 3.3; W24, 6.9). SF-36 PCS was significantly improved in both FIL arms vs. PBO at W4 (FIL 200 mg, p<0.001; FIL 100 mg, p=0.005), W12 (FIL 200/100 mg, p<0.001 for both) and W24 (FIL 200 mg, p<0.001; FIL 100 mg, p=0.002) vs PBO. SF-36 MCS scores were significantly improved by FIL 200 mg vs. PBO at W4 (p=0.019) and W12 (p=0.045) with the difference maintained through W24 (p not significant). Data for SF-36 PCS and MCS will be shown. [Conclusions] FIL (with csDMARDs) provided rapid and sustained improvements in key PRO measures of pain, HRQoL, and fatigue in pts with refractory disease and an inadequate response to biologic DMARDs.

ICW12-1

Comparing the efficacy and safety of tofacitinib and baricitinib in patients with rheumatoid arthritis in clinical practice using propensity score-based inverse probability of treatment weighting and growth mixture modeling

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Conflict of interest: None

[Objective] The differences of efficacy between each Janus kinase (JAK) inhibitors have not been clarified in the patients with rheumatoid arthritis (RA) in clinical practice. Here, we compared the efficacy between tofacitinib (TOFA) and baricitinib (BARI) in clinical practice. [Methods] The efficacy of TOFA (n=156) in patients with RA (n=353) was compared with BARI (n=138). Selection bias was adjusted bypropensity score-based inverse probability of treatment weighting (IPTW). The clinical disease activity index (CDAI) trajectory for patients who started TOFA or BARI was analyzed using growth mixture modeling (GMM). Primary endpoint was CDAI remission rate at 12 weeks. [Results] There was no significant difference in patient background (TOFA: BARI, n = 153:141) and in retention rates during the 12 week after IPTW. The BARI group had a significantly higher CDAI remission rate at 12 weeks than the TOFA group (TOFA=24.8%, BARI=37.1%, odds ratio, 1.8, p=0.02). There was no difference in the incidence of adverse events. Based on analysis of the CDAI trajectory with GMM, 3 response trajectory groups were identified. The first group included patients who had moderate disease activity at baseline. The second group included patients who had high disease activity (HDA) at baseline. In the first and second group, disease activity rapidly improved and most patients achieved low disease activity (LDA) at 12 weeks. In the third group, the disease activity at baseline was HDA, there was only partial or poor therapeutic effect, and the majority of patients could not achieve LDA at 12 weeks (treatment resistant group). The patients who had used a large number of biological disease-modifying antirheumatic drugs (bDMARDs) before receiving TOFA tended to belong to the treatment resistance group by the multivariate analysis. [Conclusions] BARI had higher CDAI remission rate than TOFA at 12 weeks. BARI might have more efficacy than TOFA after the resistance to multiple bDMARDs.

ICW12-2

Impact of Upadacitinib or Adalimumab as Initial Therapy on the Achievement of 48-Week Treatment Goals in Patients with Rheumatoid Arthritis and Inadequate Response to Methotrexate: Post hoc Analysis of a Phase 3 Study

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Conflict of interest: Yes

Objectives: In Phase 3 SELECT-COMPARE study for RA patients (pts) with inadequate response to MTX, pts with an insufficient response to the initial therapy were switched from upadacitinib (UPA) to adalimumab (ADA) (and vice versa) based on treat-to-target (T2T) principles. To assess the effectiveness of this strategy, we analyzed 1-yr outcomes by initial therapy. Methods: Patients (Pts) were initially randomized to UPA 15 mg once daily (iUPA) or ADA 40 mg every other week (wk) (iADA) (both + MTX) for up to 48 wks. Therapy were switched when initial one was insufficient (defined by protocol). Efficacy outcomes included CDAI and DAS28 (CRP) remission (REM)/low disease activity (LDA), and "deep response" (CDAI REM, HAQ-DI <0.5, and pain score <20). Results: At Wk 48, similar rates of iUPA or iADA achieved CDAI and DAS28 (CRP) REM/LDA. A small but significantly greater proportion of pts achieved a deep response with iUPA vs iADA, as well as time-averaged response rates over 48 wks. In addition, similar proportions of pts maintained Wk 26 responses [CDAI and DAS28 (CRP) REM/LDA] with iUPA vs iADA during 6-month follow-up. Conclusions: Rates of LDA or REM at 1 yr were similar between iUPA and iADA. iUPA led to more frequent deep responses and higher time-averaged response rates vs iADA.

ICW12-3

Long-Term Safety and Effectiveness of Upadacitinib or Adalimumab in Patients With Rheumatoid Arthritis: Results at 72 Weeks From the SELECT-COMPARE Study

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Conflict of interest: Yes

Objectives: To report safety and efficacy of upadacitinib (UPA) vs adalimumab (ADA) up to 72 weeks (wks) in RA patients (pts) in the ongoing long-term extension (LTE) of SELECT-COMPARE. Methods: Pts were randomized to once daily UPA 15 mg, placebo (PBO), or ADA 40 mg every other wk (all pts + MTX). The study was double-blind for 48 wks. Between Wks 14-26, pts were rescued (from PBO to UPA, UPA to ADA, or ADA to UPA) if the response did not meet protocol-defined criteria. Pts continued UPA or ADA until the last patient's Wk 48 visit; pts received open-label treatment thereafter. Treatment-emergent adverse events (AEs) and efficacy were summarized. Results: UPA + MTX was generally well-tolerated as assessed by the frequency of AEs, including serious AEs, AEs leading to discontinuation of study drug, and AEs of special interest. At both Wks 60 and 72, significantly greater rates of pt with UPA + MTX achieved ACR20/50/70, low disease activity and remission compared to those with ADA + MTX, as well as improvements in pain and function in the UPA vs ADA group through Wk 72. Conclusion: The safety profile for UPA + MTX was consistent with that reported previously. UPA + MTX maintained significantly higher clinical response compared to ADA + MTX through Wk 72.

ICW12-4

Radiographic Outcomes in Patients With Rheumatoid Arthritis Receiving Upadacitinib as Monotherapy or in Combination With Methotrexate: Results at 2 Years From the SELECT-COMPARE and SELECT-EARLY Studies

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Conflict of interest: Yes

Objectives: To describe the radiographic progression up to 2 years (96 wks) among patients (pts) with RA receiving upadacitinib (UPA) either as monotherapy or in combination with MTX. Methods: Both the SELECT-EARLY and SELECT-COMPARE phase 3 trials enrolled pts at high risk for progressive structural damage with baseline (BL) erosive joint damage and/or seropositivity. In SELECT-EARLY, MTX-naïve pts (N=945) were randomized to UPA 15 mg or 30 mg once daily (QD) or MTX monotherapy. In SELECT-COMPARE, pts with an inadequate response to MTX (MTX-IR pts) (N=1629) were randomized to UPA 15 mg, placebo (PBO), or adalimumab (ADA) 40 mg every other wk, with all pts continuing background MTX; at wk 26, all pts receiving PBO were switched to UPA 15 mg. In both trials, mean changes from BL in modified Total Sharp Score (mTSS), joint space narrowing, and joint erosion as well as the rates of pts with no radiographic progression were evaluated based on X-rays at wks 24/26, 48, and 96 for those patients in whom wk 96 X-rays were available. Results: In the SELECT-EARLY study, at wk 96 UPA monotherapy (15 mg and 30 mg) significantly inhibited radiographic progression compared with MTX as measured by mean change in mTSS

and by the rates of patients with no radiographic progression. When analyzed without patients who were rescued (MTX added to UPA or UPA added to MTX), changes in mTSS from BL remained similar. By the same measures, in SELECT-COMPARE, inhibition of structural progression was comparable between UPA and ADA. Following the switch of all PBO patients to UPA, the rate of progression slowed and was comparable to that in pts receiving UPA from BL. Among pts from both trials that had no radiographic progression at wk 24/26, >90% remained without radiographic progression at wk 48 and 96. Conclusion: UPA was effective in inhibiting the progression of structural joint damage through 2 years both in MTX-naïve pts receiving UPA monotherapy and MTX-IR pts receiving UPA + MTX.

ICW12-5

Impact of Concomitant Glucocorticoids on the Clinical Efficacy and Safety of Upadacitinib in Patients with Rheumatoid Arthritis: An Ad Hoc Analysis of Data from Three Phase 3 Studies

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Conflict of interest: Yes

Objectives: To evaluate the impact of baseline (BL) Glucocorticoids (GCs) on the efficacy and safety of upadacitinib (UPA) with or without concomitant conventional synthetic DMARDs (csDMARDs) using ad hoc analysis of three Phase 3 studies of UPA in RA. Methods: Patients (pts) with inadequate response to MTX (MTX-IR) receiving UPA 15 mg once daily (QD) or placebo (PBO) + csDMARDs in SELECT-NEXT, and MTX-IR/MTX-naïve pts receiving UPA 15 mg QD monotherapy or MTX monotherapy in SELECT-MONOTHERAPY/SELECT-EARLY, respectively, were included. Efficacy outcomes, including remission and low disease activity (LDA) based on DAS28 (CRP) and, were assessed and stratified by BL GC use. Safety was reported as number and rates of pts with adverse events (AEs). Results: 737/1506 pts (48.9%) were receiving BL GCs. BL characteristics were similar across treatment groups; SELECT-EARLY (MTX-naïve) generally had the shortest duration of RA and higher CRP. Across UPA treatment groups, concomitant GCs generally did not influence the rates of pts achieving remission. In SELECT-NEXT, clinical responses with UPA 15 mg + csDMARDs were similar irrespective of concomitant GC use. Within SELECT-MONOTHERAPY, responses in pts receiving UPA 15 mg without concomitant csDMARDs or GCs were higher than those in pts receiving MTX alone, but were numerically lower than in those receiving UPA 15 mg with GCs. However, this was not observed within SELECT-EARLY, where clinical responses in pts receiving UPA 15 mg monotherapy without GCs were higher than in those pts receiving UPA 15 mg with GCs for both DAS28 (CRP) <2.6 and CDAI ≦2.8. A trend was similar for LDA. Serious AEs, AEs leading to discontinuation, and AEs of special interest, including infections, were similar in the UPA groups irrespective of concomitant GC use. Conclusions: UPA 15 mg in combination with csDMARDs or as monotherapy was effective irrespective of concomitant GC use. Safety of UPA appeared largely unaffected by concomitant GC use.

ICW12-6

Frequency and Risk for Deep Vein Thrombosis Complicated in Patients with Rheumatoid Arthritis Requiring Molecular-Targeted Disease Modifying Anti-Rheumatic Drugs

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Conflict of interest: None

[Introduction] The increased risk of venous thromboembolism (VTE) in RA patients treated with Janus kinase inhibitors (JAKinhibs) has gathered attention mainly in western countries. We investigated the frequency and risk of deep vein thrombosis (DVT) in RA patients that initiated molecular-targeting DMARDs. [Methods] RA patients admitted from January 2019 to August 2020 to introduce molecular-targeting DMARDs who had received lower limb venous ultrasound (LVUS) and blood coagulation tests were retrospectively analyzed. [Results] We enrolled 29 of 64 admitted patients, 8 males and 21 females at the age of 61.3 ± 13.5 (mean ± SD) y.o. Disease duration was 10.7 ± 10.9 years, BMI 23.1 ± 4.72 treated with PSL 4.03 ± 4.05 mg/d and DAS28-ESR 4.45 ± 1.39, CDAI 17.3 ± 12.1. FDP and D-dimer were elevated, 8.21 ± 7.96 μg/mL and 3.15 ± 4.08 μg/mL, with history of smoking (N=13), DVT (N=1) and malignancy (N=1). DVT was observed in a single patient (3.4%) evidenced by LVUS, who had common risk factors for DVT, obesity (BMI 26) and older age (74 y.o.) but did not have DVT history and malignancy. However, FDP 4.8 μg/mL and D-dimer 1.89 μg/mL was close to normal without complicated malignancy or coagulopathy. Importantly, there was no symptoms or physical findings suggesting the presence of DVT. [Conclusion] Our results indicated that RA patients with high disease activity may potentially complicate with clinically asymptomatic DVT without FDP and D-dimer elevation, which should be screened by LVUS before introducing molecular-targeting DMARDs like JAKinhibs. However, further studies are required to reveal the real-world incidence and risk of DVT/VTE in RA patients.

ICW13-1

A case undergoing haemodialysis revealed to be correlated with ankylosing spondylitis and treated with IL-17 antagonist secukinumab

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Conflict of interest: None

A patient, who had been undergoing haemodialysis for 3 years, and had anaemia which was erythropoiesis-stimulating agents were not effective, admitted our hospital. He was 64 years old and weighed 43 kilograms. His wrist joint was swollen and the ultrasonogram revealed severe tenosynovitis of the wrist and shoulder joint. Salazosulfapyridine was prescrbed first because methotrexate was contraindicated for haemodialysis patient, but granulocytopenia progressed. Carbapenem-resistant Enterobacteriaceae infection had ocuured during these periods. Blood-transfusion, antibiotics, granulocyte colony- stimulating factor: filgrastim were used for life saving. Sacroiliatis was detected by computed tomogram (CT), therefore the diagnosis of ankylosing spondylitis (AS) was determined. IL-17 antagonist secukinumab was administered subcutanously. Successively tenosynovitis became alleviated. A marked diagnostic delay among Japanese patients with AS is pointed out. This case, who had anaemia, was not diagnosed as AS for years. The evaluation of enthesitis with ultrasound is a helpful tool for the diagnosis of patients with AS. This case shows us 3 important points: diagnostic difficulty of chronic state, clinical severity of the teatment for the fragile person with complications and appropriate indication of a novel biological agent.

ICW13-2

The clinical outcome of tumor necrosis factor inhibitors in patients with ankylosing spondylitis

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Conflict of interest: None

[Objective] This study aimed to evaluate the clinical outcome of tumor necrosis factor (TNFi) in patients with ankylosing spondylitis (AS). [Methods] Twelve patients (5 men and 7 women) who were fulfilled with

modified New York criteria (1984) were recruited for the observational study. The average age was 34 ± 18 years old (range was 12 - 67 years old), the disease duration was 5.1 years on average at the administration of tumor necrosis factor inhibitors (TNFi). The first administered TNFi was adalimumab in 11 cases and infliximab in 1 case. Human leukocyte antigen (HLA) antigen type, the Bath ankylosing spondylitis disease activity index (BASDAI), the retention rate of adalimumab, and adverse events were examined. [Results] The antigen type od HLA was B52 in 5 cases, B27 in 4 cases, and B62 in 3 cases. The average BASDAI was 6.8 at the administration of TNFi and was 6.4 at 6 months after the administration of TNFi, and 5.2 at 2 years. The first dose of adalimumab was 40 mg/2 weeks for all 11 cases, and the dose was increased to 80 mg/ 2 weeks for 9 cases. Adalimumab was ceased due to inefficacy in 4 cases. Three cases were switched to infliximab and 1 case was switched to sekukinumab. The 1-year retention rate of adalimumab was 73% and 2-years retention rate was 67%. Infliximab was continued until 2 years after the administration. For adverse evets, the elevated liver enzymes such as aspartate aminotransferase and alanine transferase, suppurative bursitis in right knee, and paramenia was 1 case each, respectively. [Conclusions] Adalimumab was the first administered TNFi for most cases of ankylosing spondylitis. However, the dose up of adalimumab from 40 mg to 80 mg/2 weeks was required due to inefficacy.

ICW13-3

Clinical features and HLA serotypes of spondyloarthritis in SAPHO syndrome

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Conflict of interest: None

[Objective] Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome has been proposed to be a subtype of spondyloarthritis (SpA). Although human leukocyte antigen (HLA) class I molecule B27 is strongly associated with SpA, the genetic association of HLA with SpA in SAPHO syndrome has not been elucidated. In this study, we examined the clinical features and HLA serotypes of SAPHO syndrome associated SpA. [Methods] We enrolled 32 patients with SAPHO syndrome at the University of Tokyo Hospital between January 2005 and May 2020. The diagnosis of SAPHO syndrome was based on the diagnostic criteria proposed by Benhamou in 1988 and Kahn in 1994. Axial and peripheral SpA was clinically diagnosed according to the ASAS classification criteria. We retrospectively reviewed clinical, laboratory, and imaging data of the patients and compared the features between those with and without SpA. We further evaluated the HLA-A and -B serotypes in the 14 patients. [Results] Among the 32 patients with SAPHO syndrome, 18 (56.3%) had peripheral and axial SpA (8 were axial and 10 were peripheral SpA). Although sex, dermatological manifestation, presence either of synovitis, tendosynovitis, osteitis, or uveitis, serum levels of C-reactive protein were not different between the patients with and without SpA, the age of the disease onset was significantly lower in the patients with SpA than those without SpA (mean, 39 and 58, respectively). HLA-B27 was not present in all of the 14 patients, but alternatively 4 of the 8 patients (50%) with axical SpA were HLA-B39. [Conclusions] Our retrospective study revealed that about half of the patients in SAPHO syndrome had axial SpA, and their disease onset was younger than those without SpA. Also, HLA-B39, but not HLA-B27, could be associated with the axial SpA in SAPHO syndrome.

ICW13-4

Quality of life score calculated from EuroQOL-5th dimension 5-L correlates with Health Assessment Questionnaire Disability Index

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Conflict of interest: None

[Objective] Validity of quality of life score (QOLS) calculated from EuroQOL-5th dimension 5-L and correlation with clinical parameters in patients with rheumatoid arthritis (RA) were investigated. [Methods] A total of 24,075 times of monitoring for RA was performed. Contents of monitoring included tenderness joint count (TJC), swollen joint count (SJC), patient's global assessment (PGA), evaluator's global assessment (EGA), C-reactive protein (CRP), and pain score with visual analog scale (PS-VAS), and Health Assessment Questionnaire Disability Index (HAQ-DI), and QOLS. Correlation of these parameters and patient's sex, age, rheumatoid factor level (RF), anti-cyclic citrullinated polypeptide antibodies level (ACPA), and disease duration with QOLS was analyzed with multivariate linear regression analysis. Same statistic analysis with average values of these same parameters was also performed using the same analysis. Change from baseline to average value of these parameters were also analyzed with a same manner. [Results] QOLS demonstrated significant correlation with patient's age, ACPA, RF, PGA, EGA, CRP, PS-VAS, and HAQ-DI in 24,075 measurements ($p<0.05$). Average value of QOLS demonstrated significant correlation with average values of patient's age, PGA, CRP, HAQ-DI, and PS-VAS ($p<0.05$). Change of QOLS value demonstrated significant correlation only with change of the HAQ score ($p<0.01$). [Conclusions] QOLS closely correlated with the HAQ score. The other candidates of correlation would be patient's age, PGA, CRP, and PS-VAS. From these results, it is suggested that QOLS is valid index for evaluation of patient's quality of life. QOLS corelates with patient reported outcomes rather than objective inflammation composites.

ICW13-5

Predicting factor for survival in connective tissue disease-associated pulmonary arterial hypertension patients

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Conflict of interest: None

Objectives: The aim of this study to assess the priority of interstitial lung disease (ILD) and systemic sclerosis (SSc), as a predicting factor, for survival in connective tissue disease-associated pulmonary arterial hypertension (CTD-PAH) patients treated with PAH-specific drugs. Methods: CTD-PAH (N=63) diagnosed by right heart catheterization and treated in our institute from 2001 to 2019 were enrolled. ILD was semi-quantified from HRCT. Patients without ILD were grouped to ILD_0, patients with ILD were grouped into ILD_1, ILD_2, ILD_3 and ILD_4 by quartiles. We utilized event as a death related to PAH and observation period as survival. Kaplan-Meier's survival curve was compared among 5 ILD groups, and with or without of SSc. Survival factor was predicted by decision tree with classification and regression tree algorithm (CART). Results: The CTD-PAH (N=63) including 56 females (89%) were Age 50.6±15.0 (mean±SD) at diagnosis of PAH with SSc (N=26), systemic lupus erythematosus (N=11) and mixed connective tissue disease (N=18). CTD-PAH were treated with Phosphodiesterase type 5 inhibitor (N=54, 86%), Endothelin receptor antagonist (N=47, 75%) and Prostacyclin analogs (N=59, 94%). ILD_0 (N=24, 38%), ILD_1 (N=15, 24%), ILD_2 (N=10, 16%), ILD_3 (N=6, 10%) and ILD_4 (N=6, 10%) were compared. There was significant difference in survival among 5 ILD groups (p=0.007). Prognosis of CTD-PAH with SSc was slightly poor than those without SSc (p=0.40). Decision tree with CART revealed that ILD_2 or ILD_3 was first strong Node (p=0.011) and with or without SSc was second Node (p=0.949). Conclusion: Our result demonstrated that the occupancy of ILD was less than half of lung filed was primary predicting factor for good prognosis in CTD-PAH patients under treated with PAH-specific drugs. The careful evaluation of ILD is crucial for success of CTD-PAH treatment.

ICW13-6

Prognostic factors for the short-term mortality of patients with rheumatoid arthritis admitted to intensive care units

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) have high mortality risk and are frequently treated in intensive care units (ICUs). [Methods] This was a retrospective observational study. This study included 67 patients (20 males, 47 females) with RA who were admitted at the ICU of our institution for ≧48 h between January 2008 and December 2017. We analyzed the 30-day mortality of these patients and the investigated prognostic factors in RA patients admitted to our ICU. [Results] Upon admission, the median age was 70 (range, 33-96) years, and RA duration was 10 (range, 0-61) years. The 5-year survival after ICU admission was 47%, and 30-day, 90-day, and 1-year mortality rates were 22%, 27%, and 37%, respectively. The major reasons for ICU admission were cardiovascular complications (24%) and infection (40%) and the most common ICU treatments were mechanical ventilation (69%), renal replacement (25%), and vasopressor (78%). In the 30-day mortality group, infection led to a fatal outcome in most cases (67%), and nonsurvival was associated with a significantly higher glucocorticoid dose, updated Charlson's comorbidity index (CCI), and acute physiology and chronic health evaluation (APACHE) II score. Laboratory data obtained at ICU admission showed that lower platelet number and total protein and higher creatinine and prothrombin time international normalized ratio (PT-INR) indicated significantly poorer prognosis. The multivariate Cox proportional hazard model revealed that nonuse of csDMARDs, high updated CCI, increased APACHE II score, and prolonged PT-INR were associated with a higher risk of mortality after ICU admission. [Conclusions] Our study demonstrated that the nonuse of csDMARDs, high updated CCI, elevated APACHE II score, and coagulation abnormalities predicted poorer prognosis in RA patients admitted to the ICU.

ICW14-1

Approach to establish a novel evaluation method for Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) -LOOPS Registry-

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Conflict of interest: None

[Objective] We used new evaluation indicators in addition to conventional indicators in an attempt to improve diagnostic and classification accuracy and to identify high-risk cases. [Methods] This study was conducted in 210 patients with SLE admitted to our department between January 2017 and April 2020. Conventional evaluation methods were used to diagnose NPSLE (153 without NPSLE, 57 with NPSLE). We then investigated features characteristic to NPSLE in greater detail using psychiatric symptom rating scales (PSRS), cerebrospinal fluid monoamines, and MRI with intracranial vessel wall imaging (VWI). [Results] (1) A close relationship between cerebrospinal fluid monoamines and psychiatric disorders has been suggested. Cerebrospinal fluid levels of HVA, 5-HIAA, and NA were significantly lower in SLE patients (n=72) than healthy controls (HCs) (n=10); however, we found no link between these monoamines and the presence of NPSLE or NPSLE activity. (2) Thirty-two patients (23 with NPSLE and 9 without NPSLE) were assessed using PSRS. MADRS-J (depression) results indicated mild in 13, moderate in 3, and severe in 2 patients. YMRS (mania) results were > 12 points in 1 patient. BPRS (psychiatric) results indicated mild in 5, moderate in 0, and marked illness in 3 patients. (3) Intracranial VWI of HCs (n=50) and SLE patients (n=60) confirmed wall thickening of the major cerebral arteries in SLE patients, selectively in NPSLE patients. (4) Abnormal results on PSRS and intracranial VWI were more commonly seen in patients with highly active NPSLE. These abnormal results were also detected in SLE patients without NPSLE. [Conclusions] Lower concentration of monoamines in SLE patients regardless of the presence of NPSLE or disease activity suggests that latent CNS abnormalities may be present in SLE. Adding new evaluations, such as MRI with intracranial VWI and PSRS could improve the rate of NPSLE diagnosis and be useful as new indicators of disease severity.

ICW14-2

Relationships between anti-SS-A antibody and Achievement of Lupus Low Disease Activity State (LLDAS) in patients with systemic lupus erythematosus: A cross-sectional analysis using the LUNA registry

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Conflict of interest: None

[Objective] Anti-SS-A antibody (ab) has been suggested to affect the pathogenesis of systemic lupus erythematosus (SLE) such as B cell differentiation. Here we investigated the relationship between anti-SS-A ab seropositivity and LLDAS achievement in patients with SLE. [Methods] Using the multicenter SLE registry "LUNA", we collected the patients' data such as background, anti-SS-A ab seropositivity, whether LLDAS achievement or not, and the components of LLDAS, including physician global assessment (PGA) and SLE Disease Activity Index 2000 (SLEDAI-2K). And we performed multiple logistic regression analysis using the patients' background including age, sex, weight, disease duration, maximum PSL dose in the past, current use of cyclophosphamide, mycophenolate mofetil, mizoribine, methotrexate, azathioprine, tacrolimus, rituximab, belimumab, and hydroxychloroquine as independent variables. [Results] Nine hundred forty-two patients (anti-SS-A ab positive rate 61.8%) were included. We couldn't concluded that anti-SS-A ab seropositivity affects LLDAS attainment (OR 0.895, 95% CI 0.629-1.271, p =0.534), low prednisolone (PSL) dose (≦7.5 mg/day; OR 1.024, 95% CI 0.735-1.427, p =0.886), low SLEDAI-2K score (≦4; OR 0.756, 95% CI 0.535-1.071, p =0.114), and low PGA (≦1; OR 1.044, 95% CI 0.715-1.525, p =0.824). Among the components of SLEDAI-2K, anti-SS-A ab seropositivity was a risk factor for pyuria (OR 1.445, 95% CI 1.010-2.069, p =0.044) and leukopenia (OR 3.217, 95% CI 1.485-6.966, p =0.003). [Conclusions] This study did not reveal the relationship between anti-SS-A ab seropositivity and LLDAS achievement. Anti-SS-A ab seropositivity was related to pyuria and leukopenia in the components of SLEDAI-2K.

ICW14-3

Remission induction therapy with mycophenolate mofetil in patients with lupus nephritis -LOOPS registry-

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Conflict of interest: None

[Objective] To clarify the effectiveness and safety of remission induction therapy with mycophenolate mofetil (MMF) in patients with lupus nephritis (LN). [Methods] Patients with LN who were hospitalized in our department between August 2015 and April 2020 and received remission induction therapy were divided into two groups: MMF-treated (37 pts) and IVCY-treated (25 pts), in addition to high-dose glucocorticoid therapy. We

compared the persistent rate and remission rates and adverse events (AEs) between the two groups 6 months after therapy initiation. [Results] No significant differences were observed between the two groups in age (MMF/IVCY 47/45 y), sex (female 86/88%), disease duration (105/118 m), classifications of lupus nephritis (III 13, VI 20, V 4/III 12, IV 11), SLEDAI (18/18), eGFR (68/68 mL/min), or urine protein-to-creatinine ratio (UPCR; 3.7/2.9 g/gCre). An average of 2.4 g/d of MMF was administered, and IVCY was administered an average of 3.9 times. 28 patients (76%) continued using MMF, while 12 patients (48%) completed 6 courses of IVCY; the continuation rate in the MMF group was significantly higher than that in the IVCY group (p=0.033, following analysis using the last observation carried forward method). 29 patients (78%) in the MMF group and 14 (56%) in the IVCY group achieved remission at 6 months; no significant difference was noted (p=0.092). The eGFRs at 6 months were also similar between the two groups, while the UPCR improvement rate in the MMF group was significantly higher than that in the IVCY group (51.3/16.5%, p=0.002). Grade ≧3 AEs per the CTCAE occurred in 6 patients (16%): aspergillosis, herpes zoster, CMV infection, liver dysfunction, and anemia (2 pts). The incidence rate of AEs was lower in the MMF group than in the IVCY group (16 pts: 64%; p=0.002). [Conclusions] MMF induces fewer AEs, resulting in higher tolerability than that associated with IVCY. MMF may be more effective than IVCY if sufficiently administered.

ICW14-4

The vitamin D levels and its association with disease activity in Japanese patients with systemic lupus erythematosus and rheumatoid arthritis

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Conflict of interest: None

[Objective] This cross-sectional study aimed to investigate vitamin D levels and their association with disease activity of SLE and RA in Japanese patients. [Methods] Consecutive patients, both outpatient and inpatient, who fulfilled ACR 1997 classification criteria for SLE or 2010 EULAR/ACR classification criteria for RA with measurements of 25 (OH) vitamin D3 levels between January 2017 and December 2019 were enrolled. Demographic, clinical and laboratory data were obtained from electronic medical records. Disease activity was assessed using the SLEDAI and DAS28-CRP. We analyzed the association between 25 (OH) vitamin D3 and SLEDAI scores in SLE patients or DAS28-CRP scores in RA patients by linear regression. [Results] Two-hundred fifty-three patients had measurements of 25 (OH) vitamin D3 during the study period. Five patients with SLE and 17 patients with RA were excluded because of the supplementation of vitamin D. In total, 98 SLE [91.8% women; median (*IQR*) age 45.9 (29.3, 56.7) years; disease duration 8.3 (4.5, 15.4) years; PSL 4.0 (4.0, 7.0) mg/day; SLEDAI 4.0 (2.0, 8.0)] and 133 RA patients [75.9% women; median (IQR) age 70 (61.2, 77.7) years; disease duration 9.2 (2.9, 17.4) years; PSL 0.0 (0.0, 3.0) mg/day; DAS28-CRP 2.0 (1.4, 3.0); MDHAQ 0.2 (0.1, 0.7)] were enrolled. Seventy (71.4%) patients with SLE and 73 (54.9%) patients with RA had vitamin D deficiency (<15 ng/ml) (*P*=0.016). The 25 (OH) vitamin D3 level correlated inversely with daily PSL dose (β=-0.13; *P*=0.003) and female sex (β=-2.36; *P*=0.03). On multivariate linear regression analysis, SLEDAI and DAS28-CRP were not significantly associated with 25 (OH) vitamin D3 levels in SLE (*P*= 0.39) or RA (*P*=0.97) patients, respectively. [Conclusions] This cross-sectional study of Japanese patients with SLE and RA showed that vitamin D deficiency are highly prevalent. The disease activity of SLE and RA is not associated with vitamin D levels.

ICW14-5

Risk factors for adverse drug reactions to trimethoprim-sulfamethoxazole in systemic lupus erythematosus

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Conflict of interest: None

[Objective] Trimethoprim-sulfamethoxazole (TMP-SMX), a prophylactic agent against pneumocystis pneumonia (PCP), can cause adverse drug reactions (ADRs) particularly in patients with systemic lupus erythematosus (SLE). The prevalence of ADRs varies among connective tissue disease (CTD) patients and the risk factors for ADRs remain unclear. Thus, we examined the prevalence of TMP-SMX related ADRs in patients with SLE and other CTDs, and identified specific risk factors for ADR development in SLE patients. [Methods] We retrospectively reviewed data from CTD patients who were administered TMP-SMX as a PCP prophylactic. The prevalence of ADRs was compared between patients with SLE and those with other CTDs. Univariate and multivariate analyses were conducted to identify risk factors for ADR in patients with SLE. [Results] Of the 426 CTD patients included in our study (SLE, n = 164; other CTDs, n = 262), 22 with SLE (13.4%) developed ADRs, with the rate being significantly higher than that observed in patients with non-SLE CTDs (7.3%, p=0.043). In SLE patients, univariate analyses revealed direct associations of ADRs with anti-Sm (p<0.001), anti-RNP (p = 0.02), and anti-Ro/SS-A antibodies (p = 0.02). The multivariate analysis identified a significant association between anti-Sm antibody and the development of ADRs (adjusted odds ratio 5.08, 95% confidence interval 1.74-14.80, p=0.002). [Conclusions] SLE patients who are prophylactically administered TMP-SMX are at high risk of ADRs. Among these patients, those who display positive anti-Sm antibody staining should be carefully monitored for ADRs.

ICW14-6

Dose hydroxychloroquine have a protective effect on infectious disease in patients with systemic lupus erythematosus or not?: The longitudinal study from the LUNA registry

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Conflict of interest: None

[Objective] Infectious disease is an important prognostic issue for patients with systemic lupus erythematosus (SLE). Previous reports suggest a protective effect of hydroxychloroquine (HCQ) against infection in SLE patients. Here we report a retrospective longitudinal analysis of the effects of HCQ against infection using a multicenter registry. [Methods] Six hundred sixty-nine patients registered in the multicenter SLE registry "LUNA" were included. We divided them into two groups based on the use of HCQ (HCQ and non-HCQ groups) and compared the patient background and incidence of severe infection requiring hospitalization. [Results] One hundred thirty in the HCQ group and 538 in the non-HCQ group were included. The observation period was shorter in the HCQ group compared to the non-HCQ group (1.14 ± 0.43 vs 1.97 ± 1.00 years, $p = 8.9 \times 10^{-31}$). The HCQ group had several background conditions that are more prone to infection at baseline compared to the non-HCQ group, such as high SLE disease activity (SLEDAI score 7.0 ± 4.2 vs 5.1 ± 5.0, $p = 1.5 \times 10^{-4}$), a high usage rate of mycophenolate mofetil (22.3% vs 9.9%, $p = 3.5 \times 10^{-4}$) and low IgG (1,316 ± 483 vs 1,436 ± 483 mg/dL, p = 0.015). The average frequency of severe infection in individual patient in HCQ group (0.04 ±

0.19 vs 0.10 ± 0.35, p = 6.0 × 10^{-3}). However, the multivariate logistic regression analysis, in which age, sex, HCQ, MMF, SLEDAI score, and the observation period was used as independent variables, did not identify HCQ use as an independent variable for the average frequency of severe infection (OR 1.46, 95% CI 0.51-4.18; p = 0.48). [Conclusions] SLE patients treated with HCQ tended to have fewer severe infections than those without HCQ, although we did not find a statistically significant difference. The result may be due to a lack of detection power due to the small sample size and short observation period. We plan to reanalyze more accumulated data of LUNA in the future.

ICW15-1

Usefulness of nailfold video-capillaroscopy for diagnosing patients positive for anti-centromere antibody

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Conflict of interest: None

[Objective] To evaluate usefulness of nailfold video-capillaroscopy (NVC) for differential diagnosis in patients with Anti-centromere antibody (ACA). [Methods] We consecutively registered patients positive for ACA who were performed NVC from April 2018 to October 2020, and categorized them into three groups (Systemic sclerosis (SSc), primary Sjogren's syndrome (pSS), undiagnosed patients) with regards to their clinical features retrospectively. Patients previously treated with corticosteroids or immunosuppressants prior to evaluation were excluded. The assessment of NVC was performed according to the methods proposed by Cutolo M et al. (Best Pract Res Clin Rheumatol. 2013;27:237-48.) with Optipix capillaroscopy system. The 2013 ACR / EULAR classification criteria was used for the diagnosis of SSc. The diagnosis of SS was made by satisfying at least one of the three in diagnostic criteria of Ministry of Health in Japan, excluding autoantibodies. [Results] A total of 105 patients with ACA were categorized into 56 SSc, 18 pSS, or 31 undiagnosed patients. All patients except one with pSS were women. Patients with SSc showed 54 Raynaud's phenomenon (RP, 96.4%), 54 NVC abnormalities (96.4%, Early 14, Active 25, Late 15). Patients with pSS showed 8 RP (44.4%), 8 NVC abnormalities (44.4%, Early 6, Active 2). Thirty one undiagnosed patients showed 16 RP (51.6%) 5 NVC abnormalities (16.1%, Early 4, Active 1). When comparing SSc and non-SSc, the sensitivity (Sn) of RP was 0.964, the specificity (Sp) was 0.51, and the positive likelihood ratio (PLR) was 1.97. The Sn of NVC was 0.964, the Sp was 0.735, and the PLR was 3.64. When compared between the group diagnosed with SSc or pSS and undiagnosed group, the Sn of NVC was 0.838, the Sp was 0.839, and the PLR was 5.20. When compared between SSc and pSS, the Sn of NVC (Active or Late) was 0.714, the Sp was 0.889, and the PLR was 6.43. [Conclusions] NVC is a useful tool for diagnosing ACA-positive patients into SSc, pSS, and the others.

ICW15-2

Prediction of myocardial fibrosis and inflammation in systemic sclerosis, assessed in cardiac magnetic resonance imaging, by using artificial neural networks models

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Conflict of interest: None

[Objective] Myocardial abnormalities strongly influence the prognosis of systemic sclerosis (SSc). Assessing asymptomatic myocardial abnormalities at an early stage is considered important. Cardiac magnetic resonance imaging (CMR) is useful for the early assessment of myocardial abnormalities. Images are assessed for myocardial late gadolinium enhancement (LGE) and T2-weighted imaging (T2WI). In the last years, artificial neural networks (ANNs) could be a useful prediction tool in medical scenarios. We aimed prediction of myocardial fibrosis and inflammation in SSc assessed by LGE and T2WI, by using ANNs models. [Methods] SSc patients with no known heart disease or risk factors were enrolled. A three-layered feedforward neural network model was structured to detect a myocardial abnormality from LGE and T2WI, respectively. Inputs for the network were totally 19 variables including attributes (e.g. Age, cutaneous subtype) and observed values (e.g. total skin score, CRP). Output of the network was existence or non-existence (1 or 0) of abnormity in each target index. The back-propagation learning algorithm was used to train the ANN structure. We selected the leave-one-out cross validation method as an evaluation. [Results] All 49 patients with SSc underwent gadolinium-enhanced CMR. LGE was present in 27 (55%) and T2WI in 10 (20%), 8 of whom also had LGE. We created a mathematical model with an AUC value of 0.81 and 0.70, respectively, able to predict LGE and T2WI positive. The accuracy, sensitivity, specificity, positive predictive value and negative predictive value for prediction of LGE and T2WI positive value were 81%, 64%, 90%, 85%, 84%, and 69%, 63%, 81%, 70%, 82%, respectively. [Conclusions] We applied ANNs to identify a prediction model for myocardial fibrosis and inflammation in SSc assessed by CMR. This prediction tool could be used potentially in a clinical practice setting to stratify SSc patients according to myocardial abnormalities.

ICW15-3

Long-term effects and safety of treatment with bosentan on digital ulcers related to systemic sclerosis

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Conflict of interest: None

[Objective] Digital ulcers related to systemic sclerosis (SSc-DU) make worse quality of life of patients with SSc. Bosentan, a dual endothelin receptor antagonist, is used for prevention of newly developed DU. We evaluated the long-term effectiveness and safety of bosentan therapy for SSc-DU. [Methods] A retrospective single center study was performed in 13 patients with SSc-DU who were treated with bosentan over 3 years. We recorded characteristics of the patients, dosage of bosentan, healing of SSc-DU, continuous rate, concomitant drug, complications, adverse events. Healing was defined as disappearance of DU. The diagnosis of SSc was based on 2013 the American College of Rheumatology criteria. [Results] Thirteen patients consisted of 11 female, 2 male, 12 diffuse cutaneous SSc. Mean age, disease duration, final dose of bosentan and use of duration were 63.0 ± 10.3 years, 15.6 ± 11.0 years, 192.3 ± 69.7 mg/day and 5.3 ±1.4 years, respectively. 8 patients were complicated with pulmonary fibrosis. Concomitant drugs were oral corticosteroid (n=7). beraprost (13), oral cyclophosphamide (2), phosphodiesterase 5 inhibitor (8), and antithrombotic drugs (9). Continuous rate was 92.3%. All patients were healed, however, 5 patients were relapsed; they all required phosphodiesterase 5 inhibitor, antithrombotic drugs, and more dose per body weight compared with non-relapsed group (4.0±0.7 vs 2.9±0.8 mg/day/kg; P= 0.04). There was no difference between relapsed and non-relapsed group about disease duration (9.1±3.1 vs 15.5±8.5 years; P=0.18), and during the bosentan start from SSc onset (3.2±4.2 vs 11.8±8.8 years; P=0.21). Major adeverse events was leukopenia in 1 patient, and liver dysfunction was not observed. [Conclusions] Bosentan has favorable effects for SSc-DU, however, does not prevent the development completely. Refractory SSc-DU required high dose bosentan and combination therapy.

ICW15-4

Poor additive effects of glucocorticoids combined with intravenous cyclophosphamide against systemic sclerosis-related interstitial lung disease

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Conflict of interest: None

[Objective] Systemic sclerosis (SSc)-related interstitial lung disease (ILD) is a fatal complication. Cyclophosphamide (CYC) has been proposed as induction therapy. However, there has been little evidence regarding whether glucocorticoids (GCs) should be combined with CYC during induction therapy for treatment of SSc-ILD. The aim of this study is to determine whether GCs have additive effects for SSc-ILD treated with CYC. [Methods] We registered consecutive patients diagnosed with SSc-ILD treated with CYC and retrospectively compared the clinical characteristics and sequential changes in pulmonary function and serological parameters between those who were treated with GC (GC group) and those who were not (non-GC group). [Results] A total of 18 patients with SSc-ILD were included. The median age was 61.0 years, and 14 (77.8%) were women. Ten patients (55.6%) were classified as having diffuse cutaneous type and the number positive for anti-topoisomerase antibody was nine (50.0%). Ten patients were classified as the GC group, and the remaining eight were the non-GC group. At 12 months after starting induction therapy with CYC, the improvement ratio of predicted forced vital capacity (GC vs. non-GC (median); -1.7% vs -1.8%, p = 0.8137) and diffusing capacity (-1.0% vs. 11.2%, p = 0.6056), or the rate of decrease in Krebs von der Lunge 6 levels (10.0% vs 13.1%, p =0.9025) did not differ between the two groups. In multivariable analyses adjusting for the ILD treatment, high CRP levels at baseline were identified as poor prognostic factors for SSc-ILD progression. [Conclusions] GGs combined with CYC did not show additive therapeutic effects in terms of improvement in pulmonary function. This suggests that routine use of GCs with CYC is not necessary for induction therapy of SSc-ILD. In high inflammatory phenotype of SSc-ILD, more intensive therapy would be appropriate to improve or maintain pulmonary functions.

ICW15-5

The effects of nintedanib on immunophenotype in patients with systemic sclerosis associated interstitial lung disease (SSc-ILD)

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Conflict of interest: None

[Objective] Nintedanib, a triple tyrosine kinase inhibitor, has recently been shown to slow progression of interstitial lung disease (ILD) in systemic sclerosis (SSc) patients in the SENSCIS trial. This study aimed to analyze the effects of nintedanib on immunophenotype in patients with SSc-ILD. [Methods] Peripheral blood mononuclear cells were serially isolated from 8 SSc-ILD patients at baseline, 3 months, and 6 months after nintedanib treatment, as well as 18 SSc patients without nintedanib and 12 healthy donors. Comprehensive immunophenotyping, covering detailed subtypes of T cell, B cell, and monocyte subsets was conducted by multi-color flow cytometry. [Results] In SSc patients, the percentage of $CD161^{+}CCR6^{+}$ Th17, $CD8^{+}$ effector memory, $CD8^{+}$ effector T, memory B cells, and M2 monocytes increased compared to those in healthy donors. After nintedanib treatment, percentages of circulating $CD4^{+}$ T, Th1, Th17 cells, and $CD161^{+}CCR6^{+}$ Th17 cells were increased, while there was no difference in $CD8^{+}$ T cells and B cells before and after nintedanib treatment. Interestingly, the percentages of classical monocytes and $CD163^{-}$ monocyte increased and those of M1+M4 monocytes decreased after nintedanib treatment. [Conclusions] Th1, Th 17, classical monocytes, $CD163^{-}$ monocytes and M1+M4 monocytes altered by nintedanib in patients with SSc. The effects of nintedanib observed on immune cells may be associated with its effect on the CSF1 receptor or src signaling pathway.

ICW15-6

Establishment of iPSc and differentiated endothelial cells of systemic sclerosis associated pulmonary arterial hypertension; functional and molecular analysis

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Conflict of interest: Yes

[Objective] Pulmonary arterial hypertension associated with systemic sclerosis (SSc-PAH) is of particularly clinical significance since its outcomes remain unfavorable despite modern PAH therapies. Previous studies have indicated the abnormality of endothelial cells (ECs) in SSc-PAH, but details have yet to be shown. We aimed to clarify the pathogenesis of SSc-PAH using disease-specific induced pluripotent stem cells (iPSc). [Methods] Peripheral blood mononuclear cells were obtained from a patient with SSc-PAH and a healthy donor. 4 kinds of Yamanaka factors were transfected to establish iPSc. ECs were differentiated with the culture system containing BMP-4, Activin, bFGF, CHIR99021, Y-27632, VEGF and SB431542. Vasculogenesis and cell proliferation of ECs were evaluated by the tube formation assay and the BrdU assay. RNA sequencing (RNA-seq) was also performed in SSc-PAH ECs and healthy ECs. [Results] The cellular uptake of BrdU was higher (0.49±0.05 (abs) vs 0.30±0.01 (abs), $p<0.05$, n=3) while the tube formation was impaired (31.2±2.0 (mm) vs 47.0±1.3 (mm), $p<0.01$, n=3) in SSc-PAH ECs compared to healthy ECs. RNA-seq revealed some differentially expressed genes and significantly enriched Gene Ontology terms, including blood vessel development, vascular endothelial growth factor-activated receptor activity and cell adhesion. According to RNA-seq data, one downregulated gene in SSc-PAH ECs, GeneX, was picked up since as it has been shown to be related to vasculogenesis. To assess the function of GeneX, siRNA-mediated knockdown experiment was performed in human umbilical vein endothelial cells. BrdU uptake was higher in GeneX-downregulated cells compare to control cells (0.70±0.05 (abs) vs 0.46±0.01 (abs), $p<0.001$, n=6). [Conclusions] We detected ECs abnormalities in patients with SSc-PAH, such as impaired vasculogenesis, facilitated cell proliferation, differentially expressed genes and enriched Gene Ontology terms. These findings might be related to the pathogenesis of SSc-PAH.

ICW16-1

A susceptibility SNP in IL12B region, but not in LILRA3 region, is associated with vascular damage in Takayasu Arteritis

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Conflict of interest: None

[Objective] We have previously identified single nucleotide polymorphism (SNP) rs6871626 in IL12B region and rs103294 in LILRA3 region as susceptibility loci in Takayasu arteritis (TAK). In this study, we aimed to examine the association of these SNPs with clinical features and vascular damage in TAK. [Methods] We retrospectively reviewed medical records of 99 TAK patients who visited Kyoto University Hospital between 1997 and 2020, and whose genotypes for both rs6871626 and rs103294 were tested in the genomic database of our institute. To assess vascular damage, Takayasu Arteritis Damage Score (TADS) and Vasculitis Damage Index (VDI) were measured at the last clinical visit. In addition, the presence or absence of aortic regurgitation (AR), ischemic heart disease, cerebrovascular disease, and visual loss were evaluated. [Results] The numbers of patients with CC, CA, and AA genotypes of rs6871626 (A: risk allele) were 19, 53, and 27, respectively. Among organ damages, the prevalence of AR in patients with CC, CA, AA genotypes was 42%, 61%, 81%, respectively. Significant difference was observed between CC and AA genotypes (p=0.011). TADS of patients with CC, CA, AA genotypes was 3.42, 4.05, 6.00, respectively. TADS of patients with AA genotype was significantly higher than that of patients with CC, CA genotypes (p=0.004 and 0.005, respectively). VDI of patients with CC, CA, AA genotypes was 3.47, 4.39, 5.48, respectively. VDI of patients with AA genotype was significantly higher than that of patients with CC genotype (p=0.005) The numbers of patients with CC, CT, and TT genotypes of rs103294 (T: risk

allele) were 1, 38, and 60, respectively, and biased to T risk allele. No significant difference was observed in the prevalence of arterial involvement, any organ and vascular damages in the three genotypes. [Conclusions] Rs6871626 in IL12B region, but not rs103294 in LILRA3 region, was associated with vascular damage and clinical features in TAK in the present analysis.

ICW16-2

A 74-Year-Old Japanese Woman with Right Hydronephrosis Caused by Takayasu Arteritis

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Conflict of interest: None

A previously healthy 74-year-old Japanese woman presented to our department with hydronephrosis. One year prior to presentation, she started having pain in her bilateral shoulders, proximal arms, and femurs. Bilateral shoulder and proximal arm pain resolved in 8 months, but bilateral femoral pain remained. Two months before her admission, she visited a primary care physician for abdominal discomfort. She was referred to our urology department after an abdominal echo revealed right hydronephrosis. Computed tomography with IV contrast revealed thickening of the right external iliac arterial wall, involving the right ureter and causing right hydroureteronephrosis. Ureteroscopy revealed no evidence of ureteral tumor, and a ureteral stent was placed. Because CRP levels were around 1.5 mg/L and CT showed thickening of the iliac artery, arteritis was suspected. We ordered positron-PET-CT which showed intense FDG uptake in the walls of her bilateral carotid and subclavian arteries, descending aorta, bilateral common iliac arteries, and proximal internal iliac arteries. On admission (day 0), the patient reported bilateral femoral pain. On physical examination, temperature was 37.1°C, blood pressure was 147/78 mmHg in both arms. No carotid bruits were heard. Blood tests showed a CRP of 1.54 mg/L, and ESR of 82 mm. Vascular echo revealed thickening of all layers of arterial wall, and she was diagnosed with Takayasu arteritis. Treatment with prednisolone was started on day 4 at a dose of 30 mg per day, which was tapered as an outpatient. On day 11, CRP was 0.09 mg/L, ESR was 22 mm, and her bilateral femoral pain had resolved. On day 14, we repeated vascular echo, which showed the right external iliac arterial-wall thickening to be 3.3 mm, down from 10.2 mm on day 3. The ureteral stent was removed on day 130 after ureteroscopy revealed no more ureteral stricture. To our knowledge, this is the first case of hydronephrosis caused by Takayasu arteritis.

ICW16-3

Effects of tocilizumab on immunophenotypic features in patients with large vessel vasculitis: results of a 1-year FLOW study

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Conflict of interest: Yes

[Objective] Immunophenotypic features and pathological immune cell subsets targeted by immunosuppressants and/or molecular target therapy in patients with large vessels vasculitis (LVV) are unknown. Here, we analyzed the immunophenotype and responsiveness to the treatment such as tocilizumab (TCZ) in patients with LVV. [Methods] Patients with new-onset LVV (GCA, n=22, TAK, n=18) and age- and sex-matched healthy controls (HC: n=44) were enrolled. Based on the standard human immune cell subset classification protocol by NIH/FOCIS, peripheral immune cell phenotypes at baseline and at 1 year after induction therapy were analyzed. We classified LVV patients by cluster analysis of immunophenotypes before treatment. [Results] Patients with high disease activity had a higher proportion of activated Th17 cells and a lower proportion of activated Treg cells compared to the HC. Cluster analysis revealed that the patients could be classified into 3 subgroups. The acquired immunity dominant group (n=19) had a higher proportion of memory CD4, CD8 T cells, activated Th17 cells and a lower proportion of activated Treg cells than other groups. This group had significantly lower remission rates at 1 year than other groups. In this group, patients who received with TCZ (n=9) resulted in significantly higher remission rates than those who did not (n=10) (66.6% vs 10.0%). The proportion of activated Treg cells was increased and that of activated Th17 cells was decreased in patients who received with TCZ; however, those changes were not seen in patients who did not receive TCZ. [Conclusion] Three immunological subgroups were identified based on peripheral blood immunophenotypic features in patients with LVV. The group with a high percentage of activated Th17 cells and fewer activated Treg cells were resistant to treatment. TCZ may correct the impaired balance of Th17 and Treg cells. The results also suggested that stratification by immunophenotypic features may lead to optimized treatment for LVV.

ICW16-4

Advantage of Tofacitinib (TOF) on maintaining corticosteroid (CS)-independent low disease activity of Takayasu Arteritis (TA) Complicated in Ulcerative Colitis (UC)

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Conflict of interest: None

[Introduction] TA complicated with UC is occasionally experienced and steroid still remains as the mainstay of the treatment. Limited number of case reports have indicated the utility of TOF in these patients. [Methods] Retrospectively reviewed three consecutive patients with TA complicated UC. [Results] Three patients; 19 y.o. male, 26 y.o. female and another 26 y.o. female who were suffering with precedent UC for 2 to 7 years developed TA during the maintenance phase, which was diagnosed based on CT angiography and PET-CT. Common clinical findings were general fatigue, low-grade fever and chest pain with sustained elevation of serum inflammatory responses which was unrelated to UC. High dose prednisolone (PSL) was initiated in two patients who had been treated with infliximab or mesalamine, and add-on TOF resulted in complete disappearance of symptoms as well as inflammatory reactions in three weeks. Interestingly, a female patient who had a 2-year history of UC developed TA during TOF monotherapy, required high dose PSL where her symptoms ameliorated in several days. Patients were able to taper-off PSL, and the followed-up PET-CT reassured the improvement and maintenance of remission of both TA and UC. [Conclusion] These cases indicate that high dose CS is absolutely necessary for remission induction of TA and treatment with TNF inhibitors or TOF cannot avoid the occurrence of TA. Whereas TOF can be appreciated for maintenance therapy with the proper multicytokine inhibition, hopefully leading to tapering off CS, and can potentially reduce the drug-associating burden in patients complicated with TA and UC.

ICW16-5

HMGB1 is highly expressed in injured muscle fibers and accelerates inflammation and muscle injury in inflammatory myopathies

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Conflict of interest: None

[Objective] We have revealed that the cell death of muscle fibers induced by cytotoxic T lymphocytes (CTLs) in polymyositis (PM) is necroptosis, suggesting that the injured muscle fibers release inflammatory mediators including damage-associated molecular patterns (DAMPs) to accelerate inflammation and muscle injury in PM. The objective of this study is to clarify the involvement of high mobility group box-1 (HMGB1), which is one of DAMPs, in the pathophysiology of PM. [Methods] Muscle tissue of PM patients were examined with immunofluorescence staining for the expression of HMGB1. As an in vitro model of PM, OT-I CTLs were cocultured with myotubes differentiated from C2C12 cells that were

retrovirally transduced with the genes encoding MHC class I ($H2K^b$) and SIINFEKL peptide. The levels of HMGB1 in the supernatant of the coculture was measured by ELISA. C protein induced-myositis (CIM) was used as a murinemodel of PM. The expression of HMGB1 in the muscle was examined with immunofluorescence staining. The level of HMGB1 in the serum was measured by ELISA. The effect of anti-HMGB1 antibody on CIM was examined. [Results] HMGB1 was highly expressed in the injured muscle fibers of PM patients. The coculture of the myotubes and OT-I CTLs resulted in elevated levels of HMGB1 in the supernatant compared to the monoculture of the myotubes. The level of HMGB1 in the supernatant of the coculture was suppressed by the pretreatment of the myotubes with a necroptosis inhibitor. In CIM mice, HMGB1 was expressed in the injured muscle fibers. The level of HMGB1 in the serum was elevated in CIM compared to the control mice. The treatment with anti-HMGB1 antibody on CIM suppressed muscle weakness, muscle weight loss, inflammatory infiltrates, and necrotic areas in the muscles. [Conclusions] HMGB1 is highly expressed in the injured muscle fibers and contributes to the pathophysiology of PM. HMGB1 could be a novel therapeutic target in PM.

ICW16-6

Contrast of muscle magnetic resonance imaging and pathological findings of muscle tissue in patients with anti-aminoacyl transfer RNA synthetase antibodies

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Conflict of interest: None

[Objective] Anti-aminoacyl transfer RNA synthetases (ARS)-associated myositis has been recognized as the independent disease entity in terms of muscle pathology to show the fascicular necrosis irrespective of clinical diagnosis of polymyositis (PM) or dermatomyositis (DM). The aim of this study is to reveal whether those pathological features are associated with the findings detected with magnetic resonance imaging (MRI). [Methods] Consecutive patients with PM or DM diagnosed with Bohan and Peter criteria in our university between 2005 and 2020 were reviewed, and those with anti-ARS antibodies detected with enzyme linked immunosorbent assay or immune precipitation assay were analyzed. Fat-suppressed T2-weighted images on MRI were assessed for the distribution and frequency of high signal intensity, and the specimens of muscle biopsies were assessed for the pathological findings. [Results] Twenty five patients (14 PM and 11 DM) with anti-ARS positive and 37 patients (22 PM and 15 DM) with anti-ARS negative patients were included. High signal intensity in subcutaneous tissue and fasciae with MRI were more frequently observed in DM than PM in anti-ARS negative patients (71% vs 29%, $p < 0.05$ and 67% vs 33%, $p < 0.05$, respectively). In contrast, high signal intensity in subcutaneous tissue and in fasciae were comparably detected between DM and PM in anti-ARS positive patients (45% vs 21%, $p = 0.2$ and 63% vs 57%, $p = 1.0$, respectively). In 7 anti-ARS positive patients (2 PM and 5 DM) who had undergone muscle biopsy, fascicular lesions were detected in 6 patients (85.7%), and the fascicular lesions in muscle tissues were reflected by fascicular high signal intensity with MRI. [Conclusions] Fascial high signal intensity on MRI in anti-ARS positive patients reflects distinctive pathological features of muscle specimens.

ICW17-1

Identification of predictors associated with death due to interstitial lung disease in patients with ANCA-associated vasculitis

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Conflict of interest: Yes

[Objective] The prevalence of interstitial lung disease with ANCA-associated vasculitis (AAV-ILD) patients is higher in Japan compared with that in Western countries. ILD involvement is associated with increased mortality. However, how AAV-ILD develop during treatment was not well discovered. The aim of this study was to determine the clinical course of AAV-ILD, and to assess the predictors associated with death due to ILD activity. [Methods] We retrospectively reviewed 121 patients from Keio University Hospital who had been newly diagnosed with AAV from 2005 to 2019. We collected clinical information and the chest high-resolution computed tomography (HRCT) images of consecutive AAV patients before and after they received treatment. Disease extent based on the area of interstitial fibrosis on the chest HRCT was obtained and compared with clinical parameters. We first compared mortality rate and cause of death between AAV patients with and without ILD. We then compared baseline characteristics and clinical course of AAV-ILD between patients with and without death due to ILD activity. [Results] ILD was observed in 30% of AAV patients. Ninety-seven% had MPO-ANCA and 81% was diagnosed as MPA. Mortality rate was significantly higher in AAV-ILD than those without ILD (42% vs 4%, $p<0.0001$). Of 15 patients who died, 9 were due to ILD activity. We obtained HRCT extent of disease from 449 consecutive images from AAV-ILD, and found that they positively correlated with serum KL-6 ($p<0.0001$) and negatively correlated with serum ANCA-titer ($p<0.0001$). Univariate analysis revealed that age (81 vs 73 years, $p=0.0015$), HRCT extent of disease (49% vs 25%, $p=0.0002$) and serum KL-6 (840 vs 464 U/mL, $p=0.025$) at AAV diagnosis were significantly higher in patients with death due to ILD activity than those without. [Conclusions] ILD was the most frequent cause of death in Japanese AAV patients. Treatment may be effective for young patients, low HRCT extent of disease, and low serum KL-6.

ICW17-2

Clinical features of mononeuritis multiplex associated with ANCA-associated vasculitis

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Conflict of interest: None

[Objective] This study aimed to determine the clinical features of mononeuritis multiplex associated with AAV. [Methods] Consecutive patients with AAV who visited our department between 2006 and 2020 were included in our study. We examined the following clinical features, with and without motor neuropathy (MN) and sensory neuropathy (SN): the worst blood test values before the initial therapy (white blood cell count (WBC), WBC differentiation, and C-reactive protein (CRP) levels). [Results] A total of 93 patients with AAV were identified. Among them, 22 patients had eosinophilic granulomatosis with polyangiitis (EGPA), 10 patients had granulomatosis with polyangiitis (GPA), and 61 patients had microscopic polyangiitis (MPA). Of the 93 AAV patients, 30 had SN (17/22 EGPA, 13/61 MPA, and 0/10 GPA). MN was observed in 21 patients (EGPA 15/22, MPA 6/61, GPA 0/10). 17 patients had both sensory and motor neuropathies (EGPA 13/22, MPA 4/61, GPA 0). In patients with both SN and MN, sensory impairment preceded in all cases. Between the patients with EGPA with and without SN, lymphocytes were significantly lower in those with sensory disorder than those without (Ly 1300±179 vs. 2300±370/μL ($p=0.02$)) before the initial therapy. On the other hand, comparing the EGPA patients with and without motor neuron disorder, CRP levels were significantly higher in those with motor impairment than those without (CRP 5.39±0.84 vs. 1.92±1.24 mg/dL ($p=0.03$)). Between the patients with MPA with and without SN or MN, there were no significant differences in the following: WBC, Ly, Eo and CRP before the initial therapy. [Conclusions] We determined the clinical feature of mononeuritis multiplex associated with AAV. Worst CRP levels before the initial therapy can be a poor prognosis factor for MN in patients with EGPA. Therefore, EGPA patients with high CRP levels need to be paid more attention to because of possible development of MN. S.H. and Y.H. contributed equally.

ICW17-3

Examination of the relationship between cerebrovascular disease associated with microscopic polyangiitis and serum cytokine levels

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Conflict of interest: None

[Objective] We examined the relationship between cerebrovascular disease (CVD) associated with microscopic polyangiitis (MPA) and serum cytokine levels. [Methods] The subjects were 38 consecutive MPA patients whose head MRI was taken and serum could be preserved before treatment. Based on head MRI findings of the head, subjects were divided into two groups: CVD group (Fazekas scale ≧2) and non-VCD group. In addition, the Shelten score and the ARWMC score were used to semi-quantify the extent of CVD lesions. Serum cytokines associated with Th1 cells (GM-CSF, IL-2, IFN-γ), Th17 cells (IL-17A, IL-23), monocytes/macrophages (IL-1β, TNF-α, CCL2), B cells (IL-6), and neutrophils (G-CSF, IL-8) were comprehensively measured, which have been reported to be related to the pathophysiology of MPA. [Results] There was no difference in age, sex, existing atherosclerosis risk factors, and MPA pathological indicators (CRP, MPO-ANCA, BVAS, FFS, EUVAS) between the CVD group and the non-CVD group. The median pretreatment serum GM-CSF level was significantly higher in the CVD group (1.5, range 0.3-9.5) than that in the non-CVD group (0.3, range 0.3-2.0) (P = 0.03), but there was no difference in other serum cytokine levels. The cut-off value of pretreatment serum GM-CSF to predict CVD complication was 0.5 pg/mL (AUC 0.693, sensitivity 68.4%, specificity 68.4%). Multivariate analysis including confounding factors (age, arteriosclerosis risk factors) showed that pretreatment serum GM-CSF elevation was an independent risk factor for CVD complication in MPA (Odds ratio 6.25, 95%CI 1.35-28.94, P = 0.02). [Conclusions] Pretreatment serum GM-CSF levels may be useful biomarkers in predicting complication and assessing severity of CVD in MPA patients.

ICW17-4

High bilateral lower lobe fibrosis scores on chest HRCT are associated with respiratory-related death in microscopic polyangiitis complicated by interstitial lung disease

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Conflict of interest: None

[Objective] We investigated prognostic factors of respiratory-related death in patients with microscopic polyangiitis (MPA) complicated by interstitial lung disease (ILD). [Methods] We enrolled 80 patients with MPA in this study, of whom 47 also had ILD. We retrospectively reviewed baseline demographic, clinical, laboratory, and radiological findings, treatments, and outcomes between MPA patients with and without ILD. The presence of ILD was assessed by high-resolution computed tomography and evaluated by ground-glass opacity and fibrosis scores. We also compared demographic significances between the alive and dead patients with MPA-ILD. [Results] Fourteen patients with MPA died due to respiratory diseases, of whom 10 died due to respiratory infections. The presence of ILD was consistent with a high risk of respiratory-related death (hazard ratio, 4.8; P=0.04). Multivariable logistic regression analyses using propensity scoring showed right or left lower lobe fibrosis score to be significantly associated with respiratory-related death (P=0.0005 and 0.0045, respectively). A right or left lower lobe fibrosis score ≧2, which indicates the presence of honeycomb lesions at 1 cm above the diaphragm, was determined to be the best cut-off value indicating a poor prognosis. The 5-year survival rate was significantly lower in patients with right or left lower lobe fibrosis score ≧2 (survival rates: 37% and 19%, respectively) than those with a score <2 (71% and 68%, respectively) (P=0.002 and 0.0007, respectively). [Conclusions] The extent of lung fibrosis and the presence of honeycomb lesions in bilateral lower lobes on chest HRCT were associated with respiratory-related death in Japanese patients with MPA-ILD.

ICW17-5

Mepolizumab is able to reduce Corticosteroids dose in Patients with Eosinophilic Granulomatosis with Polyangiitis under Remission

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Conflict of interest: None

[Objective] The utility of additive mepolizumab (MEP) treatment in patients with eosinophilic granulomatosis with polyangiitis (EGPA) under remission is unknown. This study aims to investigate the prednisolone (PSL) reduction by additive MEP. [Methods] We defined remission as treated with prednisolone (PSL) ≦ 7.5 mg/d. EGPA patients under remission were recruited and compared the clinical outcome of patients that initiated MEP (MEP group, N=6) and those that did not (control group, N=14). Clinical information was collected at baseline; at the time of MEP initiation for the MEP group or at the time when PSL was reduced to 7.5 mg/d for the control group, and 6 months later. [Results] In the MEP group, daily PSL dose significantly reduced from 6.5 mg [4-7.5] to 2.5 mg [1-5] (p=0.031) and eosinophil count significantly decreased from 435 /μl [301-858] to 32.5 /μl [11-171] (p=0.031) without exacerbation of Birmingham Vasculitis Activity Score (BVAS) (0.5 to 0). On the other hand, in the control group, daily PSL also decreased from 7 mg [5-7] to 6 mg [1-9] (p=0.040) with no change in BVAS (3 to 3) whereas eosinophil count increased from 197.5 /μl [19-488] to 234 /μl [54-775] (p=0.037) and PSL was increased in 3 patients. Overall, PSL was reduced to less than half from baseline in 66.7% of the MEP group while it was 7.1% in the control group (p=0.014). Additive MEP was a significant factor for reducing daily PSL (odds ratio: 25.99, 95% confidence interval: 2.44-694.9, p=0.016). [Conclusions] MEP was able to reduce daily PSL dose without an increase in the eosinophil count and disease activity in EGPA patients under remission.

ICW17-6

Effectiveness and Safety of Mepolizumab in Combination with Corticosteroids in patients with Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: None

Objectives: Mepolizumab (MPZ), an anti-interleukin-5 antibody, is effective for treating eosinophilic granulomatosis with polyangiitis (EGPA). However, its effectiveness has not been adequately evaluated in real-world clinical practice. In this study, we assessed the effectiveness and safety of 300 mg MPZ for relapsing/refractory EGPA resistant to corticosteroids (CS) for 1 year in real-world settings. Objectives **Methods:** We administered MPZ (300 mg) to 16 patients with relapsing/refractory EGPA resistant to CS (with-MPZ) (month 0 to month 12). We also retrospectively collected data from the same patients for 12 months before administering MPZ (without-MPZ) (month -12 to month 0). The primary endpoint was the 12-month remission rate after MPZ administration, and the secondary endpoints were the Birmingham vasculitis activity score (BVAS), vasculitis damage index (VDI), eosinophil count, changes in concomitant CS doses/concomitant immunosuppressant use, MPZ retention rate, and incidence of adverse events. The clinical course was compared between Without-MPZ and With MPZ. **Results:** The 12-month remission rate after initiating MPZ was 75%. No change was observed in BVAS, eosinophil count, or concomitant CS dose in the without-MPZ (BVAS 0 [0-2]→1.0 [0-3.8], CS 8.0 [5.0-10]→6.5 [2.6-10] mg/dL, eosinophil count 303 [55-483]→183 [60-2478]), whereas all these parameters were significantly decreased in the with-MPZ (BVAS 1.0 [0-3.8]→0 [0-0], CS 6.5 [2.6-10]→2.5 [0.1-3.8] mg/dL, eosinophil count 183 [60-2478]→28.8 [20.5-68]). The number of patients on concomitant immunosuppressants also decreased in the with-MPZ. VDI did not increase in both groups (Without-MPZ 3.5 [3.0-4.8]→4.0 [3.0→5.5], With-MPZ 4.0 [3.0-5.5]→4.0 [3.0-5.5]). The MPZ retention rate was 100%, and only three patients (18.8%) had infections. **Conclusion:** This study demonstrated that MPZ is

effective and safe for EGPA, furthermore, compared to Without-MPZ, MPZ improves disease activity and possesses a higher remission rate and CS sparing effect.

ICW18-1

Granulocyte-macrophage colony-stimulating factor and tumor necrosis factor alfa in combination is a useful diagnostic biomarker to distinguish familial Mediterranean fever from sepsis

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Conflict of interest: None

[Objective] To identify potential biomarkers to distinguish familial Mediterranean fever (FMF) from sepsis. [Methods] We recruited 28 patients diagnosed with typical FMF according to the Tel Hashomer criteria, 22 patients with sepsis, and 118 age-matched controls. Serum levels of 40 cytokines were analyzed using multi-suspension cytokine array. We performed a cluster analysis of each cytokine in the FMF and sepsis groups in order to identify specific molecular networks. Further, multivariate classification (random forest analysis) and logistic regression analysis were used to rank the cytokines by their importance and determine specific biomarkers for distinguishing FMF from sepsis. [Results] Seventeen of the 40 cytokines were found to be suitable for further analyses. Levels of serum Granulocyte-macrophage colony-stimulating factor (GM-CSF), fibroblast growth factor 2, vascular endothelial growth factor, interferon-γ, and interleukin-17 were significantly elevated, whereas tumor necrosis factor-α (TNF-α) was significantly lower in patients with FMF compared with those with sepsis, and cytokine clustering patterns differed between these two groups. Multivariate classification followed by logistic regression analysis revealed that measurement of both GM-CSF and TNF-α could distinguish FMF from sepsis with high accuracy (cut-off value for GM-CSF = 8.3 pg/mL; TNF-α = 16.3 pg/mL, sensitivity 92.9%, specificity 94.4%, accuracy 93.4%). [Conclusions] Determination of GM-CSF and TNF-α levels in combination may represent a biomarker for the differential diagnosis of FMF from sepsis, based on the measurement of multiple cytokines.

ICW18-2

Ratio of serum ferritin levels to erythrocyte sedimentation rate for macrophage activation syndrome in patients with adult Still's disease

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Conflict of interest: None

[Objective] Ratio of serum ferritin levels to erythrocyte sedimentation rate (ESR) has been proposed to be useful for diagnosis of macrophage activation syndrome (MAS) in patients with systemic juvenile idiopathic arthritis. Although adult Still's disease (ASD) is similar to systemic juvenile idiopathic disease, it is unclear whether the ratio is useful for patients with ASD. To investigate the utility of the ratio of serum ferritin levels to ESR for diagnosing MAS in patients with active ASD and to clarify its optimal cutoff value. [Methods] Patients with ASD in Keio University Hospital with serum ferritin levels and ESR data available were included. Patients were divided into two groups according to the presence of MAS and compared. [Results] We identified 45 patients with active ASD; 11 with MAS and 34 without MAS. In the laboratory findings, significant difference was found between the patients with MAS and those without MAS in serum ferritin levels (14043 [5931-38600] ng/ml in the MAS group vs. 1765 [705-5703] ng/ml in the non-MAS group, p=0.0049) and ESR (17 [10-55] mm/hr in the MAS group vs. 93 [65-111] mm/hr in the non-MAS group, p=0.0004). The ratio of serum ferritin levels to ESR was 539 [133-4189] in the MAS group and 30 [8-68] in the non-MAS group (p=0.0002). The receiver operating characteristic curve analysis revealed the optimal cut-off of the ferritin to ESR ratio 133.5 (area under the curve (AUC), 0.87433; sensitivity, 81.8%; specificity, 82.4%), which had significantly better accuracy than serum ferritin levels (cut off, 5931 ng/ml; AUC, 0.78610; sensitivity, 81.8%; specificity 76.5%) and showed better specificity compared to that of ESR (cut off, 64.0 mm/hr; AUC, 0.86096; sensitivity, 90.9%; specificity, 76.5%). [Conclusions] ESR and ferritin to ESR ratio showed good accuracy for diagnosing MAS in active patients with ASD with a better specificity in ferritin to ESR ratio. Ferritin levels were not useful for discriminating MAS from non-MAS.

ICW18-3

COVID-19 shares clinical features with anti-melanoma differentiation associated protein 5 positive dermatomyositis and adult Still's disease

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Conflict of interest: None

[Objective] To investigate the similarities and differences between coronavirus disease 2019 (COVID-19) and autoimmune and autoinflammatory rheumatic diseases characterised by hyperferritinaemia, such as antimelanoma differentiation-associated protein 5 (MDA5) autoantibody-positive dermatomyositis and adult Still's disease. [Methods] We reviewed consecutive, newly diagnosed, untreated patients with COVID-19, anti-MDA5 dermatomyositis, or adult Still's disease. We compared their clinical, laboratory, and radiological characteristics, including the prevalence of macrophage activation syndrome and lung involvement in each disease. [Results] The numbers of patients with COVID-19, anti-MDA5 dermatomyositis, and adult-onset Still's disease with hyperferritinaemia (serum ferritin ≧ 500 ng/dL) who were included for main analysis were 22, 14, and 59, respectively. COVID-19 and adult Still's disease both featured hyperinflammatory status, such as high fever and elevated serum C-reactive protein, whereas COVID-19 and anti-MDA5 dermatomyositis both presented with severe interstitial lung disease and hypoxaemia. While two-thirds of the patients in each group met the criteria for macrophage-activated syndrome that is used in systemic juvenile idiopathic arthritis, the HScore, an indicator of haemophagocytic lymphohistiocytosis, was low in anti-MDA5 dermatomyositis and COVID-19 even in severe or critical cases. The findings of chest computed tomography were similar between COVID-19 and anti-MDA5 dermatomyositis. [Conclusions] COVID-19 shared clinical features with rheumatic diseases characterised by hyperferritinaemia, including anti-MDA5 dermatomyositis and adult Still's disease. These findings should be investigated further in order to shed light on the pathogenesis of not only COVID-19 but also the aforementioned rheumatic diseases.

ICW18-4

Interferon-gamma producing immunocompetent cells for predicting disease activity and severity in adult-onset Still's disease

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Conflict of interest: None

[Objective] In adult-onset Still's disease (AOSD), some patients show resistance to initial immunosuppressive treatment or have a relapse. In this study, we investigated the relationship between serum levels of interferon-γ (IFN-γ), IFN-γ-producing immunocompetent cells, and clinical features in order to clarify the relevant factors related to disease activity and prognosis of AOSD. [Methods] Twenty-five patients with acute AOSD, 9 patients after remission (remission AOSD), and 12 healthy controls (HC) were included. Patients refractory to initial treatment were defined as having a refractory course (refractory patients). Natural killer (NK) cells, IFN-γ production in NK cells, and IFN-γ-producing CD4+ cells in peripheral blood mononuclear cells were evaluated by flow cytometry. Serum levels of IFN-γ were measured using ELISA. The obtained results were statistically analyzed together with clinical findings. [Results] Serum levels of IFN-γ, proportion of CD4+IFN-γ+ cells, and expression of IFN-γ in CD4+ cells and NK cells were significantly higher in acute AOSD than in

HC. The proportion of NK cells was significantly lower in acute AOSD than in HC. These data were significantly improved in remission AOSD. Serum ferritin levels were significantly correlated with serum levels of IFN-γ and expression of IFN-γ in CD4+ cells. Serum levels of IFN-γ had a significant reverse correlation with NK cells. Of the 25 patients, 18 were defined as refractory patients. A lower proportion of NK cells was significantly demonstrated in refractory patients than in non-refractory patients. [Conclusions] Increase in serum levels of IFN-γ, increased expression of IFN-γ in CD4+ cells, and decrease in NK cell proportion may be parameters of disease activity in AOSD. Furthermore, a lower proportion of NK cells may be implicated in an intractable clinical course.

ICW18-5

Utility of Tocilizumab (TCZ) to Maintain Low Disease Activity and Tapering Corticosteroid (CS) in Adult-Onset Still's Disease (AOSD) in real-world practice: a single-center analysis

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Conflict of interest: None

[Objective] The aim of this study is to investigate the efficacy of TCZ in maintaining low disease activity and reducing CS in AOSD. [Methods] AOSD patients admitted for remission induction therapy from 2010 to 2020 were enrolled. Remission rate (satisfying all of the following; no organ damage due to AOSD, negative CRP and normal ferritin levels), daily CS dose, rate of recurrence and severe infection were compared between patients treated with TCZ (TCZ group) and without TCZ (non-TCZ group). [Results] Age was 56.8±20.6 (mean±SD) y.o. (N=17) with 13 females (76.5%). There were no differences in ages, gender, white blood cell counts, ferritin and CRP on admission between TCZ group (n=9) and non-TCZ group (n=8). TCZ was initiated 24.5±10.5 days after initiation of induction therapy when receiving PSL 43.5±11.5 mg/day with CRP 1.8±1.7 mg/mL, concomitant methotrexate (MTX) (n=3) or calcineurin inhibitors (CNI) (n=6). Non-TCZ group were treated with MTX (n=5) and CNI (n=4). TCZ was discontinued (28.5%) due to newly-onset infections. The remission rate was similar, TCZ group 88.8% and non-TCZ group 100% (p=0.338). Recurrence was significantly less in TCZ group (22.2% vs. 62.5%) (p=0.018) and PSL dose reduction to 3 mg/day was observed significantly higher in TCZ group (66.6% vs. 37.5%) (p=0.047) however PSL-free rate was not different (p=0.612). Life-threatening infections in TCZ group and non-TCZ group was 88.5% and 50.0% respectively without statistical difference (p=0.087). [Conclusions] AOSD patients treated with TCZ showed significantly reduced recurrence during the maintenance phase with successful dose reduction of CS compared to those without TCZ. Our results indicate that TCZ could contribute to reduction of accumulating damages by disease activity as well as CS compared to the conventional treatment.

ICW19-1

Single-cell analysis of salivary gland epithelial cells revealed enhanced interferon signature and dysfunction of multipotent stem cells in Sjögren's syndrome

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Conflict of interest: None

[Objective] In Sjögren's syndrome (SS), lymphocytic infiltration is one of the characteristics of the pathology of salivary glands. Although several transcriptome studies has shown an increased interferon (IFN) signature of the salivary gland tissue, most studies were bulk analyses and performed without separating cell types. In this study, we focused on the salivary gland epithelial cells (SGEC) and analyzed their transcript at the bulk and single-cell levels. [Methods] Salivary gland biopsy tissues from seven SS patients and five non-SS patients were collected. Tissues were mechanically and enzymatically digested to single cell suspension and from them, SGEC were sorted as bulk samples (50-300 cells) or single cell samples. Transcriptome analysis was performed using the Smart-seq2. [Results] In bulk analysis, an enhanced IFN signature were observed in the SS group compared with non-SS group as previously reported. In single cell analysis, 291 cells were sorted and approximately 4000 genes per cell were detected on average. These cells were divided into four groups by unsupervised clustering. We examined the genes characteristic of each group by immunostaining and information from previous studies, and considered that these clusters are serous acinar cells, mucous acinar cells, duct cells, and basal cells. We then compared SS and non-SS for each cell type, and revealed that the SS group showed enhanced IFN signatures in all subsets. On the other hand, different signatures were downregulated for each cell type in SS group. In particular, in basal cells, which were considered to be multipotent stem/progenitor cells, cell cycle-related pathways were significantly downregulated in SS group. [Conclusions] The salivary gland epithelial cells are divided into four subsets, and all subsets were affected by IFN probably derived from infiltrated lymphocytes. The decreased proliferation ability of basal cells were one of the causes of long-term glandular dysfunction of SS.

ICW19-2

Transcriptome analysis and B cell receptor repertoire in IgG4-Related Disease

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Conflict of interest: Yes

[Objective] IgG4-related disease (IgG4-RD) is a disease entity characterized by lymphoplasmacytic infiltrates rich in IgG4-expressing plasma cells and fibrosis of involved organs. However, the driving mechanism of immunoglobulin class switching to IgG4 has not been elucidated to date. In this study, we assessed the mechanism via immunophenotyping and transcriptome analysis in IgG4-RD. [Methods] Eleven patients of IgG4-RD patients and 17 age- and sex-matched healthy controls were enrolled. For patients, organ involvement and disease activity was evaluated based on IgG4-RD responder index (RI). Peripheral blood mononuclear cells were isolated from whole blood by Ficoll-Paque separation, and phenotype of total 25 immune cell subsets was analyzed and sorted by flow cytometry. The gene expression data of each subset obtained by RNA-sequencing were evaluated to identify subset-specific differential expressed genes (DEGs) and detect modules of correlated genes by weighted gene co-expression network analysis (WGCNA) package. Kyoto Encyclopedia of Genes and Genomes was used for pathway analysis. Further, immunoglobulin repertoire in each B cell subset was evaluated by MiXCR software to quantitate clonotypes. [Results] Immunophenotyping analysis revealed that double negative (DN) B cell proportion was significantly increased in IgG4-RD patients and plasmablast proportion was positively correlated to IgG4-RD RI. The number of DEGs in B cells was much larger than other subsets. WGCNA identified 3 modules related to serum IgG4 in DN B cells, and pathway analysis indicated that B cell receptor signaling pathway-related genes were enriched in the modules. Further, increased IgG4 and decreased IgA1 isotype usage was observed in plasmablasts, switched memory B cells, and DN B cells by immunoglobulin repertoire analysis. [Conclusions] The increased proportion, greater DEGs, and isotype usage indicated that B cell subpopulation could play a pivotal role in IgG4 class-switching in IgG4-RD.

ICW19-3

The proportion of interleukin-21 producing TIGIT+ T follicular helper cells represents disease activity in IgG4-related disease

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Conflict of interest: None

[Objective] Recent studies has suggested the potential of T cell immunoreceptor with immunoglobulin and ITIM domain (TIGIT) as a new surface marker of T follicular helper (Tfh) cells. Interleukin (IL)-21 is one of Tfh-associated cytokines and increased in the affected sites of IgG4-related disease (IgG4-RD). The objective of this study was to examine that TIGIT expression can detect IL-21 producing Tfh cell populations and their clinical significance in IgG4-RD, a representative Tfh-associated disease. [Methods] Twenty-three untreated, active IgG4-RD patients and 21 healthy controls were enrolled. Comprehensive analysis of TIGIT expression in peripheral $CD4^+$ T cells and their subsets was carried out by multi-color flow cytometry. Intracellular IL-21 production was examined in $TIGIT^+$ and TIGIT- Tfh cells upon the stimulation with PMA and ionomycin in vitro. The significance of $TIGIT^+$ Tfh cells of IgG4-RD patients was analyzed along with their clinical parameters. [Results] Peripheral Tfh cells showed significantly higher expression of TIGIT than peripheral CXCR5-T helper cells (mean positivity, 43% versus. 19%, $p < 0.0001$). $TIGIT^+$ Tfh cells had higher ability to produce IL-21 than TIGIT- Tfh cells. IgG4-RD patients exhibited significant increase in the proportion of $TIGIT^+$ Tfh cells and $TIGIT^+$ Tfh2 cells than healthy controls. Notably, the proportion of $TIGIT^+$ Tfh cells and $TIGIT^+$ Tfh2 cells positively correlated with the scores of disease activity, number of affected organs, and serum IgG4 levels in patients with untreated, active IgG4-RD. Serial analysis demonstrated that the increased proportion of $TIGIT^+$ Tfh cells and $TIGIT^+$ Tfh2 cells significantly decreased along with the clinical improvement after 12-week glucocorticoid therapy. [Conclusions] TIGIT identifies high IL-21 producing Tfh cell populations and the increase of $TIGIT^+$ Tfh cells reflects disease activity in IgG4-RD. Our data suggest that TIGIT can be a useful marker for activity of Tfh-cell responses.

ICW19-4

Effectiveness and safety of Mizoribine for the treatment of IgG4-related Disease: A Retrospective Cohort Study

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Conflict of interest: None

[Objective] Patients with IgG4-Related Disease (IgG4RD) usually require steroid-sparing agents due to relapse with tapering glucocorticoids (GC). The aim of this study was to determine the efficacy and safetyof Mizoribine (MZR) among IgG4RD, which inhibits inosine monophosphate dehydrogenase, a rate-limiting enzyme in the de novo pathway of purine synthesis. [Methods] We retrospectively reviewed records of IgG4RD patients at the Immuno-Rheumatology Center in St. Luke's International Hospital, Tokyo, Japan. Patients were classified into the MZR combination group, and those treated with GCs alone or with other immunosuppressants were included in the control group. Disease exacerbation, GC dose, IgG-IgG4 titre, and adverse events were evaluated using univariate analyses, including the Kaplan-Meier method. The Cox proportional hazard model was used to evaluate risk factors for exacerbation. [Results] A total of 14 and 29 cases were included in the MZR combination and control groups, respectively. Multiple organ involvement (>= 3 organs) was significantly morefrequent in the MZR combination treatment group (10 [71.4%] vs. 9 [31.0%], p=0.021). Kaplan-Meier analysis revealed a significant reduction in exacerbation in patients with multiple organ involvement ($p<0.001$), but not in total (p=0.42). The adjusted hazard ratios of MZR use and multiple organ involvement for exacerbation were 0.34 [0.12-1.01] (p= 0.052), and 3.51 [1.29-9.51] (p= 0.014). The cumulative GC dosetended to belower in the MZR combination group (1448 [1003, 1642] vs 2179 [1264, 3425]; p=0.09). [Conclusions] MZR showed a significant steroid-sparing effect and decrease in exacerbation among IgG4RD patients with multi-organ involvement. MZR could be a treatment option for IgG4RD.

ICW19-5

Interleukin-4 activates eosinophils and CCR3-positive T helper type 2 cells migration to fascia and promotes fibrosis in eosinophilic fasciitis

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Conflict of interest: None

[Objective] Eosinophilic fasciitis (EF) is a rare disease that causes inflammation and fibrosis mainly in the fascia of the extremities with eosinophilia. However, its pathophysiology in the fascia remains unresolved. Therefore, we focused on fascial fibroblasts and aimed to clarify the mechanism of migration of eosinophils and T helper type 2 (Th2) cells and fibrosis. [Methods] Fascial fibroblasts were obtained from fascia biopsy of a patient with EF, and were stimulated with pre- and post-treatment serum of a patient with EF and healthy control, followed by microarray to analyze gene expression. Fascial fibroblasts were stimulated with interleukin-4 (IL-4) 10 ng/mL, and gene expression of CCR3 ligands, CCL7 and CCL11 were measured by qPCR. Transforming growth factor (TGF) -β and periostin in the pre- and post-treatment serum of a patient with EF and conditioned medium of fascial fibroblasts stimulated with IL-4 were measured by ELISA. CCR3-positive T cells in the fascial tissue of EF, dermatomyositis, and polymyositis patients were evaluated by immunostaining. [Results] By microarray analysis, CCL7 and CCL11 expression of fascial fibroblasts stimulated with pre-treatment EF serum was higher than that in post-treatment EF serum and control serum. IL-4 stimulation of fascial fibroblasts increased the gene expression of CCL7 and CCL11 by 5.1-fold and 7.3-fold, respectively and increased TGF-β and periostin in the conditioned medium. TGF-β and periostin in EF serum were gradually decreased by treatment for 4 and 10 weeks, compared to before treatment. Furthermore, infiltration of CCR3-positive T cells was specific to the fascial tissue of EF. [Conclusions] In EF, IL-4 enhances the production of CCR3 ligands, TGF-β, and periostin from fascial fibroblasts. As a result, it promotes the migration of eosinophils and CCR3-positive Th2 cells to the fascia and fibrosis. These results suggest that inhibition of IL-4 pathway could be a novel strategy for eosinophilic fasciitis.

ICW19-6

Novel compound that impacts migration and chemokine production via NFkB suppressing activity

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Conflict of interest: Yes

[Objective] Despite the advance of target-based drug discovery in the treatment of autoimmune diseases, glucocorticoids (GC) remain reliable agents. We have discovered novel compounds by high throughput screening (HTS) focusing on NF-κB activity. In this study, we assessed the potency of specific chemotypes in reducing pro-inflammatory cytokine and chemokine production from fibroblast-like synoviocytes (FLS) from rheumatoid arthritis (RA) and synergy with GC. [Methods] We examined the candidates by MTT assay and apoptotic assay, and CXCL8 production when stimulated with LPS (10 ng/ml) in THP-1 cells. The selected compounds were clustered into chemotype families based on molecular similarities and common scaffolds. We re-purchased commercially available compounds for further testing. RA-FLS were treated with TNFα (1 ng/ml), and the levels of cytokines and chemokines were measured by ELISA, the migratory potency of peripheral blood mononuclear cells (PBMC) in the conditioned medium were assessed by transwell assay. [Results] We have identified 122 compounds by reanalyzing data from two HTS and by con-

firming the results. Of these compounds, 51 met all of the biological selection criteria (90% viability and 70% CXCL8 release) and consisted of 11 chemotypes and included 17 singletons. Several compounds reduced IL-6, CXCL1, CXCL8, and CCL2 production ($p<0.05$, by ANOVA) but not MMP-3 from TNF-stimulated RF-FLS. The migration of PBMCs was inhibited in the conditioned medium derived from RA-FLS under treatment with the lead compound. Importantly the lead compound demonstrated synergistic effects with dexamethasone when co-administered to TNF stimulated RA FLS in suppressing IL-6 and CXCL8 production. [Conclusions] We identified novel compounds that reduced NF-κB activity and chemokine secretion induced by immunologic stimuli, and one lead compound that acted synergistically with dexamethasone as an anti-inflammatory agent showing a dose-sparing effect.

ICW20-1

Factors that correlates with presenting Shrunken Pore Syndrome

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Conflict of interest: None

[Objective] Shrunken Pore Syndrome (SPS) is recently focused pathophysiology that is suggested risk factor of cardiovascular events, high mortality rate, and osteoporosis risk. Factors that correlate with SPS was investigated. [Methods] A total of 813 subjects were included in the study. Correlation of subjects' sex, age, diagnosing rheumatoid arthritis (RA), serum creatinine phosphokinase (CPK), parathyroid hormone (PTH), homocysteine (Hc), albumin (ALB), calcium (Ca), phosphorus (IP), tartrate-resistant acid-phosphatase 5b (TRACP-5b), vitamin D administration (admVD), glucocorticoid steroid administration (admGCS), bone mineral density in the femoral neck (BMD), and body mass index (BMI) with presenting SPS were evaluated using linear regression analysis. The analyses were performed using univariate model (UM) first, and then using multivariate model (MLR) with factors that demonstrated significant correlation with BMD with the UM. [Results] Factors that demonstrated significant correlation with Cr/CysC with UM were sex, age, RA, CPK, PTH, ALB, Ca, IP, TRACP-5b, BMD, and BMI. In these, factors that demonstrated with MLR were sex, ALB, BMD, and BMI. [Conclusions] Presenting SPS correlates with various factors such like sex, age, nutritional condition, and bone metabolism. In another study, correlation with arteriosclerosis is suggested. However, Hc did not demonstrate significant correlation with presenting SPS. SPS includes more complicated pathophysiology.

ICW20-2

Patient stratification of systemic eosinophilic diseases based on clinical features

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Conflict of interest: None

[Objective] Systemic eosinophilic diseases such as hypereosinophilic syndrome (HES) and eosinophilic granulomatosis with polyangiitis (EGPA) are difficult to be differentiated by the sole symptom and biomarker due to the less frequent detection of ANCA and histological findings of vasculitis. We conducted this study toclarify the clinical differences between EGPA and other eosinophilic disorders. [Methods] We enrolled 58 patients with eosinophilia and signs of organ involvement having required hospitalization at our department. Non-supervised hierarchical clustering analysis with Ward's method and primary component analysis of 20 clinical parameters were performed. Further, a weighted scoring system to classify EGPA among systemic eosinophilic diseases by the group comparison analysis was established, and the sensitivity and validation analyses were conducted. [Results] Hierarchical clustering divided the patients into two distinct subgroups. The group comparison analyses indicated that clinical features including the presence of peripheral neuropathy, asthma, skin involvement, lung involvement, RF positivity, MPO-ANCA positivity, IgE elevation, CRP elevation and pathological findings of vasculitis were preferably observed in one subgroup ($p < 0.05$). Further, we established a scoring system to differentiate the subgroup by the primary component analysis to semi-quantitate each variable contributed to the subgroup differences. Validation analysis supported the indicated subgroup to have the classifying features of EGPA, and our scoring system precisely distinguished EGPA or not. [Conclusion] Our research indicated that systemic eosinophilic diseases clinically subdivided into two distinct subgroups, and the features of one subgroup were well corresponded with the classifying features of EGPA. Our proposed scoring system could be a novel method to differentiate EGPA among systemic eosinophilicdiseases.

ICW20-3

Effectiveness of tocilizumab in patients with TAFRO syndrome

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Conflict of interest: None

[Objective] TAFRO syndrome is an emerging disease entity characterized by thrombocytopenia, anasarca, fever, reticulin myelofibrosis, renal dysfunction, and organomegaly. This disease can be severe and fatal, but currently, there are no established therapies due to the extreme rarity of the disease. Patients with TAFRO syndrome present with high levels of serum interleukin (IL)-6. Thus, we aimed to investigate the effectiveness of tocilizumab (TCZ), an anti-IL-6 receptor antibody, in TAFRO syndrome. [Methods] We performed a systematic review to identify all publications in English in the PubMed database using the Medical Subject Heading "TAFRO syndrome" and "tocilizumab" from inception until July 5, 2020. [Results] Thirty-one patients treated with TCZ were identified. The mean age was 50 years, and 61% were male. The mean observation period was 13 months. TCZ was used at the standard intravenous dose (8 mg/kg) weekly or every two weeks in combination with other immunosuppressive drugs such as glucocorticoids. Eighteen patients (58%) received TCZ as a first-line treatment, while it was a second-line or a third-line treatment for 13 patients with insufficient responses to the prior treatments. Sixteen patients (52%) obtained complete response to TCZ, whereas 15 patients showed only partial or no response. The reason of ineffectiveness were persistent thrombocytopenia (n=7), persistent anasarca (n=5), persistent renal dysfunction (n=2), and persistent fever (n=2). A total of 4 patients (13%) died during their clinical course, whereas the remaining 27 patients survived. Two patients achieved drug-free remission at last visit, and disease remission was maintained with TCZ monotherapy in 5 patients. No new safety signal was observed. [Conclusions] TCZ was effective in half of the patients, indicating it can serve as a treatment choice for TAFRO syndrome. Poor clinical response to TCZ in other patients highlights the necessity for the additional therapeutic options.

ICW20-4

Report on cases of inflammatory arthritis induced by immune checkpoint inhibitors in our hospital

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Conflict of interest: None

[Background] Immune checkpoint inhibitors (ICI) can cause inflammatory arthritis, but the pathogenesis and predictive marker are unknown. [Objective] To review the cases of ICI induced arthritis in our hospital, and to consider the clinical features and genetic factors. [Methods] Patients with various cancer types who started ICI at our hospital were targeted. We extracted clinical information of patients developing ICI induced arthritis. HLA genotypes were determined using genomic DNA, and we analyzed the association between HLA types and the onset of arthritis. [Results] Among 260 ICI treated cases, 23 (8.8%) developed arthralgia that couldn't be explained by cancer. The mean period to onset was 99 days. Rheuma-

tologists intervened in only 8 cases, and 4 of which were diagnosed as arthritis and relieved with oral steroid therapy. Among 23 cases, RF / ACPA was measured in 11 / 10 cases, and 2 / 1 were positive respectively. No one had autoimmune diseases before started ICI, except for one patient with a history of rheumatoid arthritis. HLA-DQA1*01:02 was extracted as a candidate HLA type associated with the development of arthralgia (OR 2.09, p=0.09). 12 out of 23 cases have the shared epitope of HLA-DRB1, but there is no significant difference to control (p=0.858). Patients who developed arthralgia tended to have a higher rate of continued hospital visits (p=0.02), which may be associated with a better prognosis. [Conclusions] Since these events are rare, further study of the large cohort is necessary. Accumulating evidence from both rheumatologists' and oncologists' perspectives on how to treat patients with arthritis at the onset is necessary, as arthritis may be associated with prognosis.

ICW20-5

The role of immune checkpoint molecules in clinical phenotype of rheumatic diseases

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Conflict of interest: None

[Objective] Immune checkpoint molecules play an important role to regulate inflammation and immune reactions. Galectin-9 (Gal-9)/TIM-3 pathway negatively regulate not only adaptive immunity but also innate immunity. The aim of this study is to elucidate the association between Gal-9/TIM-3 pathway and rheumatic diseases including autoimmune and autoinflammatory disease. [Methods] A total of 116 rheumatoid arthritis (RA) and 47 adult Still's disease (ASD) patients were included in this study. Serum levels of Gal-9 was measured by enzyme-linked immunosorbent assay in RA and ASD patients. Serum levels of soluble TIM-3 (sTIM-3) were also determined in ASD patients. [Results] In RA patients, serum levels of Gal-9 were significantly higher than those in healthy controls. Although the serum levels of Gal-9 in RA patients with high titers of anti-CCP antibody (ACPA) (>200 U/ml) significantly correlated with the titers of ACPA (r=0.508), the serum levels of Gal-9 in RA patients with low titers of ACPA (≦200) was significantly correlated with DAS28-ESR (r=0.331). In ASD patients, serum levels of Gal-9 and sTIM-3 were significantly higher than those in healthy controls. Serum levels of Gal-9 and sTIM-3 were significantly correlated with disease activity score, serum levels of IL-18 and ferritin. The ratio of Gal-9/ferritin and sTIM-3/ferritin was significantly higher in chronic arthritis type compared to systemic type. [Conclusions] Gal-9/TIM-3 pathway reflects the disease activity of RA and ASD. Furthermore, this pathway is useful to classify disease phenotype. Gal-9/ TIM-3 pathway could become one of the biomarkers of rheumatic disease. These results suggest that Gal-9/TIM-3 pathway regulate adaptive and innate immunity in rheumatic disease.

ICW21-1

Factors that correlates with serum creatinine-to-cystatin C ratio

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Conflict of interest: None

[Objective] Serum creatinine-to-cystatin C ratio (Cr/CysC) is recently focused index for relative muscular ratio in body, in another word, called "Sarcopenia Index". Correlation of various factors with Cr/CysC was investigated. [Methods] A total of 878 subjects were included in the study. Correlation of subjects' sex, age, diagnosing rheumatoid arthritis (RA), serum creatinine phosphokinase (CPK), parathyroid hormone (PTH), albumin (ALB), calcium (Ca), phosphorus (IP), tartrate-resistant acid-phosphatase 5b (TRACP-5b), vitamin D administration (admVD), glucocorticoid steroid administration (admGCS), presence of Shrunken Pore Syndrome (SPS), bone mineral density in the femoral neck (BMD), and body mass index (BMI) with Cr/CysC were evaluated using linear regression analysis. The analyses were performed using univariate model (UM) first, and then using multivariate model (MLR) with factors that demonstrated significant correlation with BMD with the UM. [Results] Factors that demonstrated significant correlation with Cr/CysC with UM were sex, age, RA, CPK, PTH, ALB, Ca, IP, TRACP-5b, admVD, admGCS, SPS, and BMD. In these, factors that demonstrated with MLR were sex, age, CPK, ALB, IP, TRACP-5b, admGCS, SPS, and BMD. [Conclusions] Cr/CysC correlates with various factors such like sex, age, muscular volume, nutritional condition, bone metabolism, and drug administration, especially GCS. Therefore, Cr/CysC does not directly reflects lean muscle volume. We need to consider the correlation when Cr/CysC is used for index for any utility.

ICW21-2

Sustained long-term retention rates of Abatacept in Elderly Patients with Rheumatoid Arthritis in Daily Clinical Practice: a Single Center Study

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Conflict of interest: None

[Objective] Treatment of elderly RA, especially 75 years old or older, is sometimes difficult due to complication, organ disfunction or more susceptive to drug adverse events. Recently, Abatacept (ABT) is reported to be safer in elderly RA patients (over 65 years) compared to other biologics. However, clinical reports regarding ABT efficacy and long-term retention in Japanese elderly RA patients (75≦) are still limited. This study is conducted to elucidate the efficacy and long-term retention of ABT in elderly RA patients in daily clinical practice. [Methods] This study was designed for retrospective cohort study. RA patients treated with ABT between September 2010 and April 2020 in our department were collected. Among 43 patients received ABT, 41 patients who were treated more than a month were included (2 patients discontinued due to drug allergy and severe headache). These patients were divided into two groups (Elderly: 75≦ and Younger: 75>) and compared with clinical features. We also investigated the overall retention rates of ABT between the 2 groups. [Results] The mean observation period was 21.7 months (1-79 months). General characteristics of Elderly (14 cases) and Younger (27 cases) RA patients treated with ABT were similar. DAS28CRP levels at 6 months were successfully decreased in both groups (elderly, 2.66 to 1.98 and younger, 3.33 to 2.33, respectively) ($p<0.01$). Elderly RA patients with ABT received significantly less methotrexate ($p<0.01$) and more tacrolimus ($p<0.01$) or salazosulfapyridine ($p<0.05$). Overall retention rates of ABT between Elderly and Younger RA were similar (56.3% and 49.4%, respectively). Three malignancies occurred: prostate cancer, intraductal mucinous neoplasm in Elderly RA patients, and lung cancer in a Younger patient. One elderly patient died for cerebrovascular disease. [Conclusions] ABT treatment was effective enough in elderly RA patients and sustained long-term drug retention was observed.

ICW21-3

The treatment status of NSAIDs, prednisolone, and bDMARDs in patients with elderly onset rheumatoid arthritis; the evidence from Niigata Orthopedic Surgery Rheumatoid Arthritis Database (NOSRAD)

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Conflict of interest: None

[Objective] This study aimed to clarify the treatment status of nonsteroidal anti-inflammatory drugs (NSAIDs), prednisolone (PSL), and biological DMARDs (bDMARDs) in elderly onset rheumatoid arthritis (EORA). [Methods] The 383 RA patents who visited from January 2018 to December 2018 in our clinic were registered. All patients were included in

Niigata Orthopedic Surgery Rheumatoid Arthritis Database (NOSRAD). The treatment ratio of NSAIDs, PSL, and bDMARDs of EORA (65 years old and more than 65 years old at RA onset) were evaluated. In addition, estimated glomerular filtrated rate (eGFR) as renal function, erythrocyte sedimentation rate (ESR) as the degree of inflammation were evaluated. The data were compared between EORA and younger onset RA (less than 65 years old at RA onset) (YORA) by statistical analysis (SPSS software). [Results] EORA was 122 cases (32%). EORA was significantly lower in eGFR (65.82 vs 81.03 in YORA (ml/min/1.73 m^2), p<0.0001) and was significantly higher in ESR (23.6 vs 17.3 in YORA (mm/hour), p=0.016). No significant difference was detected between the 2 groups in treated rates of NSAIDs (52.5 in EORA vs 49.4 (%) in YORA, p=0.53), PSL (30.3 in EORA vs 26.2 (%) in YORA, p=0.45), and bDMARDs (39.3% in EORA vs 43.0 (%) in YORA, p=0.56). However, the treated rate of methotrexate (MTX) and the treated dose of MTX in EORA were significantly lower than those in YORA (31.1 vs 57.8 (%), p<0.0001, and 5.4 vs 5.9 (mg/week), p=0.009, respectively). [Conclusions] These data acquired in this study suggest that lower MTX treated rates and doses are due to lower renal function in EORA and that tighter control is required for EORA patients because they are still high inflammation.

ICW21-4

Factors associated with Frailty based on the J-CHS criteria in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] “Frailty” means a pre-condition of requiring nursing care. Our Objective is to find Factors associated with Frailty in Rheumatoid Arthritis. [Methods] 581 patients, who visited specialized outpatient with Rheumatoid Arthritis (three institutions) from June 2020 to August 2020, were chosen. 418 of 581 patients who could examine Japanese-cardiovascular health study criteria (J-CHS), DAS28-CRP, HAQ-DI, Locomo 25 score. 418 patients were divided into Frailty or non-Frailty groups based on J-CHS. The patients who have more than 3 points are frailty group, and who have from 0 - 2 points are a non-Frailty group. DAS-28 CRP, HAQ-DI, Locomo 25 were compared between each group. ROC analysis was used to find a cutoff value. Furthermore, multiple logistic regression analysis was used to investigate the odds ratio by adjusting age, gender, and disease duration. [Results] There were 113 patients in the Frailty group and 306 patients in the non-Frailty group. Features of the Frailty group were older (average±SD, 75±9 vs. 66±12, P<0.01), longer disease duration (13±11 vs. 11±17, P=0.02), higher DAS-28 score (2.8±1.3 vs. 2.0±1.0, P<0.01), HAQ-DI (1.0±0.8 vs. 0.3±0.6, P<0.01), and Locomo 25 (36.5± 24.0 vs. 14.8±16.5, P<0.01). The cutoff value related Frality (AUC, Sensitivity, Specificity) in each factor were DAS28-CRP: 2.5 (0.678, 57%, 74%), HAQ-DI: 0.8 (0.761, 66%, 78%), Locomo 25: 17.0 (0.787, 75%, 73%). [Conclusions] Factors associated with Frailty in Rheumatoid Arthritis patients were DAS28-CRP, HAQ-DI, and Locomo 25. We need to aim for clinical remission, functional remission, and lower Locomo 25 score (≦15) on the therapy of Rheumatoid Arthritis patients.

ICW21-5

Relationships among Habitual Fish Intake and Frailty Status in Patients with Rheumatoid Arthritis: A Transverse Study Using the KURAMA Cohort Database

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Conflict of interest: None

[Objective] To elucidate the correlations between frailty status, disease activity and dietary habits in patients with rheumatoid arthritis (RA). [Methods] In the cross-sectional study, 306 female outpatients were enrolled from KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort database, and were classified into three groups (robust, prefrail and frail) according to simplified frailty index (Study of Osteoporotic Fracture criteria). Dietary habits were obtained from a self-reported food frequency questionnaire as previously reported. Multivariate logistic analyses with or without dietary habits were performed for the presence of either frailty or prefrailty. [Results] The classification of frailty status revealed that DAS28-ESR in patients with frailty was significantly higher than that in the others. In multivariate logistic analysis, the presence of frailty/prefrailty was associated with DAS28-ESR (OR 1.71, p<0.0001) and methotrexate use (OR 0.47, p=0.0097). Trend analyses also showed that the intake frequency of 5 ingredients (meat, fish, milk, fruits and vegetables) was inversely associated with the prevalence of frailty/prefrailty. In additional multivariate logistic analyses with dietary habits, fish intake (≧three times per week) was negatively correlated with frailty/prefrailty (OR 0.33, p<0.0001). Neither the use of prednisolone nor that of biological DMARDs was significantly associated with the presence of frailty/prefrailty in the analyses. [Conclusions] Our results suggest that habitual fish intake may bring benefits to frailty prevention in patients with RA.

ICW21-6

Polymyalgia rheumatica successfully treated with ibuprofen

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Conflict of interest: None

Background The primary treatment choice for polymyalgia rheumatica (PMR) is steroids, which are best avoided for elderly patients susceptible to PMR. This report shows that PMR patients can be successfully cured with ibuprofen without concomitant steroid administration. ***Case presentation Case 1*** For a 76-year-old female patient with a CRP level of 8.54 mg/dL, loxoprofen, diclofenac, and pregabalin did not ameliorate her one-month-long pain. Ibuprofen cured it in five days. ***Case 2*** For a 78-year-old female patient with a CRP level of 12.8 mg/dL, neither loxoprofen nor nerve block cured her few-weeks-long pain. Ibuprofen cured her in two weeks. ***Case 3*** For an 81-year-old female with a CRP level of 5.1 mg/dL, celecoxib did not improve her movement disability. Ibuprofen cured her in two weeks. ***Case 4*** For a 73-year-old female patient with a CRP level of 8.81 mg/dL, ibuprofen was the first drug prescribed two weeks after the onset of pain and impaired walking. She recovered in three days. ***Case 5*** For a 76-year-old female patient with a CRP level of 1.57 mg/dL, acetaminophen did not improve her pain and stiffness. She recovered in seven days after ibuprofen dose. All the patients had severe continuing pain in the shoulders and pelvic girdles, and imaging revealed bursitides without temporal arteritis. They were negative for autoantibodies. The ibuprofen dosage was 600 mg/day, which is substantially lower than that prescribed in western countries. None of the patients were concomitantly treated with steroids. Case 1, 2, and 3 were already withdrawn from ibuprofen therapy; in Case 4 and 5, ibuprofen dosage was still being tapered. No adverse event was observed. ***Conclusion*** Ibuprofen clearly cured PMR without concomitant steroid administration. Ibuprofen could be the first-line therapy for PMR.

ICW22-1

Risk factors for pneumonia during biological treatments in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Pneumonia is one of the most serious complication during treatment with biologics (BIO). In this study, we aimed to clarify the risk factors for pneumonia in patients with rheumatoid arthritis (RA) who are undergoing BIO treatments. [Methods] We retrospectively included adult RA patients who underwent chest CT before primary BIO administration from January 2008 to October 2017 and had follow-up period of at least 3 years, at two hospitals. Subjects were extracted data from electrical medical records regarding patient characteristics, subsequent incidence of pneumonia, and detected microorganisms. Pneumonia was confirmed by the presence of new lung infiltrates with acute respiratory symptoms which required antimicrobial treatments. Underlying lung diseases were assessed by blinded reads of Chest CT taken before primary BIO, by two radiologists. Cumulative incidence of pneumonia was assessed using Kaplan-Meier method and compared using the log-rank test. Cox proportional hazards analysis was performed to analyze the risk factors for pneumonia. [Results] A total of 593 BIO-treated RA patients were extracted. Underlying Lung disease was found in 325 patients (54.8%), including airway disease (22.7%), interstitial pneumonia (26.8%), and emphysema (12.5%). Pneumonia was occurred in 61 patients (10.2%) during 3-year follow up after initiation of first BIO, and the median duration for pneumonia incidence was 8.0 months after the BIO initiation. Multivariate analysis of risk factors in BIO-treated RA patients showed that underlying lung diseases including airway lesions (P = 0.001) and interstitial pneumonias (P = 0.032) showed significant correlation with pneumonia incidence, while age, gender, smoking, or steroids were not correlated. [Conclusions] Our study demonstrated that RA patients with lung disease, especially airway diseases and interstitial pneumonias, are at increased risks of developing pneumonia during BIO treatments and should be followed up carefully.

ICW22-2

Clinical characteristics of invasive fungal infection during immunosuppressive induction therapy in connective tissue disease patients

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Conflict of interest: None

[Objective] Invasive fungal infection (IFI) is a rare life-threatening complication among immunosuppressed patients. This study aims to reveal prevalence, associated risk factors and clinical characteristics of IFI during immunosuppressive induction therapy in patients with connective tissue diseases. [Methods] We reviewed consecutive patients with connective tissue diseases who were treated with glucocorticoids equivalent to 0.5 mg/kg/day or more prednisolone dose from January 2012 to August 2020 in Keio University Hospital. The patients were divided into two groups according to IFI defined by EORTC/MSG 2008 and analyzed. [Results] Among 2701 hospitalized cases, 627 patients underwent induction therapy. Total of 24 (3.8%) patients developed IFI consisting of 7 proven cases and 17 probable cases; 14 aspergillosis, 5 candidiasis, 2 cryptococcosis, 1 phaeohyphomycosis, and 2 cases with unknown pathogen. Median duration from the start of immunosuppressive therapy to the onset of IFI was 81.5 days (IQR: 35, 215.5), and the average dose of daily prednisolone at the onset of IFI was 0.55±0.06 mg/kg. Five patients (20.8%) died due to IFI, and 4 (16.7%) died due to the exacerbation of underlying disease. The IFI patients were older than the non-IFI patients (65.8±3.7 vs. 56.1±0.7, P=0.01, respectively) and used methylprednisolone pulse therapy more frequently (50.0% vs. 20.9%, P<0.01, respectively). Initial daily dose of prednisolone tended to be related to the increased risk of IFI (0.95±0.04 vs 0.87±0.01 mg/kg, P=0.06, respectively). [Conclusions] Our study indicated that patients with older age, higher prednisolone dose or methylprednisolone pulse therapy had the higher risk of IFI.

ICW22-3

Factors associated with development of Pneumocystis jirovecii pneumonia in patients with Rheumatoid arthritis receiving methotrexate: A case-control study of 17 patients

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Conflict of interest: None

[Objective] The risk factors for the development of Pneumocystis jirovecii pneumonia (PCP) in patients with Rheumatoid arthritis (RA) receiving biologics have been clarified according to the previous reports. However, risk factors of PCP in patients receiving non-biologics has not been clarified. This study was aimed to investigate the risk factors for the development of PCP in RA patients who received methotrexate (MTX). [Methods] In this multicenter retrospective study, we conducted consecutive 17 patients with RA who developed PCP at participating hospitals and compared with 85 patients who did not develop PCP during MTX treatment at least 1 year were randomly collected from Seirei Hamamatsu General Hospital from 2006 through 2015. We excluded patients who received biologics, Janus kinase inhibitor, and PCP prophylaxis. [Results] For the PCP patients, the median age was 72 years old, the median duration of RA was 10 years and the median duration of MTX was 77 weeks. The median dosages of MTX and prednisolone (PSL) were 8 mg/week and 4 mg/day, respectively. Six patients had pulmonary diseases. One patient received iguratimod but other patients did not receive the other Disease Modifying Anti-Rheumatic Drugs. At the initiation of MTX, the patients with PCP were older (P<0.05), lower serum albumin (P<0.05), had more pulmonary disease (P<0.05), received more PSL (P<0.05) than the patients without PCP. Multivariate Cox Regression analysis revealed that age ≧ 65 years [hazard ratio (HR) 3.37, p = 0.04], Serum albumin <3.5 mg/dl [hazard ratio (HR) 6.27, p = 0.009], and PSL≧5 mg/day (HR 3,97, p = 0.01) were the risk factors for the development of PCP during MTX therapy. Patients with two or more risk factors had a significantly higher cumulative probability of development of PCP than patients with no or one risk factor (P<0.05). [Conclusions] PCP may occur during MTX therapy if two or more risk factors are present in patients with RA.

ICW22-4

Prophylactic effect of salazosulfapyridine for pneumocystis pneumonia in rheumatoid arthritis: A retrospective propensity score-matched cohort study

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Conflict of interest: None

[Objective] To investigate the efficacy of salazosulfapyridine (SASP), a conventional synthetic disease modified anti-rheumatic-drugs (csDMARDs), as primary prophylaxis for pneumocystis pneumonia (PCP) prophylaxis in patients with rheumatoid arthritis (RA). [Methods] We retrospectively reviewed medical records in RA patients who started to receive csDMARDs or biological DMARDs without PCP prophylaxis (defined as a treatment episode) from 2006 to 2019 in Hokkaido University Hospital. All treatment episodes were classified into two groups: a SASP group and a control group. We assessed the difference in the incidence of PCP between the two groups at about one year. The diagnosis of PCP was based on clinical symptoms, a value of 1, 3-b-D-glucan, chest CT findings, and respiratory specimens. Firth's penalized maximum likelihood was used to reduce statistical bias for the complete separation of the outcome. Furthermore, to minimize covariate imbalance at baseline, we performed a one to one propensity score (PS) matching using nearest neighbor matching and reviewed efficacy outcome in the post matched population (n=75 in both groups). [Results] This study included 470 treatment episodes in 346 patients. We enrolled 128 treatment episodes as the SASP group while other episodes as the control. We identified 20 PCP cases during the observation period of 464.7 person-years. Two patients (10%) died from PCP. Univariable Cox-proportional hazards regression analysis in the PS-matched population revealed that the one-year incidence of PCP significantly decreased with prophylaxis (Hazard Ratio (HR) 0.09; 95% confidence interval (CI) 0.0007-0.79, p = 0.03). This result was also consistent with multivariable analysis, including age and disease duration as covariates (adjusted HR 0.08; 95% CI 0.0006-0.72, p = 0.02). [Conclusions] SASP significantly reduces the PCP incidence in RA patients. The novel insight of SASP as the PCP-prophylactic DMARD would broaden treatment options for RA patients.

ICW22-5

Different Risk of Developing Herpes Zoster Differs by molecular-targeting disease-modifying anti-rheumatic drugs in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] This study aims to investigate the risk for developing herpes zoster (HZ) depending on the mode of action (MOA) of molecular-targeting disease-modifying anti-rheumatic drugs (DMARDs) in patients with rheumatoid arthritis (RA). [Methods] RA patients who had initiated Janus kinase inhibitors (JAKinhibs) and biological DMARDs (bDMARDs) in our hospital from 2006 to 2019 were analyzed by Cox proportional hazards model for the risks of developing HZ. [Results] RA patients (N=725) treated with JAKinhibs (n=61), tumor necrosis factor inhibitors (TNFIs) (n=389), interleukin-6 receptor inhibitors (IL-6RIs) (n=169) and abatacept (ABT) (n=106) were enrolled. Patients with TNFI were significantly younger than JAKinhibs (p=0.049) and ABT (p<0.001), and the observation period of JAKinhibs was significantly shorter than all bDMARDs (p<0.001). There were no significant differences in gender, disease duration, disease activity, and dose and use of PSL. The incidence rate of HZ was 6.85/person-year (PY) for JAKinibs and 1.86/PY for bDMARDs; 1.65/PY for TNFI, 2.09/PY for IL-6RI, and 2.56/PY for ABT, respectively. After adjusting age, JAKinhibs had a significantly higher risk for developing HZ (risk ratio (RR) 2.81, 95% confidence interval (CI) 1.06-7.44, p=0.037) than bDMARDs. Multivariate analysis revealed higher risk in JAKinhibs compared to TNFI (RR 3.18 95%CI 1.13-8.95, p=0.028), IL-6RI (RR 2.58, 95%CI 0.84-7.90, p=0.097), and ABT (RR 2.31, 95%CI 0.70-7.62, p=0.170). MTX dose was a risk only in TNFI (RR 1.16, 95%CI 1.03-1.32, p=0.0016). [Conclusions] Molecular-targeting DMARDs had a different risk for developing HZ. JAKinibs had the highest risk in our real-world data as reported previously. In order to prevent HZ in RA patients, individual treatment optimization should be based on drug MOA and use of concomitant DMARDs.

ICW22-6

Risk Factor of Cytomegalovirus Reactivation in Patients with ANCA-associated Vasculitis who Had Received Rituximab as Remission Induction Therapy

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Conflict of interest: None

[Purpose] Rituximab (RTX) for ANCA-associated vasculitis (AAV) treatment is increasingly used raising concerns on complicating infections. Aim of this study was to investigate the risk factor of cytomegalovirus (CMV) reactivation in AAV patients treated with RTX as remission induction therapy. [Methods] Patients diagnosed with AAV (microscopic polyangiitis, granulomatosis with polyangiitis, eosinophilic GPA) from 2013 to 2019 treated with remission induction therapy were enrolled. CMV reactivation was defined as positive CMV antigenemia (Ag). We analyzed the risk factor of CMV reactivation by logistic regression analysis. [Results] Among the AAV patients (N=79), 28 (35%) were treated with RTX (RTX group) and CMV reactivation was observed in 32 patients (41%). Within the RTX and non-RTX group (N=51), female was 12 (43%), 35 (69%) and age was 61.32±16.84 and 69.21±10.52 y.o. (mean±SD) respectively. There was no difference in the incident rate of CMV reactivation 12 (43%) vs 20 (39%). Next, we investigate the risk among the RTX group. Among the following factors; Age, gender, lymphocyte count on admission, serum albumin, CRP and IgG levels, complicating diabetes, renal or lung involvement due to AAV, BVAS, initial prednisolone dose, and steroid pulse administration, age was the only significant risk factor for CMV reactivation (odds ratio 1.07, 95% CI 1.01-1.15, p=0.026). The cut-off value was 60 y.o. and as a matter of fact, 4 patients who required treatment with an anti-viral drug to continue remission induction therapy within the RTX group were all over 60. [Conclusion] Monitoring CMV Ag could be useful for elderly AAV patients treated with RTX.

Poster Session

P1-1

Current status of rheumatoid arthritis medical treatment based on the National Database Japan -analysis by medical facility and prefecture-

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Conflict of interest: None

[Objective] To estimate the current status of patients with rheumatoid arthritis (RA) by prefecture based on the medical visiting to specialized institution (SI) and prescription. [Methods] We analyzed 825 thousands RA patients ≧16 years old by using the Japanese National Database (NDB Japan) in fiscal year 2017 by prefecture and visiting medical institution. [Results] The percentage of patients who never visited SI for RA was 31.8% with increasing with age (16-19 years old; 12.1%, ≧85 years; 42.8%). The percentage of patients who visited only SI in the year was 51.9% with decreasing with age (16-19 years old; 79.7%, ≧85 years; 35.2%). The number of prefectures in which the percentages of patients who never visited SI more than 10% from the overall average was 12 (25.5%). The percentage of patients prescribed methotrexate (MTX) or biologics prescription were 51.9-72.9% or 19.5-33.2% among patients who visited only SI and 44.0-71.6% or 7.2-28.0% in patients who never visited SI, respectively. [Conclusions] The current status of treatment for RA by visiting SI and by prefectures were estimated for the first time.

P1-2

Clustering of affected joint distribution in active rheumatoid arthritis (RA) patients registered in a nationwide RA database (NinJa), and its significance demonstrated by joint index vector analysis

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Conflict of interest: None

[Objective] In JCR2018, we reported that DIP involvement in RA, albeit rare, was associated with high disease activity with small-sized and upper-extremity joint predominance. The purpose of this study was to analyze the relationship of RA subsets, identified by cluster analysis of affected joints, with disease activity markers and joint vector indices (Nishiyama, Rheumatol Int, 2012). [Methods] We performed a cluster analysis of affected joints (68 joint excluding foot IP) involving 3,445 adult-onset RA patients with DAS28-CRP ≥ 2.3 registered in NinJa 2019, and evaluable for joint analysis. [Results] A combination of PIP, MCP, wrist and knee joints (group 1) accounted for 66%, and the others were characterized by predominance of shoulder (group 2), DIP (group 3), MTP (group 4), and hip joint (group 5). It was shown that the disease activities of group 2, 3, 4, and 5 were significantly higher than that of group 1 with regard to DAS28-CRP and Vxy, and that mHAQ was elevated in the order of group 5, 2, 4, 3, and 1. [Conclusions] We demonstrated the presence of RA subsets with high disease activity involving the joints not included in 28-joint evaluation. It would be necessary to raise awareness to the presence of such relatively rare RA subsets for better RA management.

P1-3

The demographic data of patients with rheumatoid arthritis and changes in treatment methods: From 10-year ANSWER cohort

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Conflict of interest: None

The Kansai Consortium for Well-being of Rheumatic Disease Patients (ANSWER) cohort is a multicenter observational registry of patients with rheumatoid arthritis in the Kansai region. Registration began in January 2011 and 10 years have passed. The number of registered people has exceeded 1000 since 2013, with a maximum of 4033. It is said that the situation of rheumatoid arthritis has changed in the last 10 years due to the aging of patients and the appearance of JAK inhibitors. We report on the characteristics of patients with rheumatoid arthritis and changes in treatment methods from the 10-year ANSWER cohort data. The mean age ± standard deviation of the patients examined was 60.5 ± 12.5 years in 2011, but increased to 64.7 ± 13.9 years in 2020. The age group of patients was the highest in their 70s since 2018. The proportion of women was 78.5-83.8%. The use of biologics or JAK inhibitors is gradually increasing, with 16.7% of registered patients using biologics in April 2011, but up to 43.5% in 2019. The breakdown was 40.0% for TNF inhibitors, 27.1% for IL-6 inhibitors, 22.3% for CTLA4-Ig, 7.4% for JAK inhibitors, and 3.1% for denosumab. Regarding disease activity, CDAI remission and low disease activity gradually increased over time from 74.9% in 2013 to 82.4% in 2020.

P1-4

Sarcopenia and dementia in elderly rheumatoid arthritis (RA) patients

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Conflict of interest: None

[Objective] Aging is associated with a progressive decline in skeletal muscle mass, with a decline in physical strength and motor function. However, there are few reports describing sarcopenia and dementia associated with elderly RA in Japan. [Methods] RA patients aged 65 years or older (mean age 75.1 ± 6.2) and non-RA patients including osteoarthritis (mean age 77.8 ± 4.5) followed up in our hospital were included in the study; they walked five times on the 5 m level ground and their speed was recorded. Bone density (lumbar spine and femur), muscle mass, MMSE (cognitive scale) and SRQ-D (depression scale) were measured. [Results] The Mean 5 m walking speed (m/min) was significantly lower in the non-RA group (57.9±16.5) than RA group (65.0±15.9). Bone density measured using femur reduced in the RA group, 0.77±0.16 in the RA group and 0.9±0.1 in the non-RA group, respectively. Bone density correlated with bone mass and disease duration in the RA group, and muscle mass and dementia in the non-RA group. Factors that correlated with 5 m walking speed were age and MMSE in both groups. MMSE and SRQ-D were not significantly different between the two groups. [Conclusions] Elderly RA patients did not decrease walking speed compared to non-RA patients plausibly due to advances in treatment.

P1-5

Clinical manifestations of polymyalgia rheumatica complicated with fever

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Conflict of interest: None

Objective: We studied the clinical features and treatments for the patients with polymyalgia rheumatica (PMR) who developed fever as the main symptom. Method: We compared 7 PMR patients with fever of 38.0°C or higher and 20 PMR patients without fever who were aged 65 years or older. The PMR patients complicating fever exhibited inflammatory reactions with CRP values as high as 23 ± 10 mg/dl and IL-6 values as high as 100 ± 22 pg/ml. The fever had continued for an average of 14 ± 10 days until diagnosis. Steroid was administered with MTX administered to 2 patients, and then Tocilizmab was administered to 2 patients. Conclusion: There is a group of patients with acute onset of PMR symptoms with fever, who exhibit high inflammatory responses and require combined administration with steroid. The combined use of tocilizumab with steroid was effective in refractory cases with high inflammatory responses. It has been demonstrated that various secretory proteins including inflammatory cytokines, chemokines, proteases such as extracellular matrix degrading enzymes, and growth factors are produced in aged cells, which is a phenomenon called cell senescence-related secretory phenomenon.

P1-6

Prospective study of secondary examination for rheumatoid arthritis in health checkup of residents

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Conflict of interest: None

Objectives: ACPA production is observed in several organs even prior to the onset of RA. To evaluate the RA development at high risk from the general population. Methods: During 2014-2016, 44 subjects were recruited to examine having RA from general population. Results: Of the 21 ACPA-positive patients, 2 were diagnosed with RA almost at the same time as the consultation, 6 with a median follow-up of 10 months (range 5-32.5 months), and a total of 8 (38.1%) were diagnosed with RA. The median CSA score was 0 (range 0-4) in 29 patients without joint swelling. out of There was no RA progress with a score of 3 or higher. Conclusions: Asymptomatic anti-CCP antibody-positive cases were rarely develop to RA. The CSA score was low and it may not effective in predicting prognosis in this small number of study.

P1-7

Relationship between grip strength and frailty in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] Grip strength is one of the diagnostic criteria for flailty. However, since patients with rheumatoid arthritis (RA) often have wrist or finger joint disorders, it is doubtful that it is appropriate to evaluate flailty based on grip strength. This study aimed to clarify the relationship between grip strength and flailty in RA patients. [Methods] Among 581 patients who visited RA outpatient clinics between June and August 2020, the patient characteristics of 184 female RA patients with clinical remission were available. In Kihon-Checklist (KCL), 8 points or more were defined as flailty. The correlation coefficient between KCL and grip strength was analyzed by age and disease duration. [Results] Of the 184 patients, 57 had flailty. Mean grip strength and KCL of less than 9 years of disease duration were 21.8/19.2/16.8 kg, 4.2/4.8/7.9 points (65>/65-75/75≦ years), and mean grip strength and KCL of 9 years or more were 21.1/18.8/14.2 kg, 5.3/6.2/8.1 points. The significant correlation coefficient between grip strength and KCL was -0.404 (65> years/9> years), -0.476 (75≦/9>), -0.432 (75≦/9≦). [Conclusions] When evaluating flailty in RA female patients based on grip strength, it is necessary to consider age and disease duration.

P1-8

Association between low back pain and quality of life in patients with rheumatoid arthritis according to patient-reported outcomes using the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ)

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Conflict of interest: Yes

[Objectives] To evaluate factors associated with low back pain (LBP) and effect on quality of life (QOL) using patient-reported outcome in patients with rheumatoid arthritis (RA). [Methods] Overall, 414 patients with RA who answered the Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ) were included in this study. LBP-positive was defined a visual analog scale (VAS) of LBP (LBP VAS) of ≧ 30 mm. [Results] The rate of LBP-positive group was 24.9%. Body mass index (BMI), tender joint count (TJC), global VAS, and Health Assessment Questionnaire Disability Index HAQ-DI were found as significant LBP-associated factors. When adjusted for sex and van der Heijde-modified total Sharp score, BMI, TJC, global VAS, pain VAS, and HAQ-DI were found to be the significant factors associated with LBP. Moreover, LBP VAS had relatively high correlations in all domains of the JOABPEQ scores (correlation coefficient: LBP, -0.601; lumbar function, -0.624; walking ability, -0.548; social life function, -0.479; and mental health, -0.463). [Conclusion] This study investigated the effect of LBP in patients with RA. The results of this study indicate that LBP is associated with the physical function and QOL in patients with RA.

P1-9

Profiles of non-administration cases of MTX in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] In principle, MTX administration is the first choice for the treatment of rheumatoid arthritis (RA) in recent years. However, in the elderly, MTX may not be administered, which is considered to be one of the causes of insufficient tight control of RA. [Methods] Patients aged 75 years and older were extracted from the 2019 Akita Orthopedic Group on RA (AORA) registry, and MTX administration status and patient background were investigated. [Results] In the entire AORA registry (2207 pts), 707 patients (32.0%) were 75 years or older. The non-usage rate of MTX was 55.1%. In cases without MTX, the average age was significantly higher. Regarding drug therapy, SASP and BUC were frequently used, and the frequency of use of b / tsDMARDs was 9.1% in the MTX non-administered group. The overall disease activity index were not significantly different in the MTX non-administered group. However, the HAQ-DI was significantly higher in the non-treated group. [Conclusions] Although

55.1% of patients with RA 75 years or older did not receive MTX, they maintained the same disease activity as those treated with MTX. However, since the HAQ-DI was significantly high, a therapeutic strategy for improving physical function in patients not receiving MTX is a task.

P1-10

Influence of COVID-19 on rheumatoid arthritis patients

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Conflict of interest: None

[Objective] We investigated the characteristics of patients with rheumatoid arthritis (RA) whose motivation reduced due to the effects of COVID-19 calamity. [Methods] The subjects were 520 RA patients who visited the RA outpatient clinic between June and August 2020 and were able to investigate the patient backgrounds. We compared the backgrounds of patients with reduced motivation. Furthermore, the relationship with reduced motivation was investigated by logistic regression analysis. [Results] Of the 520 patients, 80 RA patients showed reduced motivation. The mean ages of the motivation-reduced / non-reduced group were 69.0/66.7 years, disease duration 13.1/11.0 years, DAS28-CRP 2.5/2.2 (p=0.014), HAQ-DI 0.7/0.4 (p=0.005), “Living alone” 27.5/17.0% (p=0.041), “School education 13 years or more” 40.0%/28.4% (p=0.047). Variables that were significantly associated with reduced motivation were DAS28-CRP (OR 1.25) and “Living alone” (OR1.81), “School education 13 years or more” (OR2.15). [Conclusions] In RA patients, disease activity, living alone, and high education were significantly associated with reduced motivation due to the effects of COVID-19 calamity. At the same time as practicing tight control for RA, comprehensive medical care focusing on the social background is required.

P2-1

Single-cell RNA-sequence analysis of the synovium in gp130F759 at the preclinical phase of arthritis

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Conflict of interest: None

[Objective] To develop disease modifying therapies to prevent bone erosion in rheumatoid arthritis (RA), pathophysiology in the preclinical phase has attracted great attention. A knock-in mouse gp130F759 having gp130 with Y759F mutation is a suitable RA model to understand the pathophysiology at a preclinical phase of arthritis. Around 5 M.O. without symptoms of clinical arthritis, several pathological changes already exist in the synovium. In this study, we performed single-cell RNA-sequencing (scRNA-seq) to explore the clusters in the synovial cells of gp130F759 compared with those of wild-type (WT). [Methods] 10000 of viable synovial cells from the knee joints of WT and gp130F759 at 5 M.O. were purified by cell-sorter. Single-cell cDNA library was prepared with Chromium Controller. Sequencing with NGS was performed to a depth of 100000 reads each. [Results] 5734 cells in WT and 6514 cells in gp130F759 were divided into 10 clusters. Cell numbers of clusters of neutrophils and B cells in gp130F759 increased. IL-6-PAD4 axis in gp130F759 was confirmed in fibroblast and neutrophil clusters. [Conclusion] ScRNA-seq revealed changes of gene expression in the synovial-cell clusters in transition from innate to acquired immunity in the preclinical phase of arthritis in gp130F759.

P2-2

Clock controlled gene Tef regulates proliferation of RA-FLS via Cell Cycle regulators

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Conflict of interest: None

[Objective] We have previously reported that expressions of various clock genes are significantly altered in leukocytes of RA patients compared to healthy subjects, and their expression correlates with RA disease activity. However, the detailed relation between the pathogenesis of RA and clock genes has remained unclear. In this study, we examined effects of clock gene expression on the proliferation of RA-FLS. [Methods] After transfected *Bmal1, Clock, Per2, Nr1d1, Dbp, Hlf or Tef* siRNAs, 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. Total protein was extracted from RA-FLSs to analyze the expression of Cyclin D, Cyclin E, p21, cell cycle regulators, by western blot. [Results] By silencing *Tef* stimulation of IL-6/sIL-6R significantly increased the cellular viabilities and expressions of Cyclin D, Cyclin E and decreased expressions of p21. Simultaneously, stimulation of TNF-α significantly increased the cellular viabilities and expressions of Cyclin D, Cyclin E. [Conclusions] The results suggested that Tef modulated Cell Cycle regulators by IL-6/sIL-6R or TNF-α, subsequently induced proliferation of RA-FLS.

P2-3

IL-6 induces the resistance for apoptosis-induction via PAR-bZIP in synovial cells

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Conflict of interest: None

[Objective] We have previously reported on the function of RA synovial cells (RA-FLS) and the involvement of clock genes. In the present study, we examined the effects of Interleukin-6 (IL-6) and clock genes on apoptosis-induction of RA-FLS. [Methods] RA-FLS was cultured in Dexamethasone (DEX; 0, 10, 100, 300, and 500 μM) for 24 h, and cellular viabilities were measured by WST-8. Also, cells were cultured in the presence of IL-6/sIL-6R (0, 100 ng/mL) and DEX (0, 100 μM) for 24 h and cellular viabilities were examined by WST-8. Simultaneously, the expression of Bax/Caspase3/Cytochrome c/PARP was measured by Western blotting and the expression of Hlf/Tef/Dbp/Bik was measured by quantitative PCR. [Results] Cellullar viabilities were reduced in a DEX dose-dependent manner, which was antagonistically disturbed by IL-6/sIL-6R. IL-6/sIL-6R inhibited Bax-mediated release of cytochrome c and cleavage of caspase3/PARP. Also, expressions of circadian transcriptional factor *Hlf*, *Tef* and pro-apoptotic factor *Bik* were suppressed. by IL-6/sIL-6R. [Conclusions] Results suggested that IL-6 regulates Bcl-2 family protein and induces the resistance for apoptosis via clock genes in RA-FLS.

P2-4

Effects of an CDK6-selective inhibitor on mice collagen-induced arthritis model and TNFa-induced synovial fibroblasts proliferation

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Conflict of interest: None

[Objective] We have reported that SPACIA1 siRNA inhibited the proliferation of synovial fibroblasts, especially TNFα-induced synovial fibro-

blasts (RASFs). To elucidate the role of CDK6, a G1 cell cycle regulator, which is regulated by SPACIA1, we investigated effects of CDK6-selective inhibitor (compound) on TNFα-induced proliferation in vitro and collagen-induced arthritis (CIA) mice. [Methods] RASFs were cultured for 48 hours with or without the addition of TNFα and compound. Cell viability was evaluated by an CCK-8 assay, and Cytotoxicity was measured by an LDH detection kit. Protein expressions of CDK4, CDK6 and pRB were detected by western blotting. The CIA model was performed with the compound in DBA/1J mice. [Results] The CDK6-selective inhibitor reduced cell viability and increases cytotoxicity when treated with TNFα. Furthermore, CIA and the characteristic features of pathology in synovial tissues were markedly suppressed in treatment with the compound. [Conclusions] The suppression of TNFα-induced proliferation and the promotion of cytotoxicity correlated with down-regulation of the CDK6 and pRb expression. The selective inhibition of CDK6 was efficacious in CIA. These observations suggest that inhibition of CDK6 has potential for RA treatment.

P2-5

Peficitinib and filgotinib inhibit angiogenesis via suppression of VEGF production in rheumatoid arthritis fibroblast-like synoviocytes

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Conflict of interest: None

[Objective] Peficitinib and filgotinib are novel Janus kinase (JAK) inhibitors developed for the treatment of rheumatoid arthritis (RA). There is a difference in JAK selectivity between peficitinib and filgotinib. Peficitinib inhibits all JAKs, especially JAK3. Filgotinib is a JAK1 selective inhibitor. In this study, we examined the role of peficitinib and filgotinib in RA angiogenesis. [Methods] RA FLS supernatant was obtained from RA FLS-conditioned medium stimulated with IL-6 and IL-6R with or without adding peficitinib (5 μM) or filgotinib (5 μM). To evaluate the effects of peficitinib and filgotinib on RA angiogenesis, we performed in vitro Matrigel tube formation assays using HUVECs. Next, the amount of VEGF in RA FLS conditioned medium was determined using ELISA kit. [Results] We found peficitinib or filgotinib treated RA FLS conditioned medium reduced HUVEC tube formation compared to nontreated RA FLS conditioned medium. Next, we found peficitinib and filgotinib suppress the secretion of VEGF in RA FLS. Peficitinib significantly suppressed the secretion of VEGF in RA FLS than filgotinib. [Conclusions] Peficitinib and filgotinib suppressed the secretion of VEGF in RA FLS and RA angiogenesis through inhibition of VEGF.

P2-6

Interleukin-6 enhances gliostatin production in fibroblast-like synoviocytes derived from patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Gliostatin (GLS) is expressed in fibroblast-like synoviocytes derived from patients with rheumatoid arthritis (RA-FLSs). GLS levels in sera and synovial fluids of RA patients are higher than those of healthy controls. GLS has an inflammatory and arthritogenic effect. Our previous reports have shown that serum GLS level of IL-6 inhibitor-treated patients with RA was decreased. It suggested that IL-6 may be involved in GLS expression. However, the mechanism of GLS expression in RA-FLSs is unclear. Purpose of this study is whether the IL-6 induces gliostatin expression in RA-FLSs. [Methods] RA-FLSs were cultured and stimulated by IL-6 with or without soluble IL-6 receptor (sIL-6R). GLS expression levels were determined using reverse transcription-polymerase chain reaction (RT-PCR) and enzyme immunoassay (EIA). [Results] GLS mRNA expression increased in response to treatment with IL-6/sIL-6R (but not IL-6 alone) and peaked after 12 hours of treatment. Similarly, GLS protein expression peaked after 24 hours of treatment. GLS mRNA levels were significantly induced by IL-6/sIL-6R at dose dependent manner. [Conclusions] GLS expression in RA-FLS is regulated by the IL-6/sIL-6R pathway. IL-6 did not induce GLS without sIL-6R indicates that RA-FLS lack membrane-bound IL-6R.

P2-7

Clock gene Bmal1 regulates production of inflammatory mediator in RA-FLS

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Conflict of interest: None

[Objective] We reported that expressions of clock genes were correlated with the disease activity of rheumatoid arthritis (RA). RA-fibroblast-like synovial cell (FLS) produces a variety of inflammatory mediators, while the involvement of clock genes remains unclear. We examined here effects of clock gene expression on productions of inflammatory mediators in RA- FLS. [Methods] RA-FLSs were stimulated with TNF-α (0,20 ng/ml), IL1-β (0,20 ng/ml) and IFN-γ (0,20 ng/ml), and total RNA was extracted over time. Subsequently, the expression levels of *Bmal1*, *MMP3*, *CCL2*, *IL6*, *IL7* and *IL15* were measured by quantitative PCR. Small interfering RNA (siRNA) of *Bmal1* was introduced into RA-FLSs, and stimulated with TNF-α (0,20 ng/ml), IL1-β (0,20 ng/ml) and IFN-γ (0,20 ng/ml). Thereafter, quantitative expressions of *MMP3*, *CCL2*, *IL6*, *IL7* and *IL15* were analyzed by quantitative PCR. [Results] Stimulation with TNF-α, IL1-β and IFN-γ for 16-32h increased the expression of *Bmal1*, *MMP3*, *CCL2*, *IL6* and *IL15* in RA synovial cells. In addition, the expression levels of *MMP3*, *CCL2*, *IL6*, *IL7* and *IL15* were significantly reduced by suppressing *Bmal1* expression, under the same conditions. [Conclusions] The production of inflammatory mediators from RA-FLS was suggested to be regulated through Bmal1.

P2-8

Soluble CD14 Induces Pro-inflammatory Cytokines in Rheumatoid Arthritis Fibroblast-Like Synovial Cells via Toll-Like Receptor 4

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Conflict of interest: None

Objectives: Synovial fluids of RA patients commonly contain high concentrations of soluble CD14 (sCD14). To investigate its potential role in RA pathogenesis, we tested whether sCD14 binding transmits a signal to fibroblast-like synoviocytes from RA patients (RA-FLS). Methods: The induction of pro-inflammatory cytokines, chemokines, and mediators by sCD14 stimulation of RA-FLS was quantified by real-time PCR and ELISA. Cell proliferation was assessed by the BrdU assay. LPS-RS, a TLR-4 antagonist, was used to block TLR-4 signaling. Results: Soluble CD14 induced the expression of IL-6 mRNA and secretion of the protein. The expression of other pro-inflammatory cytokines and mediators, such as TNF-α, IL-8, ICAM-1, MMP-3, and RANKL, was also induced by sCD14. In addition, sCD14 stimulation promoted RA-FLS proliferation. LPS-RS abolished IL-6, IL-8, and ICAM-1 mRNA induction by sCD14 in RA-FLS. On the other hand, TNF-α and IL-17A increased TLR-4 expression by RA-FLS and amplified their sCD14-induced IL-6 expression. Conclusions: Soluble CD14 transmits inflammatory signals to RA-FLS via TLR-4. The effects of sCD14 may be augmented in inflammatory milieu. Our results suggest that sCD14 is involved in the pathogenesis of RA and may

be a novel therapeutic target.

P2-9

Histopathological Changes of Synovial Tissue in Rheumatoid Arthritis Patients Treated with TNF inhibitors or IL-6 inhibitors

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Conflict of interest: None

[Objective] The purpose of this study is to investigate the changes in synovial tissue in RA patients treated with TNF inhibitors (TNFi) or Interleukin-6 inhibitors (IL-6i). [Methods] The frozen sections were stained by HE. To detect apoptosis, TUNEL staining was performed. The immunohistochemical characterization was performed by using the following antibodies: CD20 and CD3 for detecting B and T lymphocytes respectively, CD86,80 and CD163,206 for detecting M1 and M2 macrophage respectively. [Results] In HE, discoid fibrosis was observed in synovium treated with TNFi, and marked degeneration of lining layers was observed in synovium treated with IL-6i. In TUNEL, apoptosis of lining cells around the discoid fibrosis was detected only in synovium with TNFi. In immunohistochemistry staining, CD86 and 80 positive cells increased in lining layer, and CD163 and 206 positive cells showed diffuse expression in synovium with TNFi. In contrast, those positive cells remarkably decreased in synovium with IL-6i. Moreover, CD20 and CD3 positive cells decreased in lining and sublining layers both TNFi and IL-6i compared to control. [Conclusions] This study showed the characteristic features of synovial tissues in RA patients treated with TNFi were different from those of synovial tissues with IL-6i.

P2-10

Comparison of T cell profiles between patients with rheumatoid arthritis and healthy subjects

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Conflict of interest: None

[Objective] To clarify the difference in T cell profile between patients with pretreatment rheumatoid arthritis and healthy subjects. [Methods] The subjects were 10 untreated RA patients who met 1987/2012 ACR/EULAR RA classification criterior and 10 healthy volunteers. Th1 cells (CXCR3 + CCR6-CC4-CCR7-), Th2 cells (CXCR3-CCR6-CCR4 + CCR7low), Th17 cells in Treg cells (CD4 + CD127lowCD25 +), effector T cells (CD4 + CD127 + CD25-CD45RA-) The relative ratios of (CXCR3-CCR6 + CCR4 + CCR7low), Tfh cells (CCR5 + PD-1 + CCR7low), and Tph cells (CCR5 + PD-1 + CCR7low) are analyzed by flow cytometry. [Results] The proportion of Th17 cells was lower (0.29% vs 1.53%, P <0.001) and the proportion of Tph cells was higher (2.24% vs 0.74%, P <0.01) in the rheumatoid arthritis patient group than in the healthy group. [Conclusions] It was shown that the ratio of PD-1 + CXCR-CD4 + T cells may be higher in untreated RA patients than in healthy subjects.

P2-11

Prevention of the chronicity of autoimmune arthritis by RORgammat+Foxp3+ regulatory T cells

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Conflict of interest: Yes

[Objective] To clarify the role of RORγt^{+}Foxp3^{+} regulatory T (Tr17) cells in the development autoimmune arthritis. [Methods] 1) Collagen induced arthritis (CIA) was induced in RORγt$^{fl/fl}$Foxp3^{cre} (cKO) mice and RORγt$^{fl/fl}$ mice as control Incidence and severity of CIA were evaluated. 2) Mononuclear cells in Lymph node (LN) and ankle joint (AJ) were harvested from C57BL/6 mice after immunization of collagen type II (CII). RORγt expression in Foxp3^{+} regulatory T (Treg) cells were analyzed by FCM. 3) LN cells were harvested from C57BL/6 mice on 10 days after CII immunization. Cytokine production from Tr17 cells was analyzed by FCM. 4) RORγt^{+}Foxp3^{+}Tr17 cells in peripheral blood mononuclear cells (PBMC) were evaluated in rheumatoid arthritis (RA) patients, and compared with that in healthy controls (HC). [Results] 1) CIA was significantly exacerbated in cKO mice from 56 days after the immunization of CII ($p = 0.042$). 2) Frequency of Tr17 cell was increased in joints AJ when CIA had been developed. 3) IL-10 production was significantly increased in Tr17 cells ($p<0.001$). 4) Tr17 cells in PBMC were significantly increased in RA patients ($p = 0.017$). [Conclusions] Tr17 cells might infiltrate into inflamed joint and regulate the inflammatory response, and resulting in amelioration of CIA.

P3-1

The citrullination pathway of inter alpha trypsin inhibitor heavy chain 4 (ITIH4) and its its potential effect in the neutrophil migration

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Conflict of interest: None

Objective: This study aimed to clarify its citrullination pathway and function as related to neutrophils. **Methods:** In pGIA-afflicted joints, ITIH4 and cit-ITIH4 levels were examined by immunohistochemistry (IHC) and Western blotting (WB) while peptidylarginine deiminase (PAD) expression was measured by RT-qPCR and IHC. The pGIA mice received anti-Ly6G or anti-Gr-1 antibodies to deplete neutrophils and the expression of cit-ITIH4 was investigated by WB. Recombinant ITIH4 and cit-ITIH4 were incubated with sera from healthy volunteers, then, its chemotactic ability and C5a level were evaluated using Boyden's chamber assay and ELISA. **Results:** During peak arthritic phase, ITIH4 and cit-ITIH4 were increased in joints while PAD4 was overexpressed especially in the infiltrating neutrophils of pGIA mice. Levels of cit-ITIH4 in plasma and joints significantly decreased upon neutrophil depletion. Cit-ITIH4 increased both neutrophilic migration and C5a levels, significantly. **Conclusion:** Cit-ITIH4 is generated mainly in inflamed joints by neutrophils via PAD4. Citrullination of ITIH4 may change its function to upregulate neutrophilic migration by activating the complement cascade. We are currently analyzing the function of ITIH4 using knockout mice in arthritic conditions.

P3-2

TRPV1 gene deficiency attenuates pain sensitivity and spinal glial/neuronal changes induced by sciatic nerve injury in mice

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Conflict of interest: None

Objective: Transient receptor potential vanilloid 1 (TRPV1) is known to modulate pain. In the present study, we aimed to examine the mechanism by which TRPV1 modulates neuropathic pain in mice. Methods: We developed neuropathic pain models by partial sciatic nerve ligation (pSNL) using adult male C57BL/6J (WT) mice and TRPV1 knockout (*Trpv1*-/-) mice, evaluated mechanical/thermal sensitivities and glial/neuronal activities in the L5 ipsilateral dorsal horn of the spinal cord, and compared the findings between WT and *Trpv1*-/- mice. Results: Mechanical/thermal sensitivities, expression levels of microglial Iba-1 and astrocytic GFAP, and numbers of FosB-positive neurons were significantly higher on days 7 and 14 in the pSNL group than in sham-operation and conrol groups of both WT and *Trpv1*-/- mice. However, increased thermal sensitivities and spinal astrocytic activities were significantly more attenuated in *Trpv1*-/- mice than in WT mice on day 14 but not on day 7 after pSNL. On the contrary, numbers of FosB-positive neurons were significantly more attenuated in *Trpv1*-/- mice than in WT mice on days 7 and 14

after pSNL. Conclusions: This study suggests that TRPV1 may modulate thermal hyperalgesia via activation of astrocytes in the dorsal horn of the spinal cord in mice.

P3-3

Novel therapeutic strategy using T-induced pluripotent stem cells derived from M3R-reactive Th1 cell clone of a patient with Sjögren's syndrome

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Conflict of interest: None

[Objective] To establish a novel therapeutic strategy using antigen-specific regulatory T cells generated from induced pluripotent stem cells (iPSCs) in Sjögren's syndrome (SS). [Methods] 1) M3R-reactive Th1 cell clones were established from peripheral blood of a SS patient by single-cell sorting. 2) T-iPSCs were generated from the T cell clones via induction of Yamanaka's factors. 3) TCRβ gene of the T-iPSCs and the original clone was compared. 4) CD34+ cells within (a) sacs generated by cultivation of T-iPSCs on 10T1/2 or (b) teratomas generated by transplantation of T-iPSCs and 10T1/2-DLL into NSG mice were analyzed by flow cytometry (FCM). 5) Human T cells in NSG mice, into which (a) T-iPSC-sacs or (b) CD34+ cells of the teratomas had been transferred after irradiation, were analyzed by FCM. [Results] 1) 35 T cell clones were established. 2) 7 T-iPSCs were generated. 3) TCRβ gene rearrangement of the T-iPSCs (TkSST3-B) was consistent with that of the original clone (4-7). 4) TkSST3-B-derived (a) sacs and (b) teratomas contained CD34+ cells (25.1% and 27.4%). 5) (a) Human T cells were detected in peripheral blood of the NSG mice on day 60. (b) Under analysis. [Conclusion] T-iPSCs were generated from M3R-reactive Th1 cell clones of a patient with SS and differentiated into CD34+ cells.

P3-4

The analysis for the inhibition of angiogenesis by JAK inhibitor

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Conflict of interest: None

[Objective] Many blood vessels are generated in the hyperplastic synovial tissue of patients with rheumatoid arthritis (RA). Janus kinase (JAK) inhibitors have inhibitory effects on multiple signaling pathway, however there were few reports concerning their effects on angiogenesis. In this study, we evaluated the influence of JAK inhibitors on angiogenesis of human umbilical vein endothelial cells (HUVEC). [Methods] HUVECs were treated with 20 ng/ml VEGF including various doses (0.1μM, 1μM, 5μM) of Tofacitinib (TOF), Baricitinib (BAR) or Peficitinib (PEF). The activity of proliferation, tube formation and migration were analyzed by cell counting assay, tube formation assay and migration assay respectively. [Results] The proliferation activity was increased by VEGF and suppressed by TOF and PEF, but was not by BAR. The tube formation and migration activities were increased by VEGF and suppressed by TOF, BAR and PEF, and the suppression in the BAR group tended to be lower than the other groups. [Conclusions] The angiogenesis of HUVEC induced by VEGF was suppressed by JAK inhibitors, and the suppression in BAR group tended to be lower than the other groups. Our results suggested that VEGF upregulate the angiogenesis of RA through mainly JAK3.

P3-5

Role of programmed cell death-1 on CD4+ T cell in lupus model mice induced by topical treatment with Toll-like receptor agonist imiquimod

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Conflict of interest: Yes

[Objective] To analyze the functional role of programmed cell death-1 (PD-1) on CD4+T cell in lupus model mice induced by Toll-like receptor agonist imiquimod (IMQ). [Methods] 1) After C57BL/6 (B6) mice were treated with topical IMQ, expression of superficial antigens and transcription factors in splenic CD4+ T cells were analyzed by flowcytometry (FCM). Cytokines production from CD4+ T cells stimulated in vitro was also evaluated with FCM. 2) Expression of superficial antigens, transcription factors, and cytokine production in splenic CD4+ T cells of PD-1 knock out (KO) mice were analyzed by FCM. 3) After PD-1 KO mice were treated with topical IMQ, lupus phenotype was evaluated with anti-DNA IgG in sera and deposition of C3 and IgG in kidneys. [Results] 1) Expression of CXCR3, PD-1, and transcription factors such as T-bet and Blimp-1 were significantly elevated, and IFNg and IL-10 producing CD4+ T cells also increased in IMQ-treated mice. 2) Expression of CXCR3 and T-bet were tended to be elevated in PD-1 KO mice compared with WT mice. IFNg and IL-10 producing CD4+ T cells also increased in PD-1 KO mice. 3) Evaluation of lupus phenotype in PD-1 KO mice is now undergoing. [Conclusions] PD-1 expressed in CD4+ T cells might play a role in generation of lupus phenotype induced by IMQ.

P3-6

Association between Serum Amphiregulin and Clinical Features in Systemic Lupus Erythematosus

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Conflict of interest: None

[Objective] Amphiregulin (AREG) is an epidermal growth factor-like molecule. A previous study showed that its expression was elevated in the blood cells of patients with systemic lupus erythematosus (SLE). However, the role of AREG in SLE has not been reported. We evaluated the association between serum levels of AREG (s-AREG) and the clinical features in patients with SLE. [Methods] ELISA was performed to measure s-AREG in patients with SLE and in healthy controls. Association of s-AREG with clinical parameters in patients with SLE was investigated. [Results] s-AREG were significantly higher in patients with SLE than in healthy controls (median 22.5 vs 13.4 pg/mL, $p = 0.024$). There was a negative correlation between s-AREG and the titer of the anti-double stranded DNA (dsDNA) antibody (correlation coefficient -0.392, $p = 0.02$). Patients with hemolytic anemia had higher s-AREG than those without hemolytic anemia (median 31.5 vs 20.1 pg/mL, $p = 0.017$). Additionally, multiple regression analysis showed that the anti-dsDNA antibody titer and hemolytic anemia were associated with s-AREG after making adjustments for age and sex. [Conclusions] s-AREG were elevated in SLE and were associated with the titer of the anti-dsDNA antibody and hemolytic anemia.

P3-7

Analysis of RP105-negative plasmablasts in systemic autoimmune disease

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Conflict of interest: None

[Objective] RP105 (CD180) is one of the Toll-like receptor-related molecules and is expressed on the surface of B cells. It regulates B cell

activation, antibody production, and B cell survival and death. RP105 lacking B cells that produce anti-dsDNA antibodies exist in SLE patients and correlate with disease activity. We report the differences in plasmablasts by various autoimmune diseases. [Methods] Late B cells from patients with SLE, IgG4-related disease (IgG4-RD), ANCA-related vasculitis (AAV), etc. were stained with anti-CD19, CD138, and CD180 antibodies. Six fractions of late B cells including mature, activated B cells, early plasmablasts, plasmablasts, late plasmablasts, and plasma cells were analyzed and their relationship with clinical features was examined. [Results] RP105-negative plasmablasts in SLE was characterized by increased expression of BCMA and decreased BAFF-R, and CXCR5 disappeared earlier. Plasmablasts in IgG4-RD were increased and prolonged expression of CXCR5. AAV pateints also had an increase in plasmablasts. Residual plasmablasts were found in treatment-resistant patients, and Baffling was observed. [Conclusions] Although abnormal plasmablasts exist in autoimmune diseases, the mechanism is different. Disease- and patient-specific strategy is required.

P3-8

Syk contributes to the development of atherosclerosis through CD11c expression

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Conflict of interest: None

[Objective] Autoimmune disease is a chronic inflammatory disease to develop atherosclerotic disease, which is also caused by chronic inflammatory processes. Then, we focus on spleen tyrosine kinase (Syk) to verify the mechanism of atherosclerosis on autoimmune and chronic inflammatory disease. [Methods] 1. The atherosclerotic lesions in $Syk^{del/del}$ were measured. 2. We evaluated the cell motility of BMDM in $Syk^{del/del}$. 3. From gene expression of monocytes, we focused on CD11c. Then, we evaluate the CD11c expression using FCM. 4. We evaluated the adhesive capacity of BMDM with anti-CD11c antibodies. 5. We evaluated the CD11c promoter region associated with Syk. [Results] 1. The cumulative area and macrophage amount of atherosclerosis in $Syk^{del/del}$ was decreased. 2. The cell motility of BMDM in $Syk^{del/del}$ was decreased. 3. The CD11c gene and cell surface expression in $SykSyk^{del/del}$ were decreased. 4. The number of adhesive cells to ICAM-1 in $SykSyk^{del/del}$ was decreased, and that in $Syk^{+/+}$ with anti-CD11c antibody was decreased. 5. Syk was associated with 937-1184 bp upstream from the CD11c gene TSS. [Conclusions] This present study showed that Syk drives to develop atherosclerosis. One of the mechanisms was suggested that Syk promotes cell migration by controlling CD11c expression positively.

P3-9

Analysis of the factors involved in CRP production from human hepatocyte cell line Hep3B

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Conflict of interest: None

[Objective] C reactive protein (CRP), one of inflammatory markers widely used, is produced mainly in the liver. Interleukin-6 (IL-6) is considered to be important for its production. In patients with collagen diseases, such as systemic lupus erythematosus, it is still unknown why the level of serum CRP tends to be low. Thus, we investigated the mechanisms of CRP production from Hep3B. [Methods] We stimulated Hep3B for 24 hours with cytokines including IL-6 and measured the level of CRP in the supernatants by ELISA. We also quantified CRP at the mRNA level by qRT-PCR. [Results] IL-6 induced more CRP mRNA in Hep3B cells. Interestingly, however, CRP protein was not detected in the supernatants even if the cells were stimulated with IL-6 alone or in combination with other proinflammatory cytokines, such as TNF. We detected CRP in the supernatant only when the cells were cultured in the conditioned medium from human peripheral blood mononuclear cells (PBMCs) stimulated with LPS. When Tocilizumab, anti-IL-6 receptor antibody, was added to the system, CRP at the protein level decreased significantly. [Conclusions] IL-6 is necessary but not sufficient for inducing CRP at the protein level in Hep3B cells. Unknow factor (s) that is derived from PBMCs stimulated with LPS is also necessary.

P3-10

The complication rate of osteoporosis and sarcopenia in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA), systemic chronic inflammation and glucocorticoid induce to decrease in bone density and muscle mass. In this study, we researched the complication rate of osteoporosis and sarcopenia in RA patients. [Methods] We reviewed 40 female RA patients aged over 40 years old and were divided into a group under 65 years old and a group over 65 years old. The bone mineral density was measured by DEXA, and the YAM value was measured. Patients with YAM 70% or less were regarded as osteoporosis. The skeletal muscle mass was measured by the impedance method, and SMI 5.7 kg / m2 or less was used as sarcopenia. [Results] In under 65 years old group, 6 of 21 patients (28.6%) had osteoporosis, 3 patients (14.3%) had sarcopenia, and no cases had both osteoporosis and sarcopenia. In over 65 years old group, 11 of 19 patients (57.9%) had osteoporosis, 10 patients (52.6%) had sarcopenia, and 5 of 11 osteoporosis patients (45.5%) had sarcopenia. In over 65 years old group, the complication rate of both osteoporosis and sarcopenia remarkably high, and only 2 of 19 patients (10.5%) had neither osteoporosis nor sarcopenia. [Conclusions] It is necessary to consider the complications of osteoporosis and sarcopenia when treating RA patients aged over 65 years old.

P4-1

Prevalence of antinuclear antibody related disorder and titer of antinuclear antibody in woman of reproductive age

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Conflict of interest: None

[Objective] There are no reports on the positive predictive value (PPV) of anti-nuclear antibody (ANA) in woman of reproductive age. We conducted this study to analyze the prevalence of ANA associated disorders in ANA positive woman of reprodictive age. [Methods] We performed a retrospective electric health record search for patients tested positive for ANA between Jan 2010 to Dec 2019 in our institute. Women of reproductive age (15yo to 45yo) with ANA titer ≧1:40 at first visit to our department were included. Patients who has past medical history of ANA associated disorders were excluded. We evaluated the PPV and cut off titer of ANA titer for ANA associated disorders [Results] 763 patients were enrolled in our study. PPV of ANA for any ANA associated disorders increased as the titer get higher, and ANA titer ≧1:80 was considered to be an prognostic marker for future development of any ANA associated disorders. ($p<0.01$) This trend was also seen in the PPV of ANA for SLE and Sjogren syndrome. [Conclusions] As the ANA titer increase, the probability of ANA associated rheumatic disorders increase even in woman of reprodictive age. In women of reproductive age with ANA titer ≧1:80, we need to be cautious for the future development of ANA associated rheumatic disorders.

P4-2

Establishment of new criteria for the early diagnosis of rheumatoid arthritis negative for both rheumatoid factor and anti-CCP antibody [The need for treatment aimed at drug-free remission (Matsui method)]

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Conflict of interest: None

[Objective] Cases in which drug-free remission can be achieved by treatment of RA are limited to early cases with a disease period of ≦6 months and DAS28-CRP value≦4.5. The ACR/EULAR classification are used for the diagnosis of early RA. However, according to these classification, seronegative RA cases in which both RF and anti-CCP antibody are negative will be given a score that does not meet the criteria for diagnosis. In the Matsui method, seronegative cases are diagnosed using the DAS28-ESR value. At this congress last year, Kurosawa et al. of the Niigata Rheumatology Center proposed diagnostic criteria that use MMP-3 value. The purpose of this study was to commpare the DAS28-ESR and MMP-3 methods. [Subjects] Of the 55 early RA cases treated with the Matsui method, 18 were seronegative RA cases. When these 18 cases were evaluated using the ACR/EULAR classification criteria, none of cases was diagnosed as RA. In the Matsui method, DAS28-ESR score of 0 to 2.8 were given 0 points; 2.9 to 4.2, 2 points; and ≧4.3, 3 points. Cases with≧6 of 10 points were diagnosed as RA. The 18 cases assessed using the MMP-3 method. [Results] By using the MMP-3 method, only 12 of 18 cases were diagnosed as RA. [Conclusions] We can infer that the DAS28-ESR method can diagnose more cases.

P4-3

The diagnostic utilities of IgG rheumatoid factor (IgG-RF) and anti-agalactosyl IgG antibody (CA-RF) in rheumatoid arthritis (RA), second report

Moemi Yabe[1], Yusuke Tarutani[1,2], Mako Yamamoto[1,2], Kenshi Inoue[1,2], Naofumi Dobashi[1,2], Kenta Misaki[1,2], Yasuhiko Imaizumi[2]
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Conflict of interest: None

[Objective] We previously reported the utilities of serum IgG-RF and CA-RF in the clinical situation of diagnosis of RA. Here, we re-analyzed it with more patients to obtain accurate data. [Methods] We retrospectively analyzed 252 patients who visited Rheumatology department at our medical center due to arthralgia. Serum IgG-RF and CA-RF were measured between April and November 2016 as their first visit examination. ROC Curve analysis was performed to evaluate the sensitivity, specificity and cut-off value of these two markers. 2010 ACR/EULAR-RA classification criteria was adapted to diagnose RA. [Results] Two-hundred fifty-two patients (M: 83, F: 169, mean age: 61.0 years old) were included in this study, and 78 patients (31.0%) were diagnosed as RA. Sensitivities and specificities of serum IgG-RF and CA-RF were Sen: 70.1%. Spe: 71.4% (PPV: 68.8%, NPV: 77.9%) and Sen: 66.2%. Spe: 88.0% (PPV: 79.5%, NPV: 63.2%) respectively. AUCs and cut-off values of serum IgG-RF and CA-RF were AUC: 0.74, cut-off: 1.25 and AUC: 0.81, cut-off: 26.7 AU/mL respectively. [Conclusions] Serum IgG-RF and CA-RF might be useful markers as an adjunct to the diagnosis of RA as mentioned above.

P4-4

The relationship between rheumatoid arthritis and obesity or its associated gene

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Conflict of interest: None

[Objective] The purpose of this study was to assess the effect of obesity and its gene on RA development. [Methods] We collected RA patients who treated in Shinko hospital between March 2016 and December 2019. Medical records including BMI, body weight, dose of PSL and MTX, laboratory dates, obesity gene, and DAS28CRP were retrospectively reviewed. The patients divided into two groups; Obesity group (BMI were 25 and higher than 25) and normal group (BMI is less than 25). [Results] A total 289 RA patients recruited, and 223 were Normal group and 66 were Obesity group. Das28CRP were significantly higher in obesity group (2.19 vs 2.36, P=0.021) and MTX dose were significantly lower in obesity group. (8.8 mg vs 7.5 mg, P=0.014) FTO gene mutation is related with DAS28CRP (P=0.030) [Conclusions] In Obesity group (BMI≧25) MTX dose were lower and RA disease activity were higher. This may explain the hepatic disorder such as fatty liver, which associated with obesity. FTO gene mutation might be associated with RA disease activity.

P4-5

Detection of anti-SARS-CoV-2 antibodies in Japanese patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19) and the outbreak of COVID-19 was reported in December 2019 in Wuhan, China. The prevalence of COVID-19 in rheumatoid arthritis (RA) patients may be higher than that in healthy individuals. We investigated seroprevalence of COVID-19 in patients with RA. [Methods] Japanese patients with RA were recruited at Sagamihara National Hospital from July 2014 to October 2015 (n=38, 2014 cohort) and at Tokyo National Hospital from June to October 2020 (n=93, 2020 cohort). Anti-SARS-CoV-2 antibodies were measured in the sera from these RA patients by electrochemiluminescence immunoassay (ECLIA) or immunochromatographic assay (ICA). [Results] Anti-SARS-CoV-2 antibodies were not detected in all the samples by ECLIA. However, anti-SARS-CoV-2 antibodies were measured in the serum samples from three (7.9%) in 2014 cohort and fifteen (16.1%) in 2020 cohort by ICA. The titers of rheumatoid factor were higher in RA patients with IgM anti-SARS-CoV-2 antibodies by ICA (P=0.0101). [Conclusions] The results from ICA would be modified by rheumatoid factors in RA patients.

P4-6

Reexamination of renal function evaluation of RA patients

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Conflict of interest: None

[Objective] The age of RA patients is aging. Renal function deteriorates physiologically with aging. Although MTX is positioned as an anchor drug in RA treatment, dose adjustment is required due to renal function. MTX clinical practice guideline 2016, there is a possibility that renal function evaluation with creatinine (cre) may be overestimated for elderly women with decreased muscle mass, such as cystatin (cys) as appropriate. However, there are many unclear points about how much the renal function evaluation will differ. Then we measured eGFRcre and eGFRcys with the same sample and compared them in RA patients. [Methods] eGFRcre and eGFRcys were measured in the same sample for cases with previously measured eGFRcre less than 60. [Results] 20 males and 56 females, 76 in total, average age 75.6 years, average eGFRcre 46.12 average eGFRcys 47.17. The cases requiring attention were eGFRcre> eGFRcys, 20 cases. The mean value was eGFRcre 46.45 eGFRcys 36.36. The 20 cases were divided into two groups, eGFRcre -eGFRcys ≧ 10 group and <10, and medications and disease activity at that time were compared, but no cause. [Conclusions] The existence of cases of eGFRcre> eGFRcys is a problem, and eGFRcys should be measured once every four months, and renal function should be evaluated.

P4-7

Comparison of two methods of measuring the erythrocyte sedimentation rate (ESR); Westergren method and Capillary photometry method in patients of the department of Rheumatology

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Conflict of interest: None

[Background] The erythrocyte sedimentation rate (ESR) is a common inflammation marker. Westergren (WG) method for ESR estimation is simple and traditional method, but time-consuming and requires a relatively large amount of blood. Recent years, several new techniques using different methods, such as capillary photometry (CP) method to measure ESR have been developed. [Methods] We measured ESR by CP method with EDTA blood samples, the unused portions of samples obtained for routine clinical blood tests in outpatients of the department of Rheumatology in our hospital and assessed the correlation with WG method, ordered by attending physicians in routine clinical practice. [Results] A total of 393 patient samples were measured and correlation coefficient between two methods was 0.927. [Conclusion] Our result reveals a good correlation between WG method and CP method, and CP method has several advantages, such as reduction of measuring time, amount of blood sampling and biohazard risk of laboratory technicians. But further precise studies and discussion with physicians are needed prior to introduction since the global gold standard for the determination of ESR is still WG method.

P4-8

Clinical profile and treatment of 23 cases of IL18 measured at our hospital

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Conflict of interest: None

[Objective] IL18 has been noted to be elevated in adult onset Still's disease (AOSD) in correlation with disease activity and may aid in the diagnosis. We studied 23 patients with suspected AOSD, HPS, and other diseases with IL18 measured. [Methods] Patients with fever and the cause of the fever was suspected AOSD were reviewed retrospectively for blood test findings, treatment, and final diagnosis. [Results] There were 10 males and 13 females, with a mean age of 40 years; IL18 ranged from 78-142000 pg/ml. The final diagnosis was AOSD, systemic juvenile idiopathic arthritis (sJIA) in 14 patients, malignant lymphoma (ML) in 2 patients. Methylprednisolone pulse therapy patients had a mean IL18 was 21780 pg/ml and the mean IL18 in patients who did not perform was 16776 pg/ml. The mean of IL18 in AOSD and sJIA was 30798 pg/ml and 11495 pg/ml in the other cases. In categories of MAS classification criteria (2016) merging with sJIA, a weak positive correlation was found for IL18 and ferritin, and a negative weak correlation was found for platelet count and IL18, but not for AST and fibrinogen. [Conclusions] Since IL18 is also elevated in other diseases such as ML, we believe that exclusionary diagnosis should be carefully made to help differentiate AOSD.

P4-9

A case of dermatomyositis with positive conversion of anti-TIF1r antibody at the time of relapse

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Conflict of interest: None

A 74-year-old male with facial rash, myalgia and bilateral shoulder pain appeared around August X-14. Diagnosis of dermatomyositis (DM) based on gottron's sign, weakness and myalgia in the proximal muscles of the extremities, CK 4,221 U/L, aldolase 1438 μg/L, nondestructive arthritis, and increased erythrocyte sedimentation ratio. He was treated with PSL 60 mg/day, PSL was tapered off on an outpatient basis, and the patient was treated with maintenance therapy at PSL 2 mg/day. The blood test in June of X-2 showed an anti-TIF1-γ antibody 12. He was diagnosed with CK 741 U/L, Gottron's sign, reversed Gottron's sign, V-neck sign and Scholl's sign, and was admitted to our department. On admission, anti-TIF1-γ antibody was found to be positively converted to 45, but no complications of malignancy were observed; the dose of PSL was increased to 30 mg/day, and AZP was started. Anti-TIF1-γ antibodies were reported to be associated with dermatomyositis with malignant tumors in 2006 and have been considered to correlate with the activity of malignant tumors, but not with the disease activity of DM. However, it has recently been reported to correlate with disease activity in DM and has been proposed as a useful follow-up maker.

P5-1

Automatic detection and evaluation whether normal or abnormal of evaluation area of sharp score by using deep neural network

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Conflict of interest: None

[Objective] We examined the automatic detection of the evaluation area of the sharp score (SS) and evaluation of normal (SS = 0) or abnormal (SS >= 1) for each area by using deep neural networks (DNN). [Methods] A total of 226 X-ray images of both hands of 40 RA patients taken at different times in 9 hospitals were prepared. 1 rheumatologist gave a SS to each X-ray image (bone erosion (BE) 16 areas, joint space narrowing (JSN) 15 areas) and used it as the ground truth (GT). First, a DNN model called deeplabcut was trained in order to automatically crop the evaluation area. Next, we trained the VGG model by using properly cropped images to predict the SS with continuous value. This predicted value was rounded to an integer, and we handled predicted SS = 0 as normal and SS >= 1 as abnormal. Finally, the prediction accuracy was calculated via 8-fold cross-validation. [Results] The automatic detection rate for BE and JSN were (98.0%, 98.8%), respectively. Regarding the evaluation of normal or abnormal for BE and JSN, sensitivity, specificity, and the prediction accuracy were (0.85, 0.91), (0.81, 0.67), (82.0%, 77.2%), respectively. [Conclusions] Automatic detection of the evaluation area of SS and evaluation of SS by using DNN was possible with relatively high accuracy.

P5-2

Reconfirmation of diagnosis by radiographic images in patients with rheumatoid arthritis under treatment

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Conflict of interest: None

[Objective] To clarify whether radiographic images can reconfirm diagnosis of rheumatoid arthritis (RA) in patients who had received treatments with disease-modifying antirheumatic drugs (DMARDs). [Methods] 347 RA patients, who had been treated with DMARDs and had been taken over treatments, were enrolled in this study. All subjects underwent radiographic examinations of hands and paws. Joint damage was assessed by Steinbrocker's staging and Larsen's grading system. [Results] 247 subjects were female and 227 had seropositivity. Patients with Stage≧II or Grade≧I were 241 of 347 patients (69.5% (95% confidence interval (CI); 64.4-74.1%)). In seropositive and seronegative patients, Stage≧II or Grade≧I were found in 177 of 227 (78.0% (95%CI; 72.1-82.9%)) and 64 of 120 (53.3% (95%CI; 44.4-62.0%)) respectively, and seropositive RA patients had higher rate in radiographic joint damage than seronegative ones ($p<0.0001$). [Conclusions] Radiographic images, especially in seropositive RA, were useful for diagnositc reconfirmation of RA under treatment, but showed low re-diagnostic ability in seropositive RA.

P5-3

A study on Incidence of cervical spine lesion and its related factors in patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] The purpose of this study is to evaluate RA cervical spine lesions in our hospital and to examine the related factors in a cross-sec-

tional manner. [Methods] 248 RA patients, 242 who had no history of cervical spine surgery and had been to the hospital for more than 1 year, and had lateral flexion of the cervical spine AAS (ADI 3 mm or more) and VS (Ranawat value less than 13 mm) are defined as having cervical spine lesions. The items to be examined were gender, age, duration of illness, rheumatoid factor, C-reactive protein (CRP) level, history of joint surgery, use of biologics or JAK inhibitors, use of methotrexate (MTX), and use of steroids. [Results] AAS was 64 cases (26.4%), VS group was 15 cases (6.2 %), severe AAS was 4 cases (1.7%), severe VS group was 4 cases (1.7%), and stenosis group was 3 cases (1.2%). Long-term disease duration and high CRP levels were predominantly associated with affected groups. [Conclusions] Long-term morbidity was predominantly associated with cervical spine lesions. Patients with severe cervical spine lesions often use biologics or JAK inhibitors, and patients with high disease activity are prone to cervical spine lesions, and once inflammation spreads, the progression of joint destruction cannot be suppressed even in the cervical spine.

P5-4

Evaluation of hindfoot alignment using hip to calcaneus view

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Conflict of interest: None

[Objective] Patients with rheumatic diseases are often associated with foot deformities, and it is important to evaluate their alignment. Hip to calcaneal view (HC view) can assess alignment including the hindfoot. However, to our best knowledge, there is no report on the reliability and usefulness of measuring tibio calcaneal angle (TCA) in HC view. [methods] Subjects were 50 healthy volunteers under 50-year old (25 men and 25 women, mean age 32.4 years) with 100 pairs of legs for three months 2020. Their TCA was measured in HC view. Measurements for them were taken twice by the first examiner and once by the second independent examiner with assessments for intra- and inter-examiner reliability. The SPSS was used to assess ICC (1, 1) and ICC (2, 1). [Results] TCA was 3.6 degrees (1st time of the first examiner), 3.6 degrees (2nd time of the first examiner), 3.6 degrees (1st time of the second examiner) and 3.9 degrees (mean measured values by two examiners). The intra-examiner reliability of TCA and the inter-examiner reliability was 0.91 and 0.76, respectively. Both was showed high reliability. [Conclusions] The results of this study suggest that the HC view is useful for the evaluation of TCA. We plan to examinate TCA in the large populations with other methods in the next study.

P5-5

The role of ultrasound-defined tenosynovitis in the ACPA positive early RA patients

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Conflict of interest: None

[Objective] We picked up ACPA positive patients who had only US-defined tenosynovitis (TS) without US-defined synovitis, and examined clinical and serological various variability. [Methods] 27 ACPA positive patients with clinically joints pain and only US-defined TS or tendonitis, who didn't have US-defined synovitis at wrists, fingers, shoulders, knees, MTP joints, were investigated CRP, SDAI, DAS (28) CRP, HAQ. [Results] 27 patients were divied into 3 Groups.14 patients in Group A were treated immediately as early RA. Patients in Group B were treated after more than 3 months later.9 patients in Group C were only follow up. The average of age in Group A: B: C=64.0:56.8:56.1. ACPA titer-260.0: 660.0:117.9. The number of patients who fulfilled EULAR criteria =8:2:3. CRP=0.8 mg/dl:0.25:0.1. SDAI=17.1:10.0:8.2. DAS (28) CRP=3.56:2.3:2.4. HAQ=0.8:0.36:0.23. The average number of TS and tendinitis for each patients=5.9:6.0:2.1. [Conclusions] There were significant difference for CRP, SDAI, DAS (28) CRP, HAQ between the result of Group A and C. In Group A, 57% patients satisfied with EULAR criteria. We suggest TS and tendinitis are signs of the early symptom of RA and sometime need to treat.

P5-6

Discrepancy between clinical assessment and echocardiographic findings in rheumatoid arthritis

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Conflict of interest: None

[objective] there have been cases of progressive cases despite clinical remission. in this study, we examined the presence or absence of findings in patients who achieved clinical remission by drug therapy by performing joint us. [methods] 49ra pts who were in remission for 6 months with das-28crp and sdai in our hospital were classified into 3 groups according to treatment drug, and us was performed on both hand joints, mcp, pip and mtp. the presence or absence of findings was examined. (1) 23mtx, (2) 14bio, (3) 12jak inhibitors, age 58.1/64.9/59.5 years, disease duration 11.5/15.1/11.4 years, rf118.9/136.6/101, crp0.3/0.2/0.1, das28crp1.4/1.6/1.5, sdai0.8/1.3/1.4. [results] residual arthritis was found in 50% of the cases of (+) in all three groups of gs/pd. among the patients with pd>grade 2, 8 (34.7%), 7 (50%), 3 (50%), 6 (50%) and 6 (50%) cases of gsonly (+) were (1) 30%, (2) 14% and (3) 17%, respectively, and both gs and pd (-) were (1) 20%, (2) 36% and (3) 33%. [conclusions] positive gs/pdeven in pts in clinical remission. such residual or asymptomatic arthritis may lead to progressive bone destruction if left untreated. however, it is difficult to perform us on all joints in every case, and in the present study, a high rate of positive results was observed in both hand and mp, so it is necessary to follow up.

P5-7

Examination of ultrasonographic findings in patients with inflammation of the long head of the biceps tendon (LHBT)

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Conflict of interest: None

[Objective] Long head of the biceps tendonitis (LHBTitis) is found in such as polymyalgia rheumatica, rheumatoid arthritis (RA), and spondyloarthritis (SpA). We examined the US findings of 154 case with LHBTitis. [Methods] The diagnosis was SpA that can be classified such as psoriatic arthritis in 11 cases, RA (RA group) in 41 cases, and crystal-induced arthritis in 6 cases, and 91 cases did not reach a definitive diagnosis (Unclassified group). US findings of RA group and unclassified group were compared. [Results] Power Doppler signal positive (PD (+)) tenosynovitis of LHBT was significantly higher in the RA group (61%) than in the unclassified group (30%) ($p = 0.0025$), PD (+) findings of supraspinatus was significantly higher in the RA group (56%) than in the unclassified group (30%) ($p = 0.0031$), PD (+) findings of deltoid was significantly higher in the RA group (22%) than in the unclassified group (5%) ($p = 0.0057$). Acromioclavicular arthritis was significantly higher in the RA group (41%) than 23% in the unclassified group ($p=0.0014$), and glenohumeral arthritis was significantly higher in the RA group but less frequently in the RA group (10%). [Conclusions] Inflammation of tendons, muscles and joints in the shoulder area was strongly observed in the RA group.

P5-8

Bodymarking using digital camera images and AI for rheumatoid arthritis ultrasound examination

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Conflict of interest: Yes

[Objective] Ultrasonography has become a common practice in rheumatoid arthritis. However, it has a disadvantage because it requires a long examination time due to many joints evaluations. To reduce the examination time, we conducted a pilot study of body marking using digital cameras and AI. [Methods] We conducted a simulated ultrasound examination in five healthy subjects. The ultrasound **probe** and the patient's body were photographed with a digital camera while performing ultrasonography of the fingers, hand joints, elbows, shoulders, and knees according to the guidelines of the Japan Rheumatology Society. Based on the digital camera images, the probe's position was estimated by object recognition AI (SSD), and the position of the body's joints was estimated by postural estimation AI (PoseNet + machine learning). We used matlab and pytorch as the programming environment. [Results] The detection rate of the probes was 94±4%. The detection rate of joints was 87±6%, 89±7% and 85±10% for elbows, shoulders and knees, but 75±12% for hands and 75±12% for fingers. [Conclusions] Automatic body-marking experiments for joint ultrasonography were conducted using camera images and AI, and good results were obtained for large joints.

P5-9

A case of irAE which started with synovitis, changed to tenosynovitis, and confirmed the therapeutic effect of SASP by Ultrasound

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Conflict of interest: None

[Background] Elucidation of the pathogenesis and pathology of irAE and the establishment of prevention and treatment methods are required, and cases are currently accumulating. [Subject] 89-years-old, male, who suffered from joint pain of his right wrist. He had been treated with Nivolumab as the 3rd-line chemotherapy of lung cancer. [Results] On his first visit, synovitis was detected in the right radiocarpal joint by ultrasound. Treatment by Nivolumab was skipped one time, and NSAIDs was prescribed. Even though his symptom disappeared for a while, it flared up. Tenosynovitis around wrist was found by ultrasound. SASP was prescribed and Inflammation of tendon was disappeared. [Conclusions] Joint pain by irAE may have various type of pathology. Ultrasound was useful to detect the lesion of inflammation, which helped to cure the symptom.

P5-10

Idiopathic retroperitoneal fibrosis with drug effect assessment by ultrasonography-Inspection and evaluation at our hospital-

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Conflict of interest: Yes

[Introduction] Retroperitoneal fibrosis is a disease that causes inflammatory cell infiltration and fibrosis in the retroperitoneum centering on the abdominal aorta and causes abdominal pain and low back pain. We report a case in ultrasonography was effective the therapeutic effect of idiopathic retroperitoneal fibrosis. [case] 47 years old, Male [Ultrasonography method] The aorta just before bifurcation of the common iliac artery was depicted as a short-axis image, and the thickness of the anterior wall and the cross-sectional area of the lesion were calculated during systole. [result] Front wall (mm): Before treatment: 12, 4 months after treatment: 2.1, 8 months later: Less than measurement sensitivity. Cross-sectional area of lesion (cm): Before treatment: 7.8, 4 months after treatment: 0.9, after 8 months: Measurement sensitivity is not possible. [Discussion] We observed changes over time in thickness and area of lesion as parameters for evaluating the degree of lesion reduction. Although both values declined after the start of treatment, the rate of reduction of the cross-sectional area seemed to reflect the therapeutic effect more sensitively than the thickness of the front wall. [Conclusions] Area measurement was considered useful for follow-up.

P5-11

Efforts to maintain and improve the quality of musculoskeletal ultrasound (MSUS) medical care in small and medium-sized hospitals

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Conflict of interest: None

[Objective] Unlike universities and clinics, there are a relatively large number of mid-career to young doctors who perform MSUS themselves (hereinafter referred to as "executive doctors") at small and medium-sized hospitals. In that facilities, the change of doctors tends to affect the examination system for MSUS, so we would like to consider countermeasures. [Methods] Questionnaire survey will be conducted with doctors from two hospitals with different examination systems (total of 6 executive / 6 non-executive doctors) and engineers (2 in total) to deepen mutual understanding between the requester and the recipient to grasp the actual situation. [Results] Through a questionnaire with free-form questions, it was found that the intentions of the executive and the non-executive doctors are different even on the side that issues the same test request, and that the needs of the executive doctors and the engineers are different even on the same recipient side. It was also found that there are some common parts even if the facilities change. [Conclusions] It seems that the common needs among doctors with different facilities and positions are general, and the dissimilar parts will lead to hints for countermeasures, which is the purpose of this study, by considering the background.

P6-1

Effective parameters of Dynamic Contrast-Enhanced MRI of finger and wrist joints to evaluate drug treatment response in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] The aim of this study was to assess the effectiveness of the empirical mathematical model (EMM) parameter analyses of DCE-MRI in patients with rheumatoid arthritis for distinguishing responders and non-responders of drug treatment. [Methods] DCE-MRI was performed twice. ROIs were placed where the highest signal increase was observed and the kinetic curves were analyzed using an EMM: $\Delta S(t) = A(1 - e^{-\alpha t})e^{-\beta t}$, ΔS is relative enhancement, t is time from, A is the upper limit of signal intensity, α is the rate of signal increase, and β is the rate of signal decrease. The initial slope of the kinetic curve ($A\alpha$), the initial area under the curve (AUC30), the time at which the kinetic curve reached its peak (Tpeak) and the signal enhancement ratio (SER) were calculated. The differences of change of parameters were assessed between treatment responders and non-responders. [Results] Non-responder group included 11 patients and responder group included 13 patients. In the EMM parameter analyses, there were significant differences in the changing amount of AUC30, α and Aα between treatment responders and non-responders. [Conclusions] The changing amount of AUC30 may contribute to evaluate the therapeutic effect determination of drug treatment.

P6-2

The difference in low-field magnetic resonance imaging findings between rheumatoid arthritis patients treated with certolizumab pegol or infliximab

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Conflict of interest: None

[Objective] To clarify the differences in the effects of each TNF inhibitor (TNFi) on low-field MRI (compacTscan; cMRI) findings. [Methods] We targeted RA patients who started administration of Certolizumab pegol

(CZP) or Infliximab (IFX), and were examined by cMRI at the start of TNFi and within 6 months. We compared 1) background and clinical course, and 2) changes in cMRI findings such as erosion, bone marrow edema (BME), and synovitis after the start of TNFi between two groups, retrospectively. [Results] 1) Between CZP (9 cases) and IFX (18) group, age, sex, disease duration, DAS28, SDAI, CDAI, and combination therapy were comparable at the start of TNFi. However, first Bio were significantly more frequent in IFX (33.3% vs 94.4%, P<0.01). After 6 months, disease activities were significantly decreased from baseline in both groups. 2) Erosion score did not change significantly in both. BME score was significantly decrease in CZP group after 6 months (4.4 ± 4.6 vs 0.4 ± 0.8, P=0.03), whereas in IFX groups there was no significant change. Synovitis score was significantly decrease in both groups after 6 months (CZP: 4.1 ± 1.8 vs 1.8 ± 1.6, P=0.01, IFX: 5.6 ± 4.8 vs 3.3 ± 3.5, P<0.01). [Conclusions] In RA patients, it was suggested that CZP might improve BME more effectively than IFX.

P6-3

Evaluation of knee disorders in rheumatoid arthritis patients using MRI

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Conflict of interest: None

[Objective] The aim of this study was to evaluate the knee joints of patients with rheumatoid arthritis (RA), using Whole-Organ Magnetic Resonance Imaging Score (WOMRS). [Methods] A total of 27 RA patients (21 females and 6 males, average 69 years old) who underwent total knee arthroplasty in our department after 2016 were enrolled. WORMS (Osteoarthritis Cartilage. 2004) was used to evaluate the preoperative knee MRI. Multivariate analysis was performed to assess the association between each score and age, duration of disease, and DAS28 values at the time of MRI imaging. [Results] Of the WORMS, Total score, Bone cysts score, Bone attrition score and Menisci score were positively associated only with the duration of the disease (p<0.05); Osteophytes score was negatively associated only with DAS28 values (p=0.03). The Cartilage score, the Marrow abnormality score, the Ligaments score, and the Synovitis score had no significant correlation with age, disease duration, or DAS28 values. [Conclusions] An overall assessment of the knee joint using MRI in RA patients showed that total assessment, bone cyst formation, degree of bone wear, and degree of meniscus damage were associated with the duration of RA disease, but the effect of age and disease activity was not evident.

P6-4

Evaluation of Laterality of Magnetic Resonance Imaging of hands in Patients with Rheumatoid Arthritis Achieving Clinical Remission

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Conflict of interest: None

[Objective] To evaluate of laterality of Magnetic Resonance Imaging of hands in patients with rheumatoid arthritis (RA) achieving clinical remission [Methods] Eligible patients had to have a diagnosis of RA, with clinical remission defined by DAS28-CRP and was obtained both hand of MRI imaging. MRI image of both hands was obtained using 1.5 T whole-body MRI unit with contrast enhancement. [Results] A total of 3 patients was included in this study. All patients were positive for RF and anti-CCP antibody test. Age, disease duration, and DAS28-CRP at MRI examination was as follow; patient 1 (71, 5, 1.31), patient 2 (87, 3, 1.28), patient 3 (72, 25, 1.31). Total RAMRIS synovitis score (R/L) of each patient was 3/1, 1/0, and 0/0, respectively. MRI-detected synovitis existed in only wrist joint and all of each score was 1. Hence, concordance rate of both hands of synovitis score in MP joint was 100% and those of wrist joints was 66.7%. [Conclusions] Concordance rate of both hands of synovitis in patient with RA achieving clinical remission was not necessarily high, especially in wrist joint.

P6-5

Two cases of systemic lupus erythematosus that diffusion-weighted whole-body imaging with background signal suppression (DWIBS) was useful for diagnosis, disease evaluation, and assessing treatment effects

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Conflict of interest: None

[Objective] We report two cases of SLE that DWIBS was useful for diagnosis, disease evaluation, and assessing treatment effects. [Case 1] A 33-year-old woman. She admitted to our hospital for the left inguinal lymph node swelling, fever and arthralgia. She met the 2019 EULAR / ACR classification criteria and was diagnosed with SLE. DWIBS showed multiple lymphadenitis in the left medial and external ilium, left inguinal region, and para-aortic region, and the pathological diagnosis was lymphadenitis due to SLE. We treated with PSL 20 mg, HCQ 300 mg, and TAC 3.0 mg. Remission was achieved 3 months after treatment, and DWIBS confirmed improvement in multiple lymphadenopathy. [Case 2] A 26-year-old woman. She admitted to our hospital for fever and cervical lymphadenopathy. She met the 2019 EULAR / ACR classification criteria and was diagnosed with SLE. DWIBS showed systemic lymphadenopathy. Lupus nephritis (ISN / RPS classification class V) was diagnosed by renal biopsy. We treated with PSL 50 mg, HCQ 200 mg and MMF 2 g. Remission was achieved 3 months after treatment, and DWIBS confirmed improvement in systemic lymphadenopathy. [Conclusions] DWIBS is useful for diagnosing lymphadenopathy in SLE patients, suggesting that it may be an alternative test to CT.

P6-6

Evaluation of sacroiliac joints in patients with coxarthrosis by CT and examination of risk factors for fusion

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Conflict of interest: None

[Objective] Patients diagnosed with coxarthrosis may be caused by spondyloarthritis. Among the patients diagnosed with coxarthrosis at our hospital, we compared the sex, age, and complication rate of rheumatic disease based on the presence or absence of sacroiliac joint fusion by CT. [Methods] 329 patients and 658 joints (234 women, mean 66.9 years) who underwent abdominal CT imaging among those with advanced coxarthrosis. The state of sacroiliac joint fusion was evaluated according to the classification criteria of Yahara et al. We also compared patient backgrounds by category (sex, age, rheumatic disease complications). [Results] There were 39 cases (20 women, 13 with rheumatic disease) of Type 4c fusion on either the left or right side, 290 cases other than Type 4c (213 and 36, respectively). As a result of multivariate logistic analysis, the odds ratio for sacroiliac joint fusion in patients with coxarthrosis was 2.50 (p <0.01) for males and 3.35 (p<0.005) for rheumatic disease. [Conclusions] From the results of this study, patients who complain of hip pain, especially men, should confirm the inflammatory reaction by collecting blood and perform MRI imaging including the sacroiliac joint and hip joint for early diagnosis of spondyloarthritis

P6-7

A case of advanced RA in which activity disappeared with biologics and HR-pQCT showed interesting changes in joint structure and bone microtrastructure

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Conflict of interest: None

[Objective] We report a case of advanced RA in which changes in joint structure and bone microstructure were observed by HR-pQCT after biologics therapy. [Case] Case is a woman in her twenties who developed RA one year ago and started MTX therapy. 2D and 3D images of HR-pQCT showed thinning of the cortical bone and the bone erosion at the left distal radius end and disappearance of the joint space in the right 3PIP joint. Ultrasonography showed synovitis in the same joints. In distal radius, inner trabecular bone mineral density (Inn. Tr. BMD: mg/cm^3) decreased to 70.4 on the left compared to the right (178.6), cortical bone density (Ct. BMD: mg/cm^3) decreased to 821.9 on the left compared to the right (939.1), cortical porosity (Ct. Po: %) increased to 0.037 on the left compared to the right (0.004)). The synovitis disappeared 6 months after starting TNFi. One year later, Inn. Tr. BMD was 75.8 on the left and Ct. BMD was 888.0 on the left and Ct. Po was 0.012 on the left. Remineralization and improvement of the bone erosion of the left distal radius end were observed. In the right 3PIP joint, the joint space appeared and the alignment deviation was improved. [Conclusions] A young female RA patient who received TNFi for 1 year showed improvement in joint structure and bone microstructure.

P7-1

Elucidation of the function of neutrophils and their extracellular traps in peptide GPI-induced arthritis

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Conflict of interest: None

[Objective] To clarify the function of neutrophils and their extracellular traps (NETs) in pathogenesis of peptide GPI-induced arthritis (pGIA). [Methods] 1) After confirming the localization of citrullinated proteins, Western blotting (WB) of citrullinated histone 3 (CitH3) was performed at the immunized skin and joints of pGIA. 2) Immunohistochemistry (IHC) of CitH3 was performed at immunized skin and joints of pGIA. Immunofluorescence (IF) of CitH3 and neutrophil elastase (NE) was performed at joints of pGIA. 3) Gene expression of articular neutrophils in pGIA were explored by quantitive PCR. [Results] 1) While CitH3 was detected by IHC in the pGIA skin on day 7, 14 and 28, it was also detected in the skin of control mice. CitH3 was detected in joints of pGIA on day 14, and it was specific in pGIA. 2) CitH3 was detected in the pGIA synovium on day 14 by IHC, and co-localization of CitH3 and NE was detected by IF. 3) The expression of HIF-1α was increased in articular neutrophils in pGIA on day 14, as compared with bone marrow neutrophils. [Conclusions] Specific co-localization of CitH3 and NE was detected in the synovium of pGIA, suggesting the formation of NETs in arthritic joints. HIF-1α might involved in formation of NETs in pGIA.

P7-2

Induced pluripotent stem (iPS) cells derived from a patient with rheumatoid arthritis are differentiated into myeloid progenitors earlier than those from a non-onset family member

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Conflict of interest: None

[Objective] Abnormal differentiation of bone marrow cells (BMCs) may contribute to RA pathogenesis. Thus, the studies using BMCs are necessary. However, human BMCs are not easily accessible and are susceptible to their disease activities and treatments. To overcome these limitations, we have used a method to differentiate iPS cells derived from RA patients into myelomonocytic cells. [Methods] During the differentiation of iPS cells derived from a RA patient (RA-iPS) and her non-onset family member (NOF) to myelomonocytic cells, the proportions of CD34+ cells (hematopoietic stem cells), CD43+ cells (erythro-myeloid progenitors) and CD45+ cells (lymphomyeloid) were analyzed by FACS. [Results] The proportion of CD34+ cells peaked at Day 10 (RA-iPS: 62.1±10.3%, NOF: 50.4±4.8%) and then decreased (< 2% at Day 22 for both). The proportion of CD43+ cells of RA-iPS were 52.0±6.5% and decreased to 14.0±3.5% at Day 30. On the other hand, those of NOF were 23.4±2.8% at Day 10 and increased to 40-48% after Day 14. The proportions of CD45+ in CD43+ cells were lowest at Day 10 (RA-iPS: 36.3±18.8%, NOF: 35.4±14.5%), and they increased to > 80% at Day 18 for RA-iPS and at Day 22 for NOF. [Conclusions] Our results indicate that RA-iPS are differentiated into myeloid progenitors earlier than NOF.

P7-3

The Significance of CD14 and Vimentin-Positive Synovial Dendritic-Shaped Cells in Rheumatoid Arthritis

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Conflict of interest: None

[Objective] There are still unknown about the nature, origin, and function of FLSs. We have previously reported that FLSs are positive for CD14 and constitute nursing phenomenon between lymph or plasma cells. In this study, we investigated the function of these CD14+ cells. [Methods] Synovial tissues collected from RA patients who underwent joint surgeries were prepared for this study. First, the proportion of CD14+ cells in RA synovial tissue and the function were analyzed using flow cytometry and ELISA. Next, the proportion of CD14+VIM+ cells was examined immunohistologically. [Results] As a result of flow cytometry, CD14+ cells were frequently observed in RA synovial tissue than control. Cultured CD14+ cells released more inflammatory cytokines than cultured CD14- cells. Also, as results of immunohistological staining, many CD14+VIM+ cells were observed in RA synovial tissue than in control. The proportion of CD14+ VIM+ cells was correlated with Krenn synovitis score and high proportion cases significantly showed high level of CRP and MMP-3. [Conclusions] CD14+VIM+ cells might be involved in the mechanism of chronic immunological inflammation in RA, but many problems still remain regarding the origin.

P7-5

A case of rheumatoid arthritis with right shoulder joint that required differentiation from soft tissue tumor

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is low incidence of large joints. And monoarthritis makes RA diagnosis more difficult. Here, we report a case of RA diagnosed by biopsy, which requires differential diagnosis from soft tissue tumor. [Case] The patient was a 55-year-old woman who developed right shoulder joint pain. CT scan and MRI scan showed bone destruction and soft tissue tumor in the glenoid of her shoulder joint. Antinuclear antibody, rheumatoid factor, and anti-CCP antibody were normal values, but the CRP level (1.39 mg/dl) and the ESR level (49 mm/hour) were increased. CT-guided needle biopsy was performed, the bacterial examination test was negative, and histological examination showed high proliferation of lymphocyte and plasma cell. Although she was not included the 2010 ACR/EULAR RA classification criteria, she was diagnosed with RA because of bone erosion on imaging and lymphocyte proliferation on histological examination. [Results] She was improved right shoulder joint pain after 6 months treatment of methotrexate (MTX) and was cured the contracture of shoulder joint. During 1.5 years of treatment, she did not appear other joint inflammatory symptoms and maintained remission with MTX 6 mg/week.

P7-6

The Clinical Manifestations at the onset of Human T-cell Leukemia Virus Type 1 (HTLV-1)-positive Rheumatoid Arthritis: a case-series analysis

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Conflict of interest: None

[Objective] To investigate the characteristics of HTLV-1-positive patients with rheumatoid arthritis (RA) at the first visit of our department. [Methods] We reviewed medical records of 10 HTLV-1-positive participants who were diagnosed with RA during April 2017 to August 2019. [Results] Seven participants were female. The mean age at the onset of RA was 61.9. Two were complicated with HTLV-1-associated myelopathy. One of them was complicated with HTLV-1-associated uveitis. Eight cases who were negative for RF or ACPA were diagnosed as RA using joint ultrasound and enhanced MRI of hands. The mean DAS28-CRP and SDAI was 3.9 and 31.4, and the mean levels of CRP, ESR, and MMP-3 was 1.99 mg/dL, 36.7 mm/hr, and 159.8 ng/mL, respectively. In 3 cases, atypical lymphocytes was observed in peripheral blood smears, however there were no cases of adult T-cell leukemia (ATL). The initial anti-rheumatic drugs were as follows; salazosulfapyridine (SASP): 7 cases, methotrexate (MTX): 3 cases, SASP+MTX: 1 case. Low-dose prednisolone was used in 7 cases. [Conclusions] Joint ultrasound or enhanced MRI should be evaluated in HTLV-1 positive patients who complains poly-arthralgia. Furthermore, checking atypical lymphocyte during anti-rheumatic treatment might be helpful for screening for ATL development.

P8-1

Sufficient clinical conditions for sustained functional remission in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] Treatments aimed at maintaining sustained clinical remission in rheumatoid arthritis (RA) patients have been recommended by several groups. Improvement and maintenance of functional status are also important for RA patients. The purpose of this study was to investigate the factors for maintaining long-term functional remission. [Methods] RA patients with usual care without specific protocols were included. DAS28-CRP, SDAI score, and HAQ-DI score were calculated every 3 months for 1 year. Patients were divided into the HAQ-DI remission (REM) group and the HAQ-DI non-remission (NO-REM) group, time-averaged values of these parameters were compared between groups. [Results] Of the 205 patients, 154 fulfilled the remission criteria. Time-averaged DAS28-CRP and SDAI score were significantly lower in the REM group than in the NO-REM group, (1.66 vs 2.59, 3.54 vs 10.68, respectively; $p<0.001$). Subsequent receiver operating characteristic (ROC) analysis for estimation of remission indicated a cut-off value of 1.65 for time-averaged DAS28-CRP and 2.85 for time-averaged SDAI score. [Conclusions] Sustained clinical remission is required to achieve sustained functional remission; the criteria for clinical remission may be more stringent.

P8-2

Large-joint-dominant patients with RA are Difficult to Treat (D2T)

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Conflict of interest: None

Background: Although goals for RA treatment is to keep good physical function as well as low disease activity (LDA) based on T2T strategy, there remains patients with D2T. We reported the large-joint-dominant (LAR) patients had high disease activity and poor physical function[1]. **Purpose:** To examine achievement rate of LDA and mHAQ in the LAR patients. **Patients:** Of patients serially registered in NinJa database from 2015 to 2019, we extracted 7011 subjects who were assessed joint involvements. Joint index and large-joint-dominance was defined as previously reported[1]. **Results:** Achievement rate of Boolean or CDAI remission was 37% in 2015, while that for five consecutive years was 8%. LDA achievement rate was 79% in 2015 and 52% for five years. Among the LAR patients, achievement of the remission/LDA for five years was as low as 0.6%/31%. HAQ remission at 2019 in patients with LDA in 2015 was 65% and >80% when they were in LAR group and others in 2015, respectively. Patients who achieved LDA for five years had higher levels of mHAQ when they were in LAR group than in others in 2015 ($p<0.0001$). **Conclusion:** Sustaining achievement of LDA was hard in LAR patients, and physical function was poor even if they reached LDA. LAR is thought to be a factor of D2T.

P8-3

Sarcopenia assessment is important for risk assessment of fracture among patients with rheumatoid arthritis - from the CHIKARA study -

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) tend to have sarcopenia due to decline of muscle mass and function. We longitudinally investigated sarcopenia condition among patients with RA. [Methods] We investigated the body compositions, laboratory data, disease activity, physical function, treatment, and history of fall and fracture among 100 patients with RA participated in the prospective CHIKARA study at baseline and 4 years. They were divided into 4 groups depending on sarcopenia condition; no sarcopenia development (N group), sarcopenia development (S group), cure (C group), and maintain (M group). [Results] Seventy-seven RA patients completed survey. 62.3% of all were N group; their BMI, muscle mass, fat percentage, estimated bone mass, and body metabolization rate at baseline were significantly high. On the other hand, 7.8% were S group; 83.3%, significantly more frequent, experienced fracture during 4 years. 16.9% were M group; baseline MMP-3 was significantly high. 13.0% were C group. There were no differences between 4 groups regarding disease activity, physical function. [Conclusion] 7.8% developed sarcopenia. They experienced fracture more frequently. Sarcopenia assessment is important for risk assessment of fracture.

P8-4

Prognosis prediction of treatment for rheumatoid arthritis using matrix transformation

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Conflict of interest: None

[Objective] The prognosis prediction of rheumatoid arthritis (RA) treatment was assessed using the transformation matrix (TM) developed by Nishiyama[1]. [Methods] The subjects were 529 RA patients who were treated for 1 year or more. The affected joints are assigned to the joint regarding upper or lower limbs / large or small joints. It was expressed in three dimensions; X: upper limbs, Y: lower limbs, Z: large or small joints. This was classified and the patients were classified into a low disease activity group (LDA), a large joint group (BJ), a large and small joint group (BSJ), and a small joint group (SJ). The affected joints 1 year after baseline (1YA) were also classified in the same manner, and the classifications cal-

culated with the TM were compared. [Results] There included 303 cases of LDA, 156 of BJ, 44 of BSJ, and 26 of SJ at baseline, whereas 380 of LDA, 48 of BJ, 89 of BSJ, and 12 of SJ at 1YA. The prediction results demonstrated 316 cases of LDA, 54 of BJ, 154 of BSJ, and 5 of SJ. The accordance rate was 52.4%, while it increased to 61.2% only in cases to whom biologics were introduced. [Conclusions] More accurate prognosis prediction may be possible by improving the TM in consideration of patient characteristics.

P8-5

Contents of medical treatment for the patients with early rheumatoid arthritis at our hospital in 2019

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Conflict of interest: None

[Objective] We investigated the contents of medical treatment for the referred or new outpatients with early rheumatoid arthritis at our hospital in 2019. [Methods] 19 patients who had symptoms and were diagnosed with RA within 1 year from their onset per one year. Their age, gender, duration of illness until consultation and diagnosis, the value of anti-CCP antibody, DAS28ESR4, CRP and MMP3, and content of medical treatment from the time of initial diagnosis to the last observation were examined. [Results] The mean age at the first visit was 57 years (25-78), the gender was 3 males and 13 females. The mean duration of RA till the consultation was 12 months (0.5-72), the mean time till the diagnosis of RA was 13 months (1-73). The mean value of anti-CCP antibody was 452 U / ml (0.5-2360), DAS28ESR4 was 4.8 (2.6-6.4) at the first visit and 1.7 (1.2-4.4) at the last observation, the MMP-3 at the first visit was 171.4 (25-920) and was 54.7 (29-64.5) at the last observation. The MMP-3 at the first visit was 171.4 (25-920) and 54.7 (29-64.5) at the last observation. [Conclusions] The number of early RA diagnosed per one year was 19 patients at our hospital in 2019. It should be aimed to make more efforts for early diagnosis and intervention of RA.

P8-6

Analysis of treatment results by age for Rheumatoid Arthritis outpatient in our hospital

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Conflict of interest: None

[Objective] We tried to analyze clinical characteristics and treatment response of rheumatoid arthritis (RA). [Methods] We reviewed the clinical data of 219 RA patients for DAS28CRP, HAQ, achievement rate for treatment goal (ARTG), eGFRR, and usage of MTX and bDMARDs/JAK inhibitor (bDMARDs/JAKi). Then we analyzed the data in accordance with age groups (<65 y.o., <80 y.o., and >= 80y.o.). [Results] There was no significant difference in change rate for DAS28CRP, HAQ, ARTG, eGFR between fisrt visit (FV) and 6 month later (6MO) although HAQ and eGFR at FV and 6MO got worse as the patients got older. In addition, MTX dose at 6MO was on a downward trend as the patients got older. While, for induction rate of bDMARDs/JAKi, the one of <65 y.o. group was lower than another groups. [Conclusions] Elderly patients are already in low ADL and low spare ability at FV, thus it is reasonable for them to be in low eGFR. Thus high dose csDMARDs (kidney elimination type) treatment should not be used for them. Our data clearly indicates that high dose multidrug therapy is useful for <65 y.o. patients but bDMARDs/JAKi therapy should be introduced for elderly individual. Indeed, early induction rate of bDMARDs/JAKi therapy is high and bDMARDs solo treatment rate is increased in our hospital.

P8-7

A comparative study of the validity of the DAS28-ESR and JADAS-27 disease activity assessment indexes for juvenile idiopathic arthritis in transition and adults

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Conflict of interest: None

[Objective] We compared the validity of DAS28-ESR and JADAS27 in transitional and adult JIA. [Methods] Patients aged 18 years or older at the time of the study with an onset of younger than 18 years were selected from the prospective observational studies of IORRA conducted by the Institute of Rheumatology, Tokyo Women's Medical University. [Results] A total of 3,528 cases (age 39.1 [SD15.1] years at the survey, 13.5 [SD3.8] years of onset) were included in the study. Activity according to both indices in order of high/medium/low disease activity/remission were DAS 28-ESR (mean 2.9 [SD1.3]: 5.5/31.7/19.5/43.3%, JADAS27 (mean 7.6 [SD6.3]: 65.2/16.3/7.8/10.7%, and JADAS 27 presented a higher disease activity configuration than DAS28-ESR. JADAS27-specific joints were active in the ankle (11.3%), neck (2.6%), and hips (1.2%), and In the 686 cases (19.4%) with these, DAS28-ESR averaged 2.8 [SD1.3] and JADAS27 averaged 7.3 [SD6.5], with no underestimation by DAS28-ESR compared to the overall population. [Conclusions] JADAS27 has been applied to severity classification of articular JIA as the designated incurable disease in Japan and is socially important in transitional and adult JIA, but it is necessary to recognize the difference between the JADAS27 and the DAS28-ESR in its application.

P8-8

Impact of subclinical synovitis detected by ultrasonography and MRI in RA patients after reaching clinical remission on patient's subjective symptoms

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Conflict of interest: Yes

[Objective] To examine the relationship between subjective residual symptoms and imaging examinations in RA patients who have achieved clinical remission. [Methods] 30 RA patients who achieved SDAI remission during RA treatment. Age, sex, disease duration, physical findings, serological markers, disease activity, HAQ, EQ-5D-5L, FACIT-F, PRO, EGA and medications were evaluated. 44 joints were assessed by US with GS and PD and contrast-enhanced bilateral joint MRI scoring with OMERACT-RAMRIS scoring. [Results] 1. In the analysis of the presence of subjective residual symptoms that led to SDAI remission, HAQ and pain VAS were extracted significantly differently as independent factors in multivariate logistic analysis. 2. Univariate analysis of HAQ and pain VAS showed that HAQ was significantly higher than MRI- Synovitis was extracted with a significant difference. [Conclusions] 1. It was suggested that Pain VAS and HAQ due to RA could be identified in patients reaching SDAI remission. 2. In patients reaching SDAI remission, Pain VAS≦10 or HAQ≦0.5 suggested that subjective residual symptoms may be eliminated. 3. HAQ≦0.5 suggests that synovitis is less likely to be detected on MRI.3. In patients who have reached SDAI remission, little residual inflammation was observed on US.

P8-9

Retrospective examination of X-ray follow up in the untreated patients of rheumatoid arthritis

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a intractable disease accompanied with irreversible joint destruction. Treatment should be aimed at reaching a target of sustained remission or low disease activity in every patient. Furthermore, it's neccesary to follow X-ray evaluation regarding structural change and physical dysfunction in addition to disease activity. [Methods] In untreated patients with RA at our hospital, the changes of joint lesions at the first time of X-ray follow-up are evaluated and classified into deterioration group or not. Clinical symptoms, blood data, and treatment contents are retrospectively compared. [Results] The majority of these groups was comprised with stage 2 or later and no significant differences were observed in therapeutic effect. The introduction rates of MTX and b/tsDMARD at the time of follow-up were about 50% and 15% in each groups. At the first time of X-ray follow up, 23.6% of patients worsened hand X-ray. [Conclusions] In our hospital, we could not point out the factors that predict early changes in hand X-ray in patients with untreated rheumatoid arthritis. Regardless of poor prognosis factors, patient self-assessment, and disease activity, it would be important to persue treat to target and ensure X-ray follow-up.

P8-10

Difficult-to-treat RA (DTRA) in our department

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Conflict of interest: None

[background] Biologics, JAK inhibitors, and T2T strategy have made prognosis of patients with rheumatoid arthritis better. However, Difficult-to-treat RA (DTRA) still remains problem. [objective] To investigate our DTRA data. [methods] We retrospectively analyzed 77 patients with RA who visited our department from April 2019 to September 2020. [results] Of the 77 patients, 15 patients (19.5%) did not reach remission or low disease activity. 6 patients (7.8%) could not receive adequate medication due to complications, 5 patients (6.4%) could not be adequately treated due to side effects, 5 patients (6.4%) were due to poor medication adherence, and 6 patients (7.8%) were refractory to multiple biologics. Pulmonary diseases such as interstitial pneumonia were the most common complications. Drug-induced adverse events were MTX in 2 cases, bucillamine in 2 cases, and corticosteroids in 1 case. In some DTRA cases, JAK inhibitors were effective. [conclusion] We should improve strategies for lung involvement, post adverse effects of DMARDs, and medication adherence.

P8-11

Examination of the rheumatoid arthritis onset from monoarthlitis of the knee

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Conflict of interest: None

[Objective] Knee monoarthritis is often experienced in daily practice, but it is often difficult to distinguish between knee osteoarthritis (OA) and RA, especially when the serologic reaction of rheumatoid arthritis (RA) is negative. [Methods] The subjects were 20 patients (3 males and 17 females) who underwent synovial pathological examination for RA seronegative knee monoarthritis. Comprehensive differential diagnosis including pathological examination was performed, and either OA or RA was diagnosed. Age, duration of illness and serum test (CRP, MMP-3) were investigated and compared between the OA group and RA group. The course of treatment was investigated for the RA group. [Results] The diagnosis was RA in 11 cases and OA in 9 cases. CRP was 4.48 ± 17.5 mg / dl in the RA group and 0.23 ± 0.55 mg / dl in the OA group, which were significantly higher in the RA group ($p = 0.023$). MMP-3 was 460.1 ± 489.1 ng / dl in the RA group and 124.0 ± 48.6 ng / dl in the OA group, which were significantly higher in the RA group ($p = 0.048$). In the RA group, 54% presented polyarthritis during the course. Drug treatment resulted in remission in 10 patients (91%) and low disease activity in 1 patient (9%). [Conclusions] Knee monoarthritis does not meet the RA classification criteria but may be RA.

P8-12

Usefulness as a predictor of treatment efficacy in blood trough concentrations after 14 weeks of infliximab

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Conflict of interest: Yes

[Objective] Infliximab (IFX) is the only biologic agent that can be easily measured in blood using the RemicheckQ (RemiQ) kit. However, there is still room for improvement in the use of qualitative results in daily clinical practice. [Methods] In the present study, we measured the RemiQ at 14 weeks after the introduction of IFX and evaluated its usefulness as a predictor of therapeutic efficacy. Methods: We measured the RemiQ after 14 weeks of IFX initiation starting in September 2015, and assessed the persistence rate, presence or absence of IFX escalation, DAS28 disease activity, and EULAR Response in 21 patients with follow-up. [Results] The results of 14 weeks after the introduction of IFX were positive in 9 cases and negative in 12 weeks, and the percentage of patients with dose escalation within 12 months (11.1% of positive vs. 75.0% of negative cases). This influenced the decision to increase the dose. The DAS28 low disease activity rate was significantly different at 6 months (57.1% RemiQ-positive vs. 10.0% negative), patients who were RemiQ-positive responded better to treatment early. [Conclusions] The results of the 14-week post-IFX RemiQ measurement may influence early treatment response and may be a predictor of treatment response at 12 months.

P8-13

Evaluation of efficacy and safety of 80 mg Adalimumab (ADA) / 2W for elderly patients

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Conflict of interest: None

[Objective] In the past, we have reported on efficacy and its predictive factors for 80 mg Adalimumab (ADA) / 2W. Here, we evaluate the efficacy and safety of ADA 80 mg / 2W for elderly RA patients. [Method] 23 patients over 70 years old patients were treated with ADA 80 mg / 2W for 24 weeks at our center. The endpoint was treatment continuation rate at 24 weeks, and the patient background and clinical course were compared 23 patients over 70 years old with 28 patients less than 70 years old. [Result] Of the 23 patients in the elderly group with follow up of 24 weeks, 16 patients (69.7%) continued treatment, which was not significantly different from in the non-elderly group (15 patients, 53.6%). The 16 elderly patients showed significant clinical improvement after 24 weeks. As for adverse events, only one injection site reaction was observed in the elderly group. Multivariate analysis found no predictors of 24-week continuation in the elderly. [Conclusion] Efficacy and safety of ADA 80 mg / 2W for the elderly patients, there was no significant difference in the continuation rate or efficacy compared to the non-elderly, and no serious adverse events were observed. Due to an aging population, ADA 80 mg / 2W can be a useful treatment option for elderly RA patients.

P8-14

Relationship between body mass index and disease activity with certolizumab pegol in the Tsurumai Biologics Communication Registry

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Conflict of interest: None

[Objective] To investigate the influence of differences in body mass index (BMI) on the effectiveness of certolizumab pegol (CZP). [Methods] BMI and Disease Activity Score-28 for Rheumatoid Arthritis (RA) with erythrocyte sedimentation rate (DAS28-ESR) was measured in 132 patients receiving CZP and again at 52 weeks of treatment to compare and examine the changes in DAS28-ESR. The patients were classified into groups A-C according to their BMI (kg/m^2) as follows: group A: BMI <18.5 (7 cases), group B: 18.5≦ BMI <25 (45 cases), and group C: BMI ≧25 (12 cases). [Results] The average age, disease duration, rate of anti-citrullinated protein antibody positivity, and rate of rheumatoid factor positivity were 65.3, 61.3, and 60.5 years old; 62, 129, and 106 months; 100%, 89%, and 92%; and 86%, 93%, and 67% for groups A-C, respectively. Patients with a measurable DAS28-ESR (6.36, 5.11, and 4.39 for groups A-C, respectively) and a higher BMI tended to have lower disease activity. The change in overall DAS28-ESR at 52 weeks was significantly improved from 5.11 to 3.36, decreasing from 6.36 to 4.68 in group A, 5.11 to 3.23 in group B, and 4.18 to 2.60 in group C ($P < 0.001$). [Conclusion] CZP might be able to control the disease activity of patients with RA without being affected by BMI.

P8-15

Efficacy and safety of JAK inhibitors in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of JAK inhibitors in elderly patients with rheumatoid arthritis (RA). [Methods] Retrospective study in a total of 35 elderly patients (≧ 65 years) with RA who were started JAK inhibitors, from July 2013 to March 2020. The efficacy and safety of JAK inhibitors were assessed, compared with 173 patients who were started biologic agents. [Results] Overall, 20 patients was treated with tofacitinib; 15 with baricitinib; 74 with abatacept; 33 with golimumab; 24 with etanercept; 22 with tocilizumab; 15 with certolizumab; 3 with adalimumab and 2 with sarilumab. One-year adherence rates were 74% with JAK inhibitors and 67% with biologic agents. Methotrexate was used in 21% of JAK inhibitors group and 30% of biologic agents group. Prednisolone was used in 51% of JAK inhibitors group and 54% of biologic agents group. The rate of the infection requiring antibiotics was 28.5/100 person-year with JAK inhibitors, and 19.2/100 with biologic agents. The rate of serious infection requiring hospitalization was 8.7/100 person-year with JAK inhibitors, and person-year 6.2/100 person-year with biologic agents. [Conclusions] This study suggests that the efficacy of JAK inhibitors is equivalent to biologic agents in elderly patients with RA

P8-16

The clinical efficacy of Sarilumab at clinical practice - The clinical efficacy and predictive factors of Sarilumab in 12 weeks at our center -

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Conflict of interest: None

[Objective] Sarilumab is the second anti-IL-6 receptor monoclonal antibody approved in February 2018 in Japan. We examined clinical efficacy and its predictors of sarilumab at 12 weeks at our center. [Methods] From February 2018 to April 2020, 52 RA patients treated with sarilumab are included. We set a persistency at 12 weeks as an endpoint, and we analyzed its predictive factors. [Results] Of the 52 patients, 29 patients (55.8%) could continue the treatment of sarilumab at 12 weeks. Comparing at the start of sarilumab between the continuation group and the discontinuation group, the duration of illness was significantly longer and the ACPA was significantly higher in the continuation group. On the other hand, the RF value was significantly higher in the continuation group. There was no difference in the number of history of biologics uses between the continuation group and the discontinuation group. There was no difference in the continuation rate regardless of the past tocilizumab use. [Conclusions] There was no difference in the persistency depending on the number of past biologics, and tocilizumab usage, suggesting that switching to sarilumab is one option at the time of inadequately efficacy or loss of response.

P8-17

JAK inhibitors showed good drug retention rates in RA patients with anemia - the ANSWER cohort study-

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Conflict of interest: Yes

[Objective] JAKi sometimes induce anemia because of erythropoietin signal inhibition. We aim to investigate the drug retention rate and hemoglobuin (Hb) levels after JAKi initiation in RA patients with anemia in a real-world setting. [Methods] RA patients treated with JAKi or BIO were extracted from KANSAI consortium ANSWER cohort database. Patients were stratified to 3 categories according to Hb levels (Hb^{low}, Hb^{int}, Hb^{high}). The 3-year drug retention rate due to inefficacy adjusted with possible confounding factors were analyzed with Cox proportional hazard model in each group. [Results] The retention rates of JAKi were comparable to TNFi in Hb^{int} and Hb^{high} groups (Hb^{int}: JAKi 73.0, TNFi 73.4, IL-6Ri 82.1, CTLA4-Ig 70.5, Hb^{high}: 70.5, 64.4, 82.3, 75.2) (%). In Hb^{low} group, the drug retention rate of JAKi was comparable to IL-6Ri and higher than TNFi (80.6, 62.3, 79.9, 73.7) (%) (Cox $p<0.001$). In Hb^{int} and Hb^{high} groups, Hb levels were unchanged or decreased 12 months after JAKi initiation (Hb^{int}: ΔHb= 0.1 [-0.5, 0.4], Hb^{high}: ΔHb= -0.4 [-0.8, 0.3]), while in Hb^{low} group, Hb levels increased (Hb^{low}: ΔHb= +1.1 [-0.5, 1.7]). [Conclusions] JAKi showed comparable drug retention rate to IL-6Ri and can improve anemia in RA patients with low baseline Hb levels.

P8-18

Prediction factor of renal prognosis in rheumatoid arthritis patients on biologics

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Conflict of interest: None

Background: It is known that rheumatoid arthritis patients experience renal impairment as a result of their increased disease activity. Nephrotoxicity of drugs, patient age, and comorbidities can also cause renal impairment. Objective: To evaluate predictors of renal prognosis in patients with rheumatoid arthritis who require treatment with biologics. Methods: Eighty patients with rheumatoid arthritis who were diagnosed by our rheumatologists and treated with biologics were enrolled. Joint echocardiography was performed by two or more of our rheumatologists at the time of and six months after the introduction of biologics, and disease activity and joint echocardiographic findings were compared between patients with and without renal dysfunction (eGFR < 60 mL/min/1.73 m2) 48 months after the introduction. Results: The patients with renal dysfunction 48 months after biologics introduction showed higher disease activity than those without at 12 months of DAS28 (ESR) (p=0.0495). Chronic inflammation at 24 months was also observed in the group with renal dysfunction (p=0.0324). Conclusion: Disease activity and persistent chronic inflammation, which remain after the introduction of biologics, may be a factor for poor long-term renal prognosis in rheumatoid arthritis patients.

P8-19

Serum Immunoglobulin A Level is Associated with Discontinuation of Biologic DMARDs

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Conflict of interest: None

[Objectives] Immunoglobulin A (IgA) plays a role in mucosal immunity, which is associated with autoimmune diseases, but it remains unclear whether serum IgA level contributes to phenotype of RA. In this study, we investigated the association between serum IgA and discontinuation of biologic DMARDs. [Methods] The subjects were affected by RA and measured serum IgA level before initiation or switching of biologics in our hospital from December 2015 to May 2019. Withdrawal of biologics within a year were analyzed in high or normal IgA group (>400 mg/dL or 100-400 mg/dL). [Results] Mean IgA levels were 240 mg/dL (186.0-321.0 mg/dL, N=138) and 486 mg/dL (415.8-554.5 mg/dL, N=31) in normal and high IgA groups, respectively. There were no significant differences between groups in the disease activity at baseline including tender or swollen joint counts and serum levels of CRP, ESR, MMP-3, rheumatoid factor (RF), and anti-cyclic citrullinated peptide antibody (aCCP), although high IgA group tended to have higher levels of RF and aCCP. Drug discontinuation rate in a year was higher in high IgA group (70% vs 56.6%). [Conclusions] Our results suggested that higher IgA levels does not affect disease activity in RA but does biologics withdrawal. Further research is needed to confirm these data.

P8-20

Effect of Anti-Ro/SSA antibody for treatment response to methotrexate in rheumatoid arthritis: retrospective multicenter observational study

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Conflict of interest: None

[Objective] We aimed to investigate the impact of anti-SS-A antibodies (Ab) on the response to treatment in methotrexate (MTX)-naive rheumatoid arthritis (RA) patients. [Methods] We retrospectively assessed desease activity at the MTX start and the 6th month in RA patients over 20 years of age newly starting MTX. [Results] 31 patients in the anti-SS-A positive group and 181 patients in the negative group were included. In the anti-SS-A Ab-positive group, there were more female (positive group 90.3%, negative group 68.5%, p=0.016), RF-positive (positive group 74.2%, negative group 53.6%, p=0.048), anti-CCP Ab-positive (positive group 83.9%, negative group 56.7%, p=0.005). There was no significant difference in the rate of achieving DAS-28 low disease activity (LDA) at the start (25.8% in positive group and 29.4% in the negative, p=0.831). The rate of achieving LDA at 6 months was significantly lower in the anti-SS-A positive group (54.8% in the positive group and 75.8% in the negative, p=0.027). In a propensity score matching analysis, the odds ratio for achieving LDA was 0.36 for anti-SS-A Ab positivity. [Conclusions] Anti-SS-A Ab-positive RA patients may have a lower rate of LDA attainment, even with MTX treatment.

P8-21

Examination of factors affecting lung-related death in patients with rheumatoid arthritis with interstitial pneumonia-Analysis by Kansai multi-institution ANSWER cohort-

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Conflict of interest: None

Objective: We investigated the background factors for lung-related death in interstitial lung disease with rheumatoid arthritis (RA-ILD). Methods: 329 RA-ILD patients who were treated at 7 Kansai facilities from January 2011 to April 2019 were included. For 17 patients in the lung-related death group and 312 patients in the other (control), at the time of ILD diagnosis, 6 months after, final point (lung-related death group; 3 months before death, control; at the time of final visit) The patient background and treatment were compared. Results: In the lung-related death group, 10 males and 7 females, average age 77 (83.5-72) years, average disease duration of 1319 (3804-503) days. In the control group, 106 males and 206 females had an average age of 70 (75.8-64) years and an average disease duration of 2390 (665-5794) days. The lung-related death group is described below in comparison with the control. At the time of diagnosis, significantly older, the KL-6 was high, and the MTX rate was low (P = 0.0001, 0.008, 0.033). Six months after, the rate of MTX was significantly low (P = 0.007) At the final point, CRP was significantly high (P = 0.003). Conclusion: It was suggested that elderly, high KL-6 at the time of diagnosis may be a risk factor for lung-related death.

P9-1

Relationship between anti-CCP antibody titer and pulmonary function tests in patients with RA

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Conflict of interest: None

[Objectives] In JCR 2018, we reported that in patients with RA within 1 year of onset, anti-CCP antibody titer (a-CCP-t) was higher in patients

with respiratory lesions. Here we studied the relationship between a-CCP-t and pulmonary function test results in patients with RA. [Methods] Subjects were 163 patients with RA within 1 year of onset who underwent pulmonary function tests and a-CCP-t assay consisting of 51 males and 112 females. Of the 163 patients, 92 were never-smokers. Data of DLco were not used in this study. [Results] Pulmonary functions measured were %VC, FEV1/FVC% (real value), %FEV1, %FEV1/FVC, %V50 and %V25. Our patients with RA showed low mean values of %V50 and %V25, i.e., 57% and 39%, respectively. There were no pulmonary function parameters that showed significant inverse correlation with a-CCP-t, but %FEV1, %FEV1/FVC and %V25 tended to show inverse correlations with a-CCP-t ($0.05<p<0.1$). When a-CCP-t were divided into 2, i.e., more and less than 45, and logistic regression analysis was done, %FEV1 and %V25 were listed up as discriminating factors to some extent ($p<0.1$). [Conclusion] At the onset of RA, a-CCP-t related to obstructive pulmonary function abnormality, particularly small airway obstruction, to some extent.

P9-2

Relation of RF titer to respiratory lesions in patients with RA within 2 months of onset

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Conflict of interest: None

[Objective] In JCR 2018, we reported that in patients with RA within 1 year of onset, RF titer (RF-t) was higher in patients with respiratory lesions (Resp-L). In this study, we selected RA patients within 2 months of onset to make the relation more clearly. [Methods] Patients were 247 RA patients with the mean age of 58±14 years. Around the first visit, blood sampling and chest CT scan were done. Resp-L was divided into 2, i.e., ILD and airway lesion (AW-L), moreover AW-L was divided into 2, bronchiectasis (BE) and bronchiolitis (Br). Relation of RF-t to each Resp-L was studied. [Results] RF-t was significantly higher in patients with Resp-L than those without it (median 65 vs 31). When patients were divided into 4 groups, i.e., patients with ILD and AW-L (group 1), with AW-L alone (group 2), with ILD alone (group 3), and no Resp-L (group 4), the median of RF-t of each group was 206, 62, 19, and 30, respectively. Significant differences were noted between group 1/3, 1/4, 2/3 and 2/4, respectively. No differences were found between group 3/4, and groups with BE alone and Br alone (72 vs 51), respectively. There was no difference between ever- and never-smokers (48 vs 38). [Conclusion] At RA onset, RF-t was higher in patients with Resp-L, particularly with AW-L.

P9-3

Association of IgA-ACPA with interstitial lung disease in rheumatoid arthritis

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) is characterized by interstitial inflammation and fibrosis of the lung. ILD is often complicated with rheumatoid arthritis (RA) as one of extra-articular manifestations. It was reported that idiopathic pulmonary fibrosis was associated with the production of IgA-anti-citrullinated peptide antibody (ACPA). However, a few studies were reported on IgA-ACPA in RA complicated with ILD. In the present study, we investigated the association of IgA-ACPA with RA complicated with ILD. [Methods] Sera from RA patients with ILD or without chronic lung diseases were collected. Serum IgA-ACPA was measured by enzyme-linked immunosorbent assay. [Results] Although IgG-ACPA was not associated with RA complicated with ILD (P=0.823), IgA-ACPA was (P=0.0486). Rheumatoid factor was also associated with RA complicated with ILD (P=0.0266). [Conclusions] IgA-ACPA was associated with RA complicated with ILD, suggesting the possibility of the involvement of IgA in the pathogenesis of ILD in RA.

P9-4

Incidence of pulmonary abnormalities in RA and their risk factors

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Conflict of interest: None

Purpose: To clarify the incidence of pulmonary abnormalities and risk factors for the development of lung lesions in RA patients. METHODS: A cohort study. Subjects were consecutive RA patients who had visited our department in April 2010. We reviewed medical records and examined the cumulative incidence and the risk factors of developing lung lesions using the Kaplan-Meier method. Results: Subjects were 499 patients (134 males / 365 females) with an average age of 59.8 years. Biologics, MTX and glucocorticoid (GC) were administered to 183 (37%), 293 (58%), and 285 (57%), respectively. At the entry, 170 patients had pulmonary abnormalities. During 10 years observation period, pulmonary abnormalities were developed in 61 out of 329 patients without the abnormalities at the entry. The cumulative incidence of pulmonary abnormalities over 10 years was 31%. Older age was a risk factor for the development of pulmonary abnormalities, while biologics and MTX were protective factors. PSL had little effect on the development of the abnormalities. CONCLUSIONS: The incidence of pulmonary abnormalities over 10 years was approximately 30% in RA. Older age was a risk factor, but MTX and biologics were protective ones for the development of pulmonary abnormalities.

P9-5

Clinical features of the acute exacerbation of rheumatoid arthritis-associated interstitial lung disease = Comparison with the acute exacerbation of idiopathic pulmonary fibrosis =

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Conflict of interest: None

[Objective] To clarify the clinical characteristics of acute exacerbation (AE) of rheumatoid arthritis-associated interstitial lung disease (RA-ILD) comparing with those of AE of idiopathic pulmonary fibrosis (IPF). [Methods] We retrospectively evaluated clinical records of the cases diagnosed as RA-ILD-AE or IPF-AE at Tokushima University Hospital from January, 2007 to December, 2019. [Results] There were 16 cases of RA-ILD (74±7 years old, 10 males) and 36 of IPF-ILD (73±8 years old, 30 males). 7 cases (43.8%) in RA-ILD-AE and 11 (30.6%) in IPF-ILD-AE died of AE. Majority of RA-ILD-AE cases had a history of glucocorticoid steroid treatment (RA-ILD vs IPF; 75% vs 8.3%, $p<0.001$), and experienced the preceding respiratory infection (56.3% vs 22.2%, $p = 0.025$). When the blood test findings of surviving cases were compared with those of fatal cases at the time of diagnosis, the serum LDH level was higher in the fatal cases (surviving cases vs. fatal cases; 270±50 U/ml vs 392±97 U/ml, $p<0.05$). [Conclusions] Because the majority of RA-ILD-AE cases had the history of glucocorticoid steroid treatment and experienced preceding infection, management of infection was thought to be important to control AE. In addition, serum LDH levels may be useful as prognostic indicator.

P9-6

A case of rheumatoid arthritis who developed aseptic splenic abscess, pyoderma gangrenosum and organizing pneumonia

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Conflict of interest: None

Case: A 74 years old woman, who had 3 years history of rheumatoid arthritis (RA), was treated with 3.0 mg daily of tacrolimus. One year before the presentation, prednisolone (PSL) was initiated for organizing pneumonia (OP) and pyoderma gangrenosum (PG) of the right big toe. After remission was achieved, PSL was tapered. She was hospitalized for fever, dyspnea, and flare of PG. Chest and abdominal computed tomography showed flare of OP and splenic abscess. Two sets of blood cultures were negative and antibiotics were not effective. Splenectomy was performed. Pathological analysis showed infiltration of neutrophils in spleen. Pulses of intravenous methylprednisolone (mPSL) were administrated and tapered. Colchicine 1.0 mg daily was added. PG and OP have not appeared under the treatment of 6 mg daily of oral mPSL, 1.0 mg daily of tacrolimus and 1.0 mg daily of colchicine. Although some cases of OP and PG were reported in patients with RA, aseptic splenic abscess is a rare complication. Early intervention of colchicine will be effective in RA patients complicated with PG and OP.

P9-7

Efficacy and safety of abatacept for interstitial lung disease associated with rheumatoid arthritis

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) occur in approximately 10-20% of patients with rheumatoid arthritis (RA). Acute exacerbations and poor prognosis due to chronic progressive respiratory failure are major clinical problems. We evaluated the efficacy and safety of abatacept (ABT) in 27 patients with RA complicated by ILD who were treated with ABT. [Methods] 27 patients with RA who had been prescribed ABT at our hospitals and who had been on ABT for at least 24 weeks and who had ILD noted on HRCT before using ABT were selected on a medical record until the end of September 2020. [Results] The mean age was 70.2±11.4 years, the mean duration of RA was 94.8±70.5 months, the mean duration of ABT was 23.5±16.8 months, the mean DAS28-ESR was 5.2±1.5, corticosteroid (PSL) use was 20 cases (74%) and the mean PSL dose was 7.6± 5.0 mg/day. With regard to the course of ILD during ABT use, 6 improved, 18 remained unchanged, and 3 worsened. Discontinuation cases were 11, adverse effects were observed in 6 cases. [Conclusions] The course of RA with ILD in our department was improved in 6 cases, unchanged in 18 cases, and worsened in 3 cases. We report the efficacy of ABT for the treatment of RA complicated by ILD in our department, including a review of the literature.

P9-8

Clinical study of 2 cases of rheumatoid arthritis (RA) with recurrent organizing pneumoniae (OP) treated with T cell inhibitors (TCI)

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Conflict of interest: None

[Clinical meaning] OP is unknown causes and therapy for RAOP is not standardized. I reported the clinical trial of 2 cases of RA with recurrent OP treated with TCI. [Case 1] 57 year-old female diagnosed RA 19 years ago and treated with MTX, became OP. After Steroid treatment, she was introduced to our clinic to treat RAOP. [physical exam] no rales were heard. [blood test] RF220 U/ml ACPA 49.7 U/ml [clinical course] Treated with Salazosulfapyridine, She had recurrent OP 3 times. After we started Abatacept 500 mg/month, she never had pneumoniae. [case 2] 57 year-old female diagnosed RA 2 years ago and she transferred to our clinic to treat RAOP. [physical exam] no rale was heard. [blood test] RF370 U/ml ACPA 341 U/ml [clinical course] Treated with Salazosulfapyridine and MTX, She had recurrent OP. After we started Tacrorimus 3 mg/day, She is under our observation. [Discussion] 2 cases of recurrent of RAOP with TCI treatment. Treatment of RA with pulmonary diseases has been non-TNF inhibitors or TCI. Cause of OP is lymphocytic inflammation, It might be a good idea to treat RAOP with TCI.

P10-1

A case of rheumatoid arthritis with ileocecal ulcers mimicking intestinal Behçet's disease

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Conflict of interest: None

A 79-years-old woman was diagnosed as rheumatoid arthritis (RA) in x-13 and treateding by iguratimod (50 mg/day) and bucillamine (200 mg/day). In March x-18 she visited a hospital because of abdominal pain, diarrhea and bloody stool. Colonoscopy (CF) revealed she had ileocecal ulcers and she was consulted to our hospital for further examination. Intestinal Behçet's disease (BD) was suspected because she had multiple ulcers in ileocecum and HLA-B51 was positive without any other typical symptoms of BD. However, the biopsy specimen showed necrotic inflammatory granulation in blood vessel suggesting vasculitis. Her disease activity of RA at the appearance of ileocecal ulcer was high (DAS-28-CRP 9.76: TJC19m SJC14, CRP 2.46) and marked high RF and low C3 levels although MPO-ANCA and immune complex were negative. She was diagnosed as ileocecal ulcer due to RA vasculitis and 10 mg/day of prednisolone was initiated as additional treatment. Arthritis and gastrointestinal manifestations including bloody stool were improved since then. This case was difficult to distinguish RA with vasculitis from BD because of ileocecal ulcers and HLA-B51 positivity.

P10-2

Factors related to RF titer in patients with RA within 2 months after onset

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Conflict of interest: None

[Objective] In JCR 2018, we reported that in patients with RA within 1 year of onset, RF titer (RF-t) was higher in patients with respiratory lesions (Resp-L). In this study, we tried to find factors related to RF-t in patients with RA within 2 months of onset to know the relation more clearly. [Methods] Patients were 247 RA patients with the mean age of 58±14 years. Around the first visit, blood sampling and chest CT scan were done. Resp-L was divided into 2, that is, ILD and airway lesion (AW-L), and was semi-quantified according to papers and a textbook (ILD 0-3, Resp-L 0-4). Other factors, such as age, gender, smoking history, ANA titer, and IgG value were involved and multivariate analysis was done to find factors related to RF-t. [Results] By univariate analysis, presence of AW-L and ILD, ANA titer, and IgG value were significantly related to RF-t. RF-t was divided into two, that is, more or less than 45, and logistic analysis was done. Significant factors related to RF-t of more than 45 were AW-L and ANA titer. Almost the same result was obtained by multi-regression analysis. [Conclusion] At the onset of RA, RF-t was higher in patients with AW-L and high ANA titer. This phenomenon may be related to high activity of acquired immunity.

P10-3

Aortic regurgitation associated with rheumatoid arthritis with a rheumatoid nodule in the aortic valve: a case-based review

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Conflict of interest: None

A 52-year-old woman. She was diagnosed with seropositive rheumatoid arthritis (RA) (Stage I, Class 3). One week later, she had dyspnea. Chest radiographs showed pulmonary edema and pleural effusion, and transthoracic ultrasonography showed aortic regurgitation (AR) and aortic valve mass shadows. She was diagnosed with heart failure associated with AR and started diuretics. Regarding the aortic valve mass shadow, the possibility of vegetation could not be ruled out, and an antibacterial drug was also used. Transesophageal echocardiography showed deviation of the left coronary apex, but no vegetation. The blood culture was also negative, and the infection was considered negative, so a diagnosis of non-infectious AR was made. After improvement of heart failure, aortic valve replacement was performed. Pathological findings revealed a rheumatoid nodule (RN) on the left coronary apex, and the diagnosis was AR associated with RA. This case was diagnosed as AR at the same time as the diagnosis of RA, and RN was found in the aortic valve. Echocardiography shows that the thickening of the valve looks like vegetation and needs to be differentiated from infected endocarditis. We report this case as a case with a lot of suggestions regarding AR associated with RA.

P10-4

Insufficiency fracture of the distal lower limb as a misdiagnosis of flare of rheumatoid arthritis; two case report

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Conflict of interest: None

[Objective/Methods] The incidence of Insufficiency fracture at distal tibia is not low. However, the absence of a history of trauma, the physical findings suggesting an inflammatory process, and the presence of arthritis make it difficult to consider fracture as the primary diagnosis in patients with rheumatoid arthritis (RA). We experienced two RA cases with late-diagnosed insufficiency fracture with a ankle. [Results] Two patients with establish rheumatoid arthritis (RA) who sustained ankle insufficiency fractures which were not detected on X-ray. Both patients were on biologic treatment, methotrexate and predonisone for RA, and diagnosed two months after onset. They required surgery for this fracture. [Conclusions] Juxta-article insufficiency fractures might be easily misdiagnosed in patients with RA, because X-ray imaging is often normal. When patients have juxta-articular pain during RA treatment, we should to consider the possibility of insufficiency fracture and carefully take the physical examination around the joint.

P10-5

Successful MTX Treatment of Multilocular Popliteal Cysts with Synovitis in PMR and EORA

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Conflict of interest: None

[Background] Popliteal cysts, known as Baker's cysts, are commonly found in OA, RA and meniscus injury. Operative treatment is often required to improve them. We report a case in which multilocular popliteal cysts with synovitis developed during the treatment of PMR and they were cured due to MTX administration. [Case] 70-year-old male. PMR occurred at the age of 61 and PSL was continuously treated thereafter. Left knee pain and lower leg swelling were recently appeared. At the first visit of our hospital, PMR symptoms were in remission, but CRP and MMP-3 were abnormally high and an elastic hard mass with a slight fever was palpable on the left posterior thigh. MRI revealed a multilocular giant popliteal cysts with synovitis and intra-articular synovitis. Therefore, we diagnosed him as EORA and started to treat him with MTX in addition to PSL dose increase. His symptoms disappeared and CRP decreased to normal level in 6 months. Finally, MRI showed that synovitis and popliteal cysts had disappeared. [Clinical Significance] There are some reports of popliteal synovial cysts associated with RA, but all of them were treated surgically. Our report firstly suggests that they can be treated and cured with DMARDs alone.

P10-6

A case of Rheumatoid Arthritis Preceded by Scleritis

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Conflict of interest: None

(objective) we report a case of rheumatoid arthritis (ra) preceded by scleritis. (case) a 42-year-old man was diagnosed left scleritis eight months before our hospital consultation. treatment with eye drops (rinderon) was ineffective. he was added prednisolone (psl) 20 mg/day internal use and scleritis was improved. both wrist, both fingers stiffness apperared one month before our hospital consultation. he was introduced our hospital. (intial findings) not joint swelling and tenderness on palpation. (x-ray) both fingers and wrist: normal, joint echo: synovitis of grade2 in power doppler to left wrist. (labo deta): rf108 iu/ml, anti-ccp antibody 5.3 u/ml, antinuclear antibody: negative, c-anca: negative, p-anca: negative. crp 1.64 mg/dl, esr 30 mm. ra was diagnosed in classification criteria of 2010 acr/eular. we started therapy of mtx 8 mg/week and igu 25 mg/day. mtx increased 12 mg/week, and igu increased 50 mg/day. scleritis was improved after the start of therapy in eight weeks. there was not decrease of the eyesight. (discussion) because joint symptom was poor in this case, a diagnosis of ra was late. it is reported that immunologic disease is complicated with 25-50% as for scleritis. it is necessary to diagnose the systemic disease in the refractory scleritis.

P10-7

A case of rheumatoid arthritis that led to a diagnosis of protein-losing gastroenteropathy 5 months after improvement of chronic diarrhea by collagenous colitis

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Conflict of interest: None

[case] 79-year-old woman developed rheumatoid arthritis 38 years ago and was receiving 50 mg of etanercept (ETN) weekly. She has had diarrhea for 5 years. Diarrhea worsened from 3 months ago and she lost 6 kg in half a year. Low serum Alb (2.1 g/dl) was also observed, and she was hospitalized for detailed examination. Fecal CD toxin / antigen negative. Stool culture negative. Mucosal biopsy of colon revealed a collagen band of 10 um or more just below the mucosal epithelium without amyloid deposition. The patient was diagnosed with collagenous colitis, the suspected drugs were discontinued and aspirin was changed to clopidogrel. Prednisolone (PSL) 10 mg was started on the 21st day of hospitalization, but diarrhea continued. On the 28th day of hospitalization, ETN was changed to tocilizumab. One month after discharge, diarrhea disappeared and the serum Alb recovered to 3.9 g / dl. Four months after discharge, he was readmitted to the hospital due to eating disorders because of severe depression, severe weight loss (27 kg), and hypoalbuminemia. She had no diarrhea. Tc-99m HSA-DTPA scintigraphy revealed protein leakage in the intestinal tract. [Discussion] Drug-induced (clopidogrel) or autoimmune (rheumatoid arthritis) PLGE were considered. Tocilizumab was effective against diarrhea.

P10-8

A case of malignant mesothelioma with the early manifestation of the pleural effusion not to respond to treatment in rheumatoid arthritis

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Osaka Medical College

Conflict of interest: None

A 87 years old man treated of rheumatoid arthritis for twenty years with predonisolone (PSL) 2.5 mg/day, methotrexate, and abatacept had dyspnea on exertion on July in X-1. He had right pleural effusion on CT, and it improved by increasing PSL. However, he had right pleural effusion again on November after tapering PSL. Although PSL was increased, it did not improve. Abatacept stopped considering infection, but no change. Then he was hospitalized on December, and took a thoracentesis for two times. The first pleural effusion was exudative, many monocytes, no malignant cell, and high titer of rheumatoid factor, CYFRA21-1, and hyaluronic acid. We thought rheumatoid pleuritis, so PSL increased from 15 mg to 35 mg. However, this treatment did not work, and then he took a second time. At last, the pleural effusion was included atypical cells suspected of malignant mesothelioma. He had history of asbestos exposure in fact. There was FDG uptake in the right pleura and bilateral pleural calcification on FDG-PET. He took thoracoscopic pleural biopsy on March in X, and was diagnosed with malignant mesothelioma. Rheumatoid arthritis overlapped with malignant mesothelioma is rare, but it is important to rule out malignancy when we see pleural effusion not to respond to treatment.

P11-1

Analysis of the effect of early introduction of adalimmab (ADA) and bio-free condition (BF) in patients with rheumatoid arthritis (RA). Results at 3 years after introduction

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Conflict of interest: Yes

[Objective] To analyze the effect of early introduction of ADA (within 3 M from the introduction of MTX) and BF in RA patients 3 years after introduction of ADA. [Methods] Among 191 patients (M37, F154) who received ADA, 54 (M12, F42) started ADA as an early introduction. Eight patients switched to other bDMARDs due to inefficacy and achieved clinical remission (CR). Six patients developed adverse events and discontinued ADA. We analyzed 28 patients (M6, F22, age 55.3±14.2 years old, disease duration 8.8±9.1 months) who were followed up more than 152 W. [Results] DAS28-CRP decreased from 4.46±1.2 to 1.46±0.53 ($p<0.0001$). 24 patients achieved CR (DAS28-CRP <2.3, 85.7%), and 17 patients (60.7%) achieved BF. Two patients relapsed and re-started ADA, but achieved CR and BF again with the adjustment of csDMARDs. MTX (mg/W) was not significantly increased (7.6±2.4 to 7.9±3.6). The numbers of other than MTX significantly increased from 0.8±0.5 to 1.4±1.2 ($p=0.026$). One patient discontinued bucillamine due to proteinuria. PSL (mg/day) decreased from 3.2±3.6 to 0.3±0.7 ($p<0.0001$). Eight patients with CR did not want BF. [Conclusions] Early introduction of ADA was effective and it might be a good choice in terms of medical cost due to BF.

P11-2

Comparison between two groups of the change and no-change to biosimilar infliximab during the maintenance of originator infliximab therapy with rheumatoid arthritis

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Conflict of interest: None

[Background] Since the cost of bDMARDs is very high and the current concern for medical finance is rising, the usefulness of biosimilar is hoping. [Purpose] We explained to RA patients treated with originator infliximab (OI) whether changing from OI to biosimilar infliximab (BI) or not. RA patients with consent switched to BI and patients without consent continued OI. Whether IFX is given with the same speed in the current IFX-infusion or the IFX-loading was decided depending on patient decision. We retrospectively examined disease activity of RA and adverse events. [Result] OI group was 8 and BI group was 12. Characteristics of both groups (OI; BI) at starting the comparison show as follows: age (years) 69.5;62.0, female (persons) 7;11, prednisolone dose (mg/day) 0;0, methotrexate dose (mg/week) 9.0;8.0, DAS28-CRP 1.63;2.02 (all value shows by median, $p > 0.05$). Disease activity and rheumatoid factor value were not significantly different between both groups. Severe adverse events were not reported. [Discussion] The change of RF and MMP-3 after changing to BI have not been reported. Our data for effectiveness and safety was similar with published articles. It should be considered to prescribe BI in the future.

P11-3

Study on long-term retention rate of golimumab treatment for rheumatoid arthrithis

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Conflict of interest: None

[Objective] To evaluate clinical features and retention rate of golimumab (GLM) in rheumatoid arthritis (RA) in clinical settings. [Methods] We enrolled 56 RA patients who received GLM from 2011 to 2019 with at least 6 months follow-up and analyzed clinical data. [Results] The median age at onset (female: 75.0%) was 67 years, with RF (75.0%) and ACPA (76.8%). MTX and PSL were used in 57.1% and 62.5% patients. The 50 mg-group (n=40) showed higher MTX use and lower pre-biologics rate than 100 mg-group (n=16) (65.0% vs 37.5%, $p=0.078$; 45.0% vs 93.8%, $p=0.0008$). The 1-, 2-, and 5-year retention rate between two groups were 74.5% vs 43.8%, 66.0% vs 37.5%, and 40.5% vs 25.0% ($p=0.027$). The withdrawal reasons were as follows: primary failure (15.0% vs 37.5%), secondary failure (12.5% vs 25.0%), infection (2.5% vs 0%), malignancy (7.5% vs 0%), drug rush (5.0% vs 0%), and interstitial pneumonia (0% vs 6.3%). The 1-, 2-, and 5-year retention rate between 50 mg-continued (n=24) and 100 mg-swiched group (n=16) were 78.9% vs 67.3%, 67.7% vs 50.5%, and 54.1% vs 25.2%; there were no significant differences in clinical background. [Conclusions] MTX concomitant use and biological history could be involved in retention rate of GLM, and further studies about effectiveness of switching to 100 mg are needed.

P11-4

Efficacy of Sarilumab on rheumatoid arthritis with a history of Tocilizumab use

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Conflict of interest: None

[Objective] We report the efficacy of Sarilumab (SRL) on rheumatoid arthritis with a history of using Tocilizumab (TCZ). [Methods] From January 2019 to January 2020, SRL was started at our outpatient department, and among the cases of rheumatoid arthritis whose progress was confirmed for 6 months or more, 8 patients with a history of using TCZ were investigated. We assessed the patient background at the time of SRL introduction, the reason for discontinuing TCZ, and the clinical course after SRL introduction. [Results] All cases were female, and the average age at the time of introduction of SRL was 66.5 years, and the average disease duration was 18.8 years. The reasons for discontinuing TCZ were insufficient effect; 3 cases, secondary ineffectiveness; 2 cases, and injection-site reaction; 3 cases. Previous DMARDs were TCZ in 5 cases and other biologic DMARDs or JAK inhibitors in 3 cases. The average duration of SRL use was 13.8 months, and there were no dropouts at the final follow-up. Disease activity was evaluated by CDAI, with remission; 1 case and low disease activity; 7 cases. No serious adverse events occurred during the follow-up period. [Conclusions] Sarilumab was considered to be effective for rheumatoid arthritis with a history of Tocilizumab use.

P11-5

The efficacy of Sarilumab to RA patients for short-term results

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Conflict of interest: None

[Objective] To evaluate Sarilumab (SAR) to RA patients for short-term results. [Methods] From August 2018, twelve cases treated with SAR were evaluated by recording DAS28 (ESR) and CDAI. The average period of treatment of SAR was 11 months. [Results] DAS28 was 4.3 and decreased to 2.0 at 12 month, CRP was also reduced from 2.5 to 0.3 at 12 month. CDAI was improved from 21.4 to 2.6 at 12 month. [Conclusions] The therapy of SAR was effective for short-term results.

P11-6

Sirukumab induced drug free remission for a patient with rheumatoid arthritis refractory to methotrexate

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Conflict of interest: None

[Case] 71-years Japanese female had been suffering from polyarthralgia since 8 years ago. She was diagnosed as RA based on polyarthritis, RF and anti-CCP antibody. Although she was referred to us for the treatment, her symptoms were improved and she was observed about 8 months. In next March, as she was pointed out PIP arthritis, she was treated with 8 mg/week of MTX, then increased to 16 mg. However, her joint symptoms were continued. She agreed to participate the double-blinded clinical study of sirukumab, anti-IL-6 humanized IgG1κ monoclonal antibody. Her symptoms became to improve after a month. One year later, MTX was decreased to 8 mg/week becuse of liver dysfunction. The clinical study was completed and she participated long-term study. Her dose of sirukumab was 50 mg every 4 weeks. Eight months later, her MTX was discontinued because of no symptom. Two years later of long-term study, the development of sirukumab was discontinued. Since then, she was observed without treatment, but any symptoms had been manifested since 3 years ago. [Significance] Sirukumab was expected to suppress the pathogenesis related with IL-6 such as RA. We wondered if sirukumab could deplete IL-6 producing cells. We believe that sirukumab has clinical significance for the treatment of RA.

P11-7

The Effects of baricitinib on early disease activity and pain in the treatment of Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We evaluated the clinical characteristics of patients with the introduction of baricitinib for the treatment of rheumatoid arthritis (RA) and its early treatment and pain relief effects. [Methods] Of the 32 RA patients treated in our outpatient clinic who were treated with BAR, we examined the efficacy of very early 4 weeks post-treatment and changes in patient Visual Analog Scale (VAS) at 4 and 12 weeks post-treatment, which is the very early stage of pain improvement, in 20 of the 32 patients with RA who were treated in our outpatient clinic and for whom BAR was available for clinical data extraction. [Results] Case background was 8 males and 12 females with a mean age of 68.75 ± 14.0 (42-88) years. The starting dose was 2 mg/day in 15 cases and 4 mg/day in 5 cases, with MTX in 4 cases (mean dose 8 mg/day) and without MTX in 16 cases. After 4 weeks of treatment, the researchers achieved 60% and 40% of low disease activity criteria for DAS28CRP and 40% for remission, and 70% and 30% for SDAI. [Conclusions] Baricitinib inhibits a variety of cytokines. This suggests that it may improve disease activity and pain quickly after treatment.

P12-1

The trends of conventional synthetic DMARDs in Japanese patients with RA by NinJa 2019 cohort

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Conflict of interest: None

[Objective] The purpose of this current study is to review the trends of conventional synthetic DMARDs in Japanese patients with RA. [Methods] In 16087 Japanese RA patients registered with NinJa2019, 9794 RA patients medicated one and more conventional synthetic DMARDs without biological DMARDs and JAK inhibitors were divided various kinds of DMARDs. We researched the number of csDMARDs, single use or combined therapies, and the rate of all patients registered with NinJa2019. [Results] The single use of csDMARD were used 4278 patients medicated MTX, 793 patients with SSZ (4.9%), 523 patients with TAC (3.3%), 278 patients with IGU (1.7%), 270 patients with BUC (1.7%), respectively. The combined therapies of csDMARD were used 847 patients medicated MTX+SSZ (5.3%), 544 patients with MTX+IGU (3.4%), 458 patients with MTX+TAC (2.8%), 285 patients with MTX+BUC (1.8%), 156 patients with SSZ+IGU (1.0%), 126 patients with MTX+SSZ+IGU (0.78%), 119 patients with MTX+SSZ+BUC (0.74%),, respectively. [Conclusion] The 60.9% of all patients registered with NinJa2019 were medicated csDMARDs therapy. The anchor drug, MTX was most currently used in RA. Iguratimod were widely used in combination therapies with other csDMARDs.

P12-2

Preparing a simplified formula for calculating area under curves (AUC) of methotrexate (MTX)

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Conflict of interest: None

[Objective] In JCR 2020, we reported that the efficacy of MTX is not only related to the dose but also to calculated AUC. The method we used was so called traditional trapezoid (rectangle) method, i.e., using speculated blood concentration curve. However, this method is complicated. Then we searched for a simplified formula and compared the results with those by the previous methods. [Methods] Subjects were 231 patients with RA on MTX. The means (range) of age, BW, eGFR, and dose of MTX were 66 years (21-88), 54.8 kg (29-96), 75.2 ml/min (39.8-118.5), and 7.2 mg (2-16), respectively. Based on the report by Suzuki T (Jap J TDM, 1998), the following pharmacokinetic parameters were used; rate of absorption 70%, Vd 0.665 (L/kg), and Kel 0.345 (/hr) when CCr is 100 ml/min. Formula for calculating AUC was quoted from a report by Takii M (Jap J Pediat Nephrol 2006) as follows; AUC = (absorption rate * dose of MTX)/clearance. Clearance = Kel * Vd. [Results] The calculated mean AUC by the formula was 576 (μg/ml * hr) ±252. The correlation coefficient with AUC by the previous method was 0.99. Transforming the formula above, the dose of MTX to obtain AUC of 700 was calculated, resulting in 9.6 mg±3.3. [Conclusion] The formula to calculate MTX AUC will be useful.

P12-3

Survey of non-use of methotrexate in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study is to evaluate the background, medication, and disease activity of elderly patients with RA who do not use MTX. [Methods] The subjects were RA patients enrolled in the AORA Registry 2019, and 652 patients who were 75 years or older at the time of enrollment. Patient background includes gender, age at survey, age at onset 60 years or older (EORA), Steinbrocker stage, HAQ, comorbidities, dementia treatment, eGFR, rheumatoid factor (RF), anti-CCP antibody. Treatment details include the presence and dose of PSL, and the percentage of the other csDMARDs and bDMARDs. MMP-3, DAS28-CRP, CDAI as indicators of disease activity were evaluated. [Results] Elderly RA patients who did not use MTX had more elderly and EORA cases and fewer cases of advanced joint destruction, but the average HAQ was high, and there were more cases of comorbidities, dementia treatment, and renal dysfunction. There was no difference in RF, but there were significantly fewer anti-CCP antibody positive cases. MMP-3 was significantly higher in non-MTX patients than in MTX patients, but no significant difference was observed in either DAS28-CRP or CDAI. [Conclusions] Elderly RA patients who did not use MTX had more EORA and seronegative RA in addition to patients with comorbidities.

P12-4

Efficiency and safety of iguratimod for patients with rheumatoid arthritis after the onset of methotrexate-related lymphoproliferative disorder

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Conflict of interest: None

[Background] To date, no definitive treatment is available for rheumatoid arthritis (RA) in patients with methotrexate-associated lymphoproliferative disorder (MTX-LPD). We investigated the effects of IGU as a therapeutic agent for RA in patients with MTX-LPD. [Method] Among the 71 patients with RA with histologically confirmed MTX-LPD, we enrolled 30 patients with temporary withdrawal secondary to MTX discontinuation. Patients were categorized into the IGU (n=8) and non-IGU (n=22) groups. We performed an intergroup comparison of the clinical background and MTX-LPD recurrence rates and the effect of IGU on RA disease activity were also evaluated in the IGU group. [Result] No statistically significant intergroup difference was observed in patient background. The MTX-LPD recurrence rate was lower in the IGU group (12.5%, one case) than those in the non-IGU group (40.1%, 9 cases); however, the difference was statistically non-significant ($p = 0.308$). The 28-joint Disease Activity Score for Rheumatoid Arthritis with C-reactive protein was significantly reduced 6 months after initiation of IGU treatment ($p = 0.045$). [Discussion] IGU could potentially reduce the MTX-LPD recurrence rate and serve as a useful therapeutic agent to control RA disease activity in patients who develop MTX-LPD.

P12-5

Relationship between intolerance symptoms when taking methotrexate and daily caffeine consumption

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Conflict of interest: None

[Objective] It is suggested that caffeine inhibit the effects of methotrexate (MTX). We aimed to investigate the relationships between MTX intolerance and caffeine intake. [Methods] Questionnaires were conducted for rheumatoid arthritis patients who attended our department. We got the answers about such as intake of caffeine-containing food and drink, patient global assessment (GA) and symptoms of MTX intake day. Patients were divided into 4 groups according to their estimated daily caffeine consumption: low (<120 mg), moderate (120-180 mg), high (>180 mg, <400 mg), and excessive (400 mg and above). [Results] We got responses from 187 patients (low 25 cases, moderate 25 cases, high 76 cases, and excessive 61 cases). The average dose of MTX was 8.2 mg/week (no difference in each group). The average GA score of MTX day was higher in excessive group than high group (14.4 vs. 7.4 mm, $p=0.03$). More patients in excessive group have anticipatory symptoms before MTX day than high group (19.7 vs. 5.3%, $p=0.05$). [Conclusions] There was no difference in the occurrence of MTX intolerance symptoms between high and low caffeine intake within the appropriate dose. The over-caffeinated patients tended to have higher incidence of anticipatory symptoms before taking MTX and higher GA on the day of MTX intake.

P12-6

Experiences of Iguratimod (IGU) therapy in RA patients in a single institute

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Conflict of interest: None

[Objectives] To assess the efficacy of Igratimod (IGU) in Rheumatoid Arthritis (RA). [Patients and Methods] Two hundred eighty-eight RA patients who had been treated with IGU were evaluated. Patients background data were as follows; mean age: 64.1 years old, female rate: 80.9%, mean duration of RA: 10.9 years, %biologics combination: 22.6%, %MTX combination: 71.3%, mean MTX dose: 9.9 mg/week, mean PSL dose: 4.5 mg/day. Clinical efficacy profiles (at 0 week, 12 weeks, 24 weeks, 1 year, 2 years) were assessed for patients enrolled in our institute and DAS28-ESR, SDAI was assessed. [Results] Mean DAS28-ESR (at 0 week, 12 weeks, 24 weeks, 1 year, 2 years) was 3.9/3.1 ($p<0.001$)/2.9 ($p<0.001$) /2.8 ($p<0.001$) /2.8 ($p<0.001$), they were significantly decreased. Remission rate at 24 weeks, 2 years were as follows; DAS28-ESR: 46.9% and 52.8%, SDAI: 34.7% and 43.9%. Remission rate by with or without MTX at 2 years were as follows; DAS28-ESR: 58.9% and 42.6%, SDAI: 51.1% and 31.8%. Remission rate by with or without biologics at 2 years were as follows; DAS28-ESR: 52.3% and 52.9%, SDAI: 41.5% and 44.6%. Remission rate by under or over 75 years old at 2 years were as follows; DAS28-ESR: 57.5% and 37.7%, SDAI: 47.9% and 30.9%. [Conclusion] Both DAS28-ESR and SDAI were significantly improved at 24 weeks and 2 years.

P12-7

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] IGU was approved in June 2012 and recommended by guideline 2014 in the treatment of rheumatoid arthritis (RA). Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant bDMARDs (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 107 patients adding IGU who had inadequate response to Bio from Janually 2014 to October 2018. Previous treatment Bio. was ADA. And baseline mean concomitant MTX was 12.3 mg/week). And baseline characteristics were Mean age 53.8 years, mean duration of illness 5.5 years, corticosteroid use 9.3% (mean 3.1 mg/day). The course of DAS28, SDAI, CDAI and remission rates were analyzed. [Results] Mean DAS28-ESR, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 24 weeks (3.1→2.3, 7.1→2.7, 6.5→2.4), at 52 weeks (2.1, 2.4, 2.0). Remission rates of DAS28-ESR, SDAI, CDAI were 69.2%, 68.2%, 70.1% at 24 weeks, 74.8%, 78.5%, 79.4% at 52 weeks. There were no side-effect that must be stopped after adding IGU. [Conclu-

sions] IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio

P12-8

Comparative study of iguratimod-salazosulfapyridine (IGU and SASP) combination therapy in methotrexate-resistant patients (MTX-IR) in combination with 2nd anti-rheumatic drugs (csDMARDs)-a 3-center clinical trial-A results from the rheumatology multicenter in the university, hospital, and clinic as a retrospective study (ARIES study)

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Conflict of interest: Yes

[Objective] The optimal combination of 2nd csDMARDs for MTX-IR is one of the most important evidence for the treatment of rheumatism, but it remains unclear. [Methods] In the present study, we compared the clinical efficacy and side effects of 2nd csDMARDs IGU and SASP as add-on therapy to 1st csDMARDs MTX-IR. [Results] Patients were retrospectively observed for 12 months in the MTX+IGU group (n=70) and in the MTX+SASP group (n=55), who had been treated with IGU and SASP at the physician's discretion in patients with MTX since 2012 and who were in remission for at least 3 months. The endpoints of DAS28-CRP disease activity, EULAR Response, and adverse effects were compared between the two groups. After 3 months of MTX+IGU and MTX+SASP treatment, ΔDAS28-CRP (-1.2 vs. -0.6), DAS remission rate (47.5% vs. 20.8%), and good response rate at EULAR Response (16.7% vs. 30.6%) were significantly higher than those in the other two groups. After 3 months of treatment, kidney damage (ΔeGFR) was significantly reduced in the MTX-+IGU group (-8.7 vs. -2.5 mL/min/1.73 m2). [Conclusions] IGU is more effective as an additional agent compared to SASP for MTX-IR patients, but renal impairment should be noted.

P12-9

Efficacy of iguratimod add-on therapy for patients with rheumatoid arthritis inadequately responding to tocilizumab alone

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Conflict of interest: None

[Objective] Tocilizumab (TCZ) monotherapy in methotrexate (MTX)-refractory patients has recently received much attention in the treatment of rheumatoid arthritis (RA), but there are also some cases of inadequate response (IR). We investigated the efficacy of iguratimod (IGU) adjunctive therapy for TCZ monotherapy IR. [Methods] The efficacy of 14 patients treated with additional IGU for TCZ monotherapy IR extracted from the registry of Nagoya University Orthopaedic was evaluated at 24 weeks. [Results] Mean age 65.6 years, 11 women, Clinical Disease Activity Index (CDAI) = 14.8, Matrix metalloproteinase (MMP)-3 = 176.8, modified health assessment questionnaire (mHAQ) = 0.62. There was a significant decrease in CDAI = 5.1, MMP-3 = 96.7, and mHAQ = 0.41 ($p<0.001$, <0.01, and <0.05) at 24 weeks after the addition of IGU, respectively. [Conclusions] TCZ inhibits the inflammatory response through the IL-6/JAK/STAT pathway, while IGU inhibits the nuclear translocation of NFκB, which is downstream of TNF-α, and thus inhibits the inflammatory response. The combination of TCZ and IGU inhibited both pathways, demonstrating the efficacy of additional IGU therapy for TCZ-IR cases.

P13-1

two case report of polyarthritis fulfilled the criteria of RA classification

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Conflict of interest: None

[Objective] treatment with immune checkpoint inhibitor give a remakable improvement for various cancer, but various autoimmune disorder was repoted. Here, we reported two cases of polyarthritis fulfilled 2010 RA classification criteria treated with pembrolizumab [Methods] estimation of two cases of polyarthritis fulfilled RA classification criteria treated with pembrolizumab [Results] first case: 70 years old famale treated with pembrolizumab due to reccurence after right upperlobe lung cancer was consulted to Rheumatology department because of polyarthritis. full fill the RA classification criteria, US shows PD positivity, MTX and lowdose prednisolone treatment was insufficient, so added Golimumab acheaved remission, then Golimumab stopped with maintain remission second case: 72 years old famale treated with pembrolizumab due to reccurence after perineum malignant melanoma opetration was consulted to Rheumatology department because of polyarthriris. fulfill the RA classification criteria. US shows PD positivity. MTX treatment effective and reached remission. [Conclusions] both case reached remisson with standard RA treatment. for clarification of feature and treatment policy, similar case accumulation are needed.

P13-2

Two cases of rheumatoid arthritis that developed after the age of 90

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Conflict of interest: None

[Purpose] The number of cases of rheumatoid arthritis (RA) is aging, but the number of elderly-onset RA is also increasing. We treated 2 RA cases that developed after the age of 90. [Case 1] A 90-year-old woman visited the hospital with her family for two weeks with complaints of swelling of the right wrist joint, pain and stiffness of the fingers. Joint echo showed abundant blood flow signals in the right wrist joint. Drug therapy was started at 100 mg / day of bucillamine (BUC). [Case 2] A 90-year-old woman was referred for the first time because of shoulder joint pain from 3 months ago, and then both knee joint pain and finger joint pain. Due to dementia, the patient was followed up by intra-articular injection of glucocorticoid. [Course] The clinical course was relatively satisfactory in both cases, but there were many complications of other diseases such as diabetes and hypertension. During the course of treatment, case 1 suffered from cellulitis of the lower extremities and case 2 suffered from pneumonia. [Clinical significance] Elderly people have a high frequency of cognitive dysfunction, complications and adverse events, but it is necessary to search for an effective treatment method in consideration of consultation with the patient's family.

P13-3

A case of rheumatoid arthritis with a huge geode in which bone repair mechanism was observed by intra-articular injection of glucocorticoid

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Conflict of interest: None

[Purpose] Rheumatoid arthritis (RA) is an inflammatory disease that causes bone erosion and joint dysfunction. Geodes with large osteolytic lesions may be associated with RA cases. We report a case in which a huge geode generated in the distal humerus showed bone formation by intra-articular injection of glucocorticoid (GC) therapy. [Case] An 82-year-old man was diagnosed with RA at the age of 75 and was treated with metho-

trexate (MTX) 6 mg / week. He came to our hospital because of increased pain in the right elbow joint, both fingers, and both wrist joints. Blood test findings were RF 67 IU / ml, anti-CCP antibody 140.5 IU / ml, MMP3 66.7 ng / ml, CRP 0.04 mg / dl, and ESR 13 mm / h. The XP image showed an osteolytic lesion in the medial condyle of the right upper humerus and the articular cartilage surface was preserved, but an osteolytic image was seen from the center of the lateral diameter of the humerus to the bone cortex. We treated him by intra-articular injection of GC (betamethasone 2 mg). Symptoms, joint pain, and range of motion limitation were improved by GC administration at intervals of 3 to 4 weeks. One year later, XP showed overall reticulated bone formation in the osteolytic region, and a clear osteosclerotic image was obtained in the peripheral region.

P13-4

Investigation of differences between rheumatoid arthritis patients in charge of internal medicine and of orthopedics using NinJa2019 database

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Conflict of interest: None

[Objective] We investigated the differences between rheumatoid arthritis patients in charge of internal medicine and of orthopedics using NinJa2019 database. [Methods] We made the investigation by using NinJa study. We examined 15392 cases of differences between rheumatoid arthritis patients in charge of internal medicine, orthopedics and both. [Results] In charge of internal medicine; orthopedics; both. Age: 66.6; 67.7; 69.3, female: 78.3%; 81.9%, 87.7%; disease duration (years): 12.9; 17.5; 23.6 CDAI: 5.70; 6.35; 7.54, HAQ-DI: 0.54, 0.69, 1.22, no NSAID use: 62.6%; 67.5%; 60.5%: no steroid: 65.8%; 73.9%; 48.0%; biologics: 25.3%; 27.2%; 31.6% Steinbrocker Stage: no NSAID use (%) Stage I: 64.9, 76.9, 70.4 /II: 63.8, 70.5, 63.6 /III: 59.1; 68.1; 65.3 /IV: 58.4; 61.9; 57.0 no steroids I:74.3; 87.2; 63.0 /II: 68.4; 80.2; 63.6 /III: 59.9; 73.3; 59.2 /IV: 54.5; 67.3; 39.7 Steinbrocker functional class exhibits a similar tendency. [Conclusions] 1) There are slightly more female patients and longer disease duration in patients of orthopedics, 2) There are more steroid free and NSAIDs free cases in orthopedic patients. 3) Cases in collaboration revields higher disease activity and Health Assessment Questionnaire Disability Index.

P13-5

Treatment options for patients with rheumatoid arthritis who maintain physical function during long periods of illness

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Conflict of interest: None

[Objective] We conducted the following studies to consider about treatment options for RA to maintain the physical function during long-term disease. [Methods] Disease duration of more than 120 months was defined as a long-term disease. 1092 RA patients with a definite duration of illness were extracted. Therapeutic agents used in patients, LL group, with long-term illness with JHAQ score of 0.5 or less were compared with a group of patients with JHAQ score more than 0.5: LH group with long-term illness and SH group without long-term illness. [Results] There were 241 patients (22.1%) in LL group, 174 (15.9%) in the LH, and 183 (16.8%) in the SH. The average age of the LL was 66.7 years, which was younger than that of LH and SH (73.2 years and 73.6 years). The frequency of MTX administration in LL was significantly higher than in the other two groups (66.8% vs 39.6%, 39.3%). Steroid was used in the LL less frequently than in the other two groups (16.2% vs 46.5%, 50.8%). The frequency of biologics use in LL was 27.8%, lower than LH (35.1%) and higher than SH (21.9%). [Conclusions] Patients who maintained physical function for a long time after the onset of RA had a relatively young onset, and it was considered important that they could continue MTX and did not use steroids.

P14-1

In adalimumab treatment, Remission induction and treatment continuation at 312 weeks in 186 patients

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Conflict of interest: Yes

[Objective] Clinical usefulness and treatment continuation following 256 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 years, mean duration of illness 6.8 years. 151 received MTX ≧10 mg/week (≧10 group) and 29 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 48% of patients from 12 weeks, and achieved 66% from 52 weeks, after that this condition continued. Changes in DAS 28 (ESR) remission rates of 4, 12, 24, 52, 80, 104, 152, 208, 256, 312 weeks for the <2 and ≧2 groups were similar to those seen in the N and S groups. Overall HAQ remission rate at 312 weeks was 81%; treatment continuation rate was 43.0%., and those of≧10 group was 44.4%. [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.

P14-2

Clinical outcomes of Golimumab for rheumatoid arthritis in our hospital: From the NOSRAD registry

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Conflict of interest: None

[Objective] To investigate the clinical outcomes of Golimumab for rheumatoid arthritis in our hospital with using the NOSRAD registry [Methods] Sixty-seven cases of rheumatoid arthritis who introduced Golimumab between February 2012 and August 2019 were included in this study. The examination items consist of 1) Changes in DAS28 from the start up to 12 months after the administration, 2) Cumulative survival rate, 3) DAS28 and survival rate in combined with or without MTX, 4) DAS28 and survival rate of each bio-naive and switch cases, 5) Administration spacing cases, 6) Cases of administrating 100 mg per month. [Results] DAS28 had gradually improved up to 12 months. The cumulative survival rate was 59% for 1 year and 45% for 2 years. There was no significant difference in the transition of DAS28 with or without MTX combination, but survival rate was significantly higher in with MTX combination cases. Also, the DAS28 declining rate and survival rate, the naive case was significantly higher. In 5 cases, remission was maintained even after spacing of the administration. Of the 12 patients whose dose was increased to 100 mg, a good response was obtained in 9 patients. [Conclusions] In combination with MTX and for bio-naive cases may be recommended in RA treatment with Golimumab.

P14-3

Therapeutic effects of certolizumab pegol in rheumatoid arthritis by methotrexate dose

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Conflict of interest: None

[Objective] Adalimumab (ADA), a TNF inhibitor used for the treatment of rheumatoid arthritis (RA), has been reported to have therapeutic

efficacy at different methotrexate (MTX) doses. At present, there are few reports comparing the therapeutic efficacy of certolizumab pegol (CZP) at different MTX doses, and we have continued to increase the number of cases and to investigate the therapeutic efficacy of MTX dosage in CZP treatment, following our presentation last year. [Methods] We conducted a retrospective, observational study of RA patients treated with CZP (N=63). We compared the persistence rate, disease activity (DAS28-ESR), and response to treatment (EULAR response) of patients with RA treated with ADA (N=30) in the high MTX dose (H group: MTX≧8 mg/week) and the medium/low MTX dose (L group: 0<MTX<8 mg/week) as a control group. [Results] There was no significant difference in the persistence rate of CZP/ADA treatment between group H and L after one year. Group L treated with CZP after one year showed a significant improvement in DAS28-ESR change and a good + moderate response to treatment. [Conclusions] The results showed that treatment with CZP was more effective at medium and low doses of MTX.

P14-4

Efficacy of etanercept biosimilar in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] To investigate the efficacy of etanercept biosimilar in rheumatoid arthritis patients. [Methods] 4 Rheumatoid arthritis patients who were treated with etanercept biosimilar from November 2019 and could follow more than 24 weeks were recruited. Efficacy in disease activity scores and adverse events were investigated. [Results] All were women. Mean age was 60.25±21.6 years old, and mean disease duration 14.8±5.2 years. Mean DAS28-CRP were, baseline: 1.13±0.02, after 4 weeks: 1.13±0.03, after 12 weeks: 1.19±0.14, after 24 weeks: 1.24±0.22, which continued remission. There were no adverse events [Conclusions] etanercept biosimilar was effective in rheumatoid arthritis treatment.

P14-5

Clinical evaluation of abatacept and golimumab in patients with rheumatoid arthritis in our department

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Conflict of interest: None

[Objectives] To investigate the efficacy and the adherence of abatacept (ABT) and golimumab (GLM) in RA patients. [Patients] 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/w)/ 17 (5.52), PSL; 19 (4.73 mg/day)/13 (1.94). Bio-naïve: 6/11. [Methods] Efficacy of ABT and GLM was evaluated by DAS28-ESR4, CDAI and SDAI for 156 weeks. [Results] 1) Mean DAS28 at the baseline (ABT/GLM): 5.87/5.80, CDAI 25.47/23.42, SDAI 28.64/27.48. The disease activity was significantly decreased in both groups. As time went by, the ratio of LDA + remission increased significantly until 24 weeks and maintained until 312 weeks in both groups. No significant difference in both groups. 2) The adherence at 52 weeks showed more than 80% in both groups and that at 104 weeks 69.2%, at 156 weeks 61.5% in ABT, 56.0%, 40% in GLM. No significant difference in both groups. 3) HAQ-DI was significantly improved after 12 weeks in ABT. 4) Both levels of CRP and MMP-3 were significantly reduced in GLM after 12 weeks, while the only CRP level in ABT after 52 weeks. 5) Drop-out reasons (ABT/GLM) inadequate response 5/7, cancer1/1, pneumonia 1/1, EBV reactivation 1/1, remission1/0 and so on. [Conclusion] The efficacy and the adherence of ABT and GLM were similar.

P14-6

Effect of Certolizumab Pegol (CZP) on Physical Function in Japanese Rheumatoid Arthritis (RA) Patients with Elevated Baseline Joint Damage

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Conflict of interest: Yes

[Objective] We assessed the correlation between mTSS and disease duration in early and established RA, and the effect of CZP on physical function in established RA patients (pts) with baseline (BL) joint damage. [Methods] Correlations in early and established RA pts were analysed using the Spearman's rank correlation coefficient (ρ). Study design and results were previously reported (C-OPERA [NCT01451203], HIKARI [NCT00791921], J-RAPID [NCT00791999]). Week (Wk) 24 HAQ-DI was reported for established RA pts (J-RAPID, HIKARI) based on BL mTSS (≦50/>50). [Results] 514 CZP and 348 placebo (PBO)-treated pts with early or established RA were included. mTSS was strongly correlated with disease duration at BL (ρ [95%CI] CZP/PBO: 0.7 [0.7-0.8]/0.7 [0.7-0.8]). The proportion of pts with mTSS>50 increased with disease duration (CZP/PBO, ≦5 years: 7%/5%; >5-10: 57%/49%; >10: 63%/67%). For established RA, more CZP vs PBO pts achieved HAQ-DI≦0.5 at Wk24 across BL mTSS groups (J-RAPID mTSS≦50: 59 vs 38%, mTSS>50: 65 vs 26%; HIKARI mTSS≦50: 59 vs 17%, mTSS>50: 43 vs 19%). [Conclusions] At BL, joint damage was strongly correlated with disease duration in early and established RA pts. At Wk24, CZP showed improvements in physical function in established RA pts, irrespective of BL joint damage level.

P14-7

Safety and Effectiveness of Certolizumab Pegol (CZP) in Patients with Rheumatoid Arthritis (RA): A Subgroup Analysis of a 24-week Japanese Post-Marketing Surveillance (PMS) Study

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Conflict of interest: Yes

[Objective] We assessed the impact of patient (pt) demographics on CZP safety and effectiveness in a PMS study in RA. [Methods] Pts newly initiated on CZP for RA were enrolled. Logistic regression was used to analyse the association between adverse event (AE)/adverse drug reaction (ADR) incidence/EULAR response (good/moderate) and age/body weight (BW). Missing data were imputed using LOCF. [Results] 3,727 pts were enrolled; safety/efficacy was evaluated in 3,586/1,794 pts. Incidence of AEs was similar across all age groups (40-<65 years: 25.6%, <40: 22.7% [OR 0.9, 95%CI 0.7-1.1], ≧65: 25.0% [1.0, 0.8-1.1]), as were ADRs (40-<65: 15.5%, <40: 14.2% [0.9, 0.7-1.2], ≧65: 14.2% [0.9, 0.7-1.1]). Pts <40 had the lowest risk of serious ADRs (40-<65: 5.4%, <40: 1.6% [0.3, 0.1-0.6], ≧65: 6.2% [1.2, 0.9-1.6]). EULAR good/moderate response was similar across all age groups. Safety was similar across all BW groups, and EULAR good/moderate response in BW groups were as follows: <40 kg: 59.7%, ≧70 kg: 67.5% [OR 1.4, 95%CI 0.8-2.5], 40-<50 kg: 63.3% [1.2, 0.7-2.0], 50-<60 kg: 66.5% [1.3, 0.8-2.3], 60-<70 kg: 68.9% [1.5, 0.9-2.6]. [Conclusions] Increased age did not impact AE and ADR incidence and

used safely in higher age group. Similar efficacy was observed regardless of body weight.

P15-1

Effect of sarilumab and extension of dosing interval in patients with rheumatoid arthritis patients in Fukushima Medical University Hospital

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Conflict of interest: None

Objective: Recently, outcome of rheumatoid arthritis (RA) has been improved by using Biological disease-modifying anti-rheumatic drugs (bDMARDs) and Janus Kinases Inhibitors (JAK). The aim of our study is to clarify the efficacy and safety of sarilumab (SAR) in patients with RA treating in our hospital. Methods: Eight patients of RA who newly treated with SAR in our hospital from February 2018 to December 2019 were included. Effects of treatment, laboratory data, side effects and reasons of therapy cessation were retrospectively reviewed. Results: The percentages of elderly RA patients (75 years or older) were 12.5%. The ratio of man to women is 1 to 3. Four of eight patients had been already treated with three or more bDMARDs, while remaining four patients were Bio-naïve. In those Bio-Switch group, three of four patients had used JAK. After 6 months of SAR, Disease Activity Score 28 decreased from 3.8 to 1.42 (P=0.04). Five cases (62.5%) could continue SAR treatment. Three of five cases could extend dosing interval and no recurrence was observed. There were no severe side effects in all eight cases. Conclusions: SAR seems to be effective in both Bio-naïve RA patients and Bio-switch RA patients. Furthermore, the effect of SAR can sustain even if dosing interval is extended.

P15-2

The efficacy of sarilumab at 1 year in patients with rheumatoid arthritis in our institution

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Conflict of interest: None

[Objective] To assess the efficacy and safety of sarilumab (SAR) in patients with rheumatoid arthritis. [Methods] Twenty-six RA patients were initiated SAR in our institution from June 2018 to June 2020, and 24 of them were continued SAR over three months. DAS28-ESR and CDAI were assessed at the point of 0, 1, 2, 3, 6, 12 months. And we investigated about adverse events within the 1 year. [Results] DAS28-ESR/CDAI after initiation of SAR decreased as follows; DAS28-ESR/CDAI 0 month: 5.45/24.9, 0.5 month: 3.94/17.62, 1 month: 3.28/11.57, 2 months: 2.47/7.76, 3 months: 2.07/6.05, 6 months: 1.89/5.15, 1 year: 1.74/4.85, with significant difference (respectively, $p<0.001$/$p<0.001$) after the first month. Remission rate of DAS28-ESR/CDAI was as follows; 0 month: 4.2%/0%, 3 months: 67%/33%, 6 months: 79%/46%, 1 year: 79%/58% and under low disease activity rate was as follows; 0 month: 4.2%/8%, 3 months: 88%/83%, 6 months: 88%/83%, 1 year: 88%/83%. The incidence of adverse events rate were 92% and 75% of them were some kinds of infectious disease and 2 cases had severe infections needed administration. There were no dead case because of AEs. [Conclusions] These data indicate that continuation of effectiveness can be expected from SAR therapy from the early phase. Infectious diseases should be cautioned as much as other biologics.

P15-3

Effect of sarilumab treatment on noninflammatory pain in Japanese patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] Noninflammatory pain (NIP) is frequently reported in overseas patients with rheumatoid arthritis (RA). This analysis aimed to describe NIP in Japanese patients with RA treated with sarilumab (SAR). [Methods] NIP was defined by the 28-joint assessment using an established formula: tender joint count minus swollen joint count $\geqq 7$. In this post-hoc analysis, we assessed baseline (BL) demographics and disease characteristics of patients with NIP enrolled in the KAKEHASI study (NCT02293902), and the effect of SAR on changes in NIP status and disease activity, stratified by the BL NIP status. [Results] 36/243 (15%) patients had NIP at BL; these patients had higher disease activity than those without BL NIP. At week 16, before rescue treatment was allowed, a lower proportion of patients with BL NIP treated with SAR had ongoing NIP versus PL (19% vs. 49%). Patients with BL NIP who received SAR had better clinical outcomes at week 24 versus PL, as assessed by CDAI, DAS28-CRP, and ACR 20/50/70 scores. [Conclusions] The proportion of patients with NIP in this Japanese study was lower compared with the global studies. Consistent with the global studies, patients with NIP had worse BL clinical assessment scores. NIP was reduced and clinical outcomes were improved with SAR versus PL.

P15-4

Investigation of cases using salilumab at Yokohama-Minami Kyosai Hospital

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Conflict of interest: None

[Objective] Salilumab (SAR) is a human anti-IL-6 receptor antibody drug. In recent years, treatment options for rheumatoid arthritis (RA) have expanded, but it is unclear which preparation should be used for what kind of patient group in clinical practice. The purpose of this study is to investigate the clinical background, efficacy, and retention rate of patients who received SAR in RA patients. [Methods] We investigated medical records of patients diagnosed with RA at our hospital who had introduced SAR. We examined the efficacy and retention rate 3, 6, 9, and 12 months after administration of SAR. [Results] There were 20 cases of SAR introduction (female / male: 19 cases / case, age 64.5 ± 10.4 years). At the start of SAR, RA activity was DAS28-ESR: 5.67 ± 1.1 and CDAI: 19.1 ± 11.6. There were 2 cases with malignant tumor and 2 cases with interstitial pneumonia. The number of patients who continued SAR until 12 months was 10 (62.5%), and the DAS28-ESR and CDAI after 12 months were 1.54 ± 1.0 and 1.39 ± 0.8, respectively. The reasons for discontinuing SAR were rash, primary ineffectiveness, nausea, and injection site reaction. [Conclusions] SAR may be expected to be effective for highly disease-active RA regardless of the history of use of biologics.

P15-5

Changes in blood complement levels in patients with rheumatoid arthritis used tocilizumab

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Conflict of interest: None

[Objective] The use of tocilizumab (TCZ) for rheumatoid arthritis (RA) reduces the concentration of acute phase reactants. However, there are few reports on the changes in complement levels. This study examined the changes in complement levels in patients receiving TCZ at our hospital. [Methods] Nine patients (8 females, 1 male) had been administered TCZ in October 2020 and were followed up for 2.5 years. The mean patient age was 75 years, and the mean RA morbidity was 6.7 years. Regarding the line of biologics, the first was TCZ in 7 cases while the second was in 2 cases. TCZ administration was started at 3 months, 6 months, and 12 months and CRP, RF, MMP-3, C3, and C4 at the final observation; disease activity was evaluated at 12 months. The DAS28-CRP at the time of the

final observation was evaluated and examined. [Results] CRP, C3, and C4 levels improved significantly after administration, and MMP-3 levels improved significantly. RF did not show a significant improvement throughout the period. The DAS28-CRP significantly improved after administration. [Conclusions] TCZ use significantly reduced disease activity, suggesting that the change in complement value due to TCZ use is results from anti-IL-6 action.

P15-6

Analysis of the effect of sarilumab in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] To analyze the efficacy of sarilumab in patients with rheumatoid arthritis (RA). [Methods] 21 RA patients (M 4, F 17) who received salilumab treatment were included. Salilumab was subcutaneously injected once every two weeks at 150 or 200 mg. The therapeutic effect from 1 month to 1 year after administration was evaluated. [Results] Mean age 63.5±10.8 years, disease duration 13.8±7.6 years. bDMARDs were used in 18 patients, with the most changes from tocilizumab (12). In all-case analysis, DAS28 decreased from 3.78±1.37 to 3.11±1.25 (p=0.003) after 1 month and 2.93±1.06 (p=0.007) at 3 months. The activity of 3 patients who received the first bDMARDs continued to improve up to 6 months (From 5.46±0.67 to 3.27±1.25 after 1 month (p=0.05), 3 months 2.6±1.01 (p=0.03), 6 months 2.15±0.63 (p=0.02)). In 18 patients who used 2 or more bDMARDs, the activity significantly improved (DAS28: from 3.51±1.25 to 3.08±1.25 after 1 month (p=0.01), 3 months 2.99±1.05 (p=0.048)). Activity was not improved in 10 patients who used 3 or more bDMARDs (DAS28: From 3.31±0.93 to 3.01±0.94 after 1 month (p=0.12), 3 months 3.12±0.74 (p = 0.29)). [Conclusions] Salilumab improved activity in patients with little history of bDMARDs, but was not effective in patients with 3 or more bDMARDs.

P15-7

Salirumab use in Rheumatoid Arthritiss: Single Center experience

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Conflict of interest: Yes

[Objective] Sarilumab is one of interleukin-6 receptor inhibitor available for treatment of Rheumatoid Arthritis (RA). Here, we report real world experience. [Methods] This is a retrospective chart review of patients who were treated with Sarilmab at St. Luke's International Hospital in Tokyo. [Results] Total 25 patients were identified (men: women=1:24). The median disease duration was 7 years (3-13). Twenty patients (80%) were positive for Rheumatoid Factor and 21 patients (84%) were positive for anti- CCP antibody. Three patients (12%) had Interstitial Lung Disease (ILD). Thirteen patients used methotrexate concomitantly as 23 patietns (92%) used a conventional synthetic DMARD. Thirteen patients used glucocorticoids. Twnety for patients prevously had used biological DMARDs or tarteted synthetic DMARDs. The median duration of observation in this study was 361 days (91-494). There were no serous adverse events recorded. We analyzed drug survival rate and factors associated with drug sruvival rate using Kaplan-Meier survival curve and log rank test. Patients with bone erosions had better continuation rate (P=0.027) [Conclusions] Sarilumab tended to be used in refractory cases in our hospital but seems to have relatively good continuation rate. No serious adverse events were observed.

P15-8

The evaluation of the radiographic advancement of articular destruction in hand of the patients with rheumatoid arthritis receiving the treatment using Tocilizumab for longer than 5 years continuously

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Conflict of interest: None

[Objective] The articular destructions in the patients of rheumatoid arthritis have being considered to be unreversible, therefore it's the most important to begin the treatment before the development of visible radiographic lesion; bone erosion and/or joint space narrowing. In current study, we evaluated the effect of the continuous long-term administration of Tocilizumab (TCZ) on radiographic lesion. [Methods] We evaluated 8 rheumatoid patients receiving the treatment using TCZ for longer than 5 years continuously by DAS 28-CRP and modified Sharp score of the roentgenogram of the hands. Seven females and 5 switched cases from other biologics were included, and the average age at introduction of TCZ was 61.8 years. [Results] In all cases, administrations of TCZ are continued without adverse event or secondary failure to date. The average duration of administration of TCZ were 98 months. The average of DAS 28-CRP was 1.88 at final examination and 5.13 at introduction (P<0.05). The change of modified Sharp score in hand were 54.6 points and 45.5 points, similarly. In 2 cases of 8, any change was not identified. [Conclusions] In several cases, at the introduction of TCZ advanced articular destructions were already identified, considered to result getting worse the modified Sharp score.

P15-9

Two cases of sarilumab treatment for rheumatoid arthritis patients undergoing hemodialysis

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Conflict of interest: None

[Case] Case 1: A 65-year-old woman. She was diagnosed with rheumatoid arthritis (RA) 25 years ago because of her clinical symptoms and laboratory findings. She was treated with prednisolone (PSL) and salazosulfapyridine (SASP). Dialysis was introduced 10 years ago. RA disease activity deteriorated, and she treated with adalimumab but RA disease activity was not improved. She was treated with sarilumab (SAR). DAS28-ESR improved from 5.32 to 3.30 at 48 weeks and no adverse effects such as complications of infectious diseases were observed. Case 2: A 65-year-old male. He was diagnosed with RA because of his clinical symptoms and positive for anti-CCP antibody two years ago. He was treated with PSL and SASP, but his symptoms did not improve. Dialysis was introduced about two months ago. He was treated with SAR. DAS28-ESR was improved from 5.33 at baseline to 1.31 at 48 weeks without adverse effects. [Clinical significance] These cases suggest that SAR treatment for RA patients undergoing hemodialysis are useful and safety.

P16-1

The study of efficacy of biologics to 5 cases of seronegative monoarthritis

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Conflict of interest: None

[Background] There is still no consensus on the efficacy of biologics for chronic seronegative monoarthritis of large joints. We examined the efficacy of biologics in 5 cases treated from 2016 to 2020 in our department. [Method and Patients] We retrospectively investigated 5 patients of 2 males and 3 females, average age 52.2 (29-75) years. They first visited to our department in average 23 (3-48) months from onset. Two cases were

left knee joint, and others were right knee joint and left ankle joint respectively. The laboratory examination showed both RF and anti-CCP antibodies were negative and Larsen classification of affected joints was 1, 0, 3, 0, 1 respectively. [Results] The joint fluid culture test was negative in all 5 cases, and an arthroscopic synovial biopsy was performed in 1 case. Biologics were administrated 105 (14-760) days after the first visit to our hospital and administered average methotrexate dose is 7.6 (0-12) mg/week. Tocilizumab was administered in 3 cases, abatacept and certolizumab pegol in 1 case. Three months after the start, laboratory examination and visual analog scale were improved, and Larsen classification was not deteriorated. [Discussion] Biologics were effective for seronegative and chronic large joint monoarthritis.

P16-2

A case of malignant rheumatoid arthritis after remission of methotrexate-related lymphoproliferative disorder requiring combination therapy of tocilizumab and rituximab

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Conflict of interest: None

Treatment of rheumatoid arthritis after the onset of methotrexate-related lymphoproliferative disorder is limited. We report a case of malignant rheumatoid arthritis after MTX-LPD remission, in which the combined use of tocilizumab and rituximab was effective for the treatment. The case is a man in his 60s. RA developed 9 years ago. Intractable RA developed MTX-LPD from the heart two years ago. Diagnosis of diffuse large B-cell lymphoma by biopsy. This was relieved only by discontinuing MTX. However, after that, he developed malignant rheumatoid arthritis. Therefore, RA was indicated overseas, and rituximab, which is effective for DLBCL, was also indicated for vasculitis in Japan, and the abnormal findings as MRA improved. However, since joint symptoms remained, the disease could be controlled by using tocilizumab in combination. Treatment of RA after the onset of MTX-LPD is often difficult due to limited treatment options. We experienced a case in which the combined use of rituximab and TCZ was effective for the onset of a rare site called MTX-LPD (DLBCL), which is the primary cardiac site, and the worsening MRA condition after MTX-LPD remission. In particular, rituximab is reported because it may be useful for the treatment of RA after MTX-LPD, which has few options.

P16-3

Abatacept and Tacrolimus Effectively Ameliorated Chronically Progressive Interstitial Lung Disease under Methotrexate and TNF inhibitors in Patient with Rheumatoid Arthritis

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Conflict of interest: None

[Patient] 63-year-old Female [Present illness] RA was diagnosed when she was 27, methotrexate and prednisolone (PSL) did not lead to remission. After initiation of Infliximab at 52, she started to suffer from persistent dry cough and was diagnosed with interstitial lung disease (RA-ILD) by chest CT. Although switched to Golimumab monotherapy, due to the appearance of additional progressive dyspnea, she was admitted. [Clinical course] Progressive ILD was observed on CT with elevated KL-6, SP-D and, spirometry test revealed intact %VC with decreased DLco% (82.5%). Abatacept (ABT) with concomitant tacrolimus (TAC) was introduced without PSL dose escalation (1 mg/2d). Her symptoms disappeared in 12 weeks with ILD amelioration. KL-6 and SP-D normalized after 30 weeks and RA was maintained in low disease activity even after tapering-off PSL. [Clinical significance] MTX and TNF inhibitors can be a risk for exacerbation of RA-ILD. On the other hand, ABT is known for its improvement in safety profile and also RA-ILD. A T cell-targeted therapy with ABT and concomitant TAC has been also reported as an effective therapy for RA-ILD which our case also suggested the utility. Moreover, our case suggests that PSL dose escalation might not be necessary in limited cases.

P16-4

The efficacy of Abatacept therapy in rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy in abatacept therapy with rheumatoid arthritis (RA). [Methods] This study comprised 22 patients with rheumatoid arthritis intolerant to biologic DMARDs. Patients received abatacept 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 3.4 to 2.9) and CDAI (from 5.6 to 3.5) decreased significantly from baseline to Week 52. DAS28ESR Remission achieved in 19 cases at Week 52. Abatacept monotherapy was also effective with RA patients of in adequate response to antiTNF inhibitor therapy. The retension rate of abatacept at 52 weeks was 90%. The average dose of methotrexate tapered from 7.7 mg to 6.6 mg. The average dose of glucocorticoid also tapered from 5.0 mg to 4.2 mg. [Conclusions] These results suggested that abatacept therapy is effective in patients with RA of an inadequate response to other biologic DMARDs.

P16-5

A case of lupus nephritis during the treatment with infliximab biosimilar

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Conflict of interest: None

[Presentation of case] A 56-year-old woman was diagnosed with rheumatoid arthritis (RA) two years ago. Her arthralgia was exacerbated despite methotrexate (MTX) treatment, therefore infliximab biosimilar (IFX-BS) was started. Several months later, proteinuria and microhematuria appeared, and skin rash developed mainly on the trunk one year after the initiation of IFX-BS. Renal biopsy showed “full-house-pattern” nephropathy in immunofluorescence, and endocapillary hypercellularity in light microscopy. Subepithelial deposits were seen in electron microscopy. With thrombocytopenia, hypocomplementemia, and antinuclear antibody positive, we diagnosed lupus nephritis (LN) (ISN/RPS class iv+v). Since drug-induced lupus was suspected, we stopped IFX-BS and started prednisolone (PSL) 30 mg/day, hydroxychloroquine (HCQ) 300 mg/day, and abatacept (ABT) 125 mg/week in addition to MTX. Thereafter LN remission was achieved. We gradually decreased PSL to 5 mg/day without any exacerbation both of RA and LN. [Clinical significance] Tumor necrosis factor (TNF) inhibitors sometimes induce lupus-like syndrome. However, most cases show only serological abnormalities and cutaneous symptoms. Nephropathy rarely have been reported but should be considered as a part of TNF inhibitor-induced lupus.

P17-1

Study of Patients who Switched to Biosimilars After Low Disease Activity was Achieved by Preceding Originator Etanercept

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Conflict of interest: None

[Objective] We focused on the outcomes of continuous therapy in patients who chose to switch to Etanercept (ETN)- Biosimilar (BS) after low disease activity was achieved by OriginatorETN. [Methods] We recom-

mended all patients with RA who were receiving ETN to switch to ETN-BS. We specifically explained the study to patients with RA who had maintained DAS-28-ESR of less than 3.2 for 3 months or longer or those whose satisfaction was very high included in this explanation. They were then asked whether they would be willing to switch. [Results] Forty Japanese patients with RA, including the elderly were asked whether they would choose to switch to ETN-BS after the disease activity was decreased and stabilized by Originator ETN. Of these, 27 patients switched to the BS. The effect was maintained in 25 of these patients, whereas the remaining 2 patients dropped out due to adverse reactions (AE). In addition, spacing was possible in 24 of the 25 patients switched to the BS. [Conclusions] Forty Japanese patients with RA, were asked whether they would choose to switch to ETN-BS after the disease activity was decreased and stabilized by ETN. Of these, 27 patients switched to the BS. The effect was maintained in 25 of these patients, whereas the remaining 2 patients dropped out due to AE.

P17-2

Tocilizumab can efficiently prevent bone destruction in patients with recent-onset rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To assess whether tocilizumab (TCZ) can prevent bone destruction in patients with recent-onset rheumatoid arthritis (RA). [Methods] DAS28-ESR and van der Heijde-modified Sharp score (mTSS) were evaluated in 50 patients who received TCZ within 1 year from the onset of RA. TCZ was consecutively administered during the observation period within the first 2 years. In 15 patients, mTSS could be evaluated at 5 years. [Results] The mean DAS28-ESR at baseline, 1, 2, and 5 years was 4.86, 1.29, 1.19, and 1.18, respectively. No patient withdrew owing to ineffectiveness. The change in mTSS (ΔmTSS) between baseline and 2 years was -0.33. The structural remission rates (ΔmTSS/year ≦0.5) were 91.8% and 92.7% during the first and second years, respectively. Only one increase in erosion score was observed in the first year in 2 patients and the erosion score of all patients did not increase in the second year. In 15 patients, the ΔmTSS over 5 years was 0.80, corresponding to 0.16 per year. The structural remission rate at 5 years (ΔmTSS ≦2.5) was 93.3%. The erosion score was 0 in all 15 patients at 5 years, indicating that bone destruction did not become apparent. [Conclusions] TCZ can efficiently prevent bone destruction in patients with recent-onset RA.

P17-3

Successive coupling hospitalization for weight loss with sarilumab treatment in a morbidly obese rheumatoid arthritis patient who did not response to tocilizumab: A case report

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Conflict of interest: None

[BACKGROUND] Compared with another interleukin-6 (IL6) inhibitor tocilizumab, sarilumab showed a similar safety profile with significantly higher affinity and longer half-life. Recently, it was reported that switching tocilizumab nonresponders to sarilumab may have favorable efficacy outcomes. Morbid Obesity can be a factor that affects response to IL-6 inhibitor. [CASE PRESENTATION] A 37-year-old woman who had previously been treated for rheumatoid arthritis by tocilizumab, methotrexate and steroids was referred to our department. Her body weight was 113 kg, body mass index was 40.5 kg/m2 and the anti-cyclic citrullinated peptide antibody was 733. Serum C-reactive protein (CRP) was 4.11 mg/dL, matrix metalloproteinase -3 was 2125.8 ng/mL and DAS28-CRP was 5.99 at first visit. She lost her weight 15 kg during hospitalization (2 months). Two weeks after initiation of sarilumab, the CRP level became negative and steroids were successfully stopped. At one and half year after initiation of sarilumab, the low disease activity are achieved with ongoing sarilumab treatment. MMP-3 decreased to 93.2 ng/mL. [Clinical Significance] This case suggests that hospitalization for weight loss and sarilumab treatment may be an effective treatment option for morbidly obese non-responders to tocilizumab.

P17-4

Characteristics of RA patients who required drug switch of bDMARD or tsDMARD and success rate of switch to each drug in JCHO Osaka Hospital

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Conflict of interest: None

[Objective] The purpose of this study is to analyze difficult to treat RA patients who has received several times of bDMARD or tsDMARD and success rate to each drug. [Methods] We extracted bDMARD or tsDMARD switch cases due to adverse effect or lack of sufficiency among RA patients receiving bDMARD or tsDMARD in our hospital. We set up two groups switch and non-switch, and we investigated female rate, age, medication term, MTX medication rate, and average dose of MTX, ACPA value, RF value and success rate of each drug. Success rate was defined as continuous bDMARD or tsDMARD medication for more than 6 months. [Results] We investigated no switch group 134 cases and switch group 89 cases, and each group characreristics was female 81.6/76.4%, mean age, 65.2/76.4%, mean age 65.2/76.4, ACPA 138/165 U/ml implied significant high disease activity, MTX added on rate 69/58%, mean dose of MTX 8.41/7.33 mg showed significant low in switch group. Successful switch was performed to TNFi 28%, to non-TNFi 54.2%, to JAKi 85.7%. [Conclusions] Switch cases tended to include high disease activity patients, and successful switch was performed to non-TNF and JAKi. We supposed part of switch cases included decrease or suspending MTX usage in long term of treatment for RA.

P17-5

Examination of additional effect of abatacept on patients with rheumatoid arthritis treated insufficiently with csDMARDs other than MTX

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Conflict of interest: None

[Objective] Methotrexate (MTX) is a key drug for the treatment of rheumatoid arthritis (RA), but it is often unusable due to complications and side effects. The 2019 EULAR recommendations state that if MTX is not available, IL-6 inhibitors or tsDMARDs have advantages than TNF inhibitors, but ABT is not mentioned. So, we examined the effect of ABT on cases in which csDMARDs other than MTX were inadequate. [Methods] We extracted the RA patients who were treated with csDMARDs other than MTX but had insufficient effect and administered TCZ or ABT for half a year, from January 2015 to October 2019, and compared effects. [Results] There were no significant differences in age, gender, duration of illness, or disease activity before the introduction of biologics between 8 patients in the TCZ group and 28 patients in the ABT group. The combined rate of tacrolimus (TAC) was significantly higher in the ABT group. When the differences in ΔDAS28ESR, ΔSDAI, ΔCDAI, and ΔmHAQ were examined between the two groups, no significant difference was observed ($P = 0.5360$, $P = 0.5777$, $P = 0.5777$, $P = 0.3504$). [Conclusions] It was suggested that ABT may have the same effect as TCZ for RA for which csDMARDs other than MTX are inadequate, but the combined use of TAC may affect the therapeutic effect.

P18-1

Examination of rheumatoid arthritis patients in which biological DMARDs discontinued due to comorbidities

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Conflict of interest: None

[Objective] The purpose of this study was to examine the reasons for discontinuation and the transition of disease activity after discontinuation of bDMARDs. [Methods] Twenty-four RA patients who did not resume for more than 6 months after bDMARDs discontinuation were included in this study. First, we examined the reasons for discontinuation of bDMARDs. Next, we compared DAS28-CRP, CDAI and SDAI before and 6 months after discontinuation of bDMARDs. [Results] Reasons for discontinuing bDMARDs were solid cancer in 3 cases, osteoarticular infection in 4 cases, cost in 4 cases, LPD in 3 cases, ML in 2 cases, pneumonia in 3 cases, liver dysfunction, rash, widespread burns, rehabilitation transfer, institutional admission in one case. The mean DAS28-CRP after discontinuation bDMARDs was significant higher than before (3.00 vs 2.38, $p<0.05$). The mean CDAI and SDAI after discontinuation bDMARDs were also significant higher than before (10.84 vs 7.28, 12.12 vs 7.59, $p<0.05$, respectively). There were two cases in which disease activity improved dramatically, both of which were treated with rituximab for LPD. [Conclusions] Clinical disease activity worsened due to discontinuation bDMARDs. It is necessary to establish a treatment strategy for difficult-to-treat cases due to complications.

P18-2

The effects of tumor necrosis factor inhibitors (TNFi), anti-IL-6 receptor antibody (tocilizumab; TCZ), janus kinase inhibitors (JAKi) and methotrexate (MTX) on diabetic control and lipid metabolism in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] To determine the comparative effects of anti-rheumatic medications (TNFi, TCZ, JAKi and MTX) on glucose tolerance and lipid profiles. [Methods] We identified RA patients in the treatments with TNFi+MTX (10 cases), TCZ ±MTX (10 cases) JAKi±MTX (5 cases) and MTX alone (10 cases) were selected between May 2013 to November 2018 at our hospital, and RA patients also have complicated with glucose intolerance (HbA1c≧5.6), had been registered. We have compared the changes of HbA1c, body weight, DAS 28-ESR, HDL-C and LDL-C before and after treatments for 6 and 12 months. [Results] Each group showed significant improvement of DAS 28-ESR after treatment for 6 and 12 months. There were no significant differences between each group for DAS 28-ESR. The mean reduction in HbA1c showed a significantly decreases in the TCZ group after treatment for 6 and 12 months, and MTX alone groups for 12 months. There were no significant decrease in the TNFi and JAKi groups. HDL-C and LDL-C in TCZ group was increased. [Conclusions] The TCZ showed a significant improvement in the glucose tolerance compared with TNFi and JAKi. However, deterioration of lipid metabolism in TCZ was observed. Although MTX have the improvement of glucose tolerance, these effects was attenuated in combination with TNF.

P18-3

A 5-year-follow-up study of patients with early rheumatoid arthritis following T2T management

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Conflict of interest: None

[Objective] Patients with RA had been treated by treat-to-target (T2T)-strategy in daily clinical practice. In this study patients with early RA were evaluated in the course of five years. [Methods] Twenty patients (male 5, female 15) who developed RA within two years and were visited to our hospital during the consecutive three months in 2013, were registrated. Average age was 62±19 years old. These patients have been observed for five years. Disease activity was checked with DAS28ESR. [Results] When registration was completed, all patients were high disease activity. Three months after registration, 25% of them were remission. At 6 months, 75% of them were remission. At one year, all patients were treated with MTX (7.9 ± 2.6 mg/w) and 20% of them were treated with bDMARD, 75% of patients were remission and 25% of patients were low disease activity. Five years after registration, 80% of patients were remission and 10% were drug free remission. No patients were treated with steroid and 25% of patients were treated with bDMARD. Three patients had been performed with operation (THA 2, synovectomy of wrist 1) and they were remission. Two patients were dead in the course of five years. [Conclusions] 80% of patients with early RA treated by T2T were remission in the course of five years.

P18-4

Different clinical features of anti-citrullinated peptide antibody-positive and anti-citrullinated peptide antibody-negative elderly-onset rheumatoid arthritis

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Conflict of interest: None

[Objective] To compare the characteristics between patients with ACPA-positive EORA and patients with ACPA-negative EORA. [Methods] We defined EORA as RA that developed in patients older than 75 years. We enrolled 66 patients (22 men, 44 women), and their median age was 83 years. Details of the patients' background, clinical parameters, and laboratory findings were obtained from the medical records. The outcome was evaluated at week 52. [Results] Among 66 patients, ACPA was positive in 35 patients. At diagnosis, CDAI, CRP, and HAQ-DI were significantly higher in the ACPA-negative group than in the ACPA-positive group (19.80 vs 15.00, $p<0.01$, 4.02 vs 1.29 mg/dL, $p<0.01$, and 1.56 vs 0.75, $p<0.01$, respectively). Improvement of CDAI (delta CDAI), CRP (delta CRP), and HAQ-DI (delta HAQ-DI) was significantly greater in the ACPA-negative group than in the ACPA-positive group (16.6 vs 4.00, $p<0.01$, 3.40 vs 0.50, $p<0.01$, and 0.88 vs 0.25, $p<0.01$, respectively). [Conclusions] Our study indicates that ACPA-negative patients develop EORA with high disease activity and high HAQ-DI, which improves dramatically after 52 weeks. Clinicians should be aware of these characteristics of both the groups.

P18-5

Comparison of MTX Combination/Non-combination at the Start of Abatacept Administration in Japanese Biologic-Naïve Rheumatoid Arthritis Patients - from the ORIGAMI Study -

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Conflict of interest: None

[Objective] To investigate the effectiveness and safety of abatacept (ABT) with or without concomitant MTX at the start of ABT treatment in Japanese biologic-naïve rheumatoid arthritis (RA) patients (pts). [Methods] Post-hoc analysis was conducted using the data obtained from the ORIGAMI study (N=279), which is a multicenter, prospective, observational study including SDAI moderate biologic-naïve pts. In the MTX combination [M (+)] and non-combination [M (-)] groups, patient background, effectiveness, retention rate, and safety information up to 52 weeks were analyzed. [Results] The proportion of M (+) was 32.3%. The mean age and the proportion of respiratory and renal comorbidities of M (+)/(-) were 62.0/69.2 years, 13.3/28.0%, and 1.1/9.0%, respectively. SDAI values of both groups decreased over time (week 0/4/24/52), with 19.3/12.6/9.5/8.3 in M (+) and 19.8/13.5/9.5/9.2 in M (-). DAS28-CRP and J-HAQ also decreased in a similar manner. In the multivariate analysis, MTX did not affect the effectiveness and retention of ABT. No apparent difference was found in serious AEs between the two groups. [Conclusions] ABT showed comparable effectiveness for disease activity and physical disability in bi-

ologic-naïve RA pts with SDAI moderate regardless of MTX use or not.

P18-6

Cost and effectiveness analysis of DMARDs therapy (annual report from NinJa 2019) -The cost-effectiveness of DMARDs improved-

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Conflict of interest: None

[Objective] To evaluate the balance between the clinical effects of recent anti-rheumatic treatment and its cost [Methods] The Data from RA patients registered in the large cohort database (NinJa) in 2002-2019 was analyzed. They included clinical indices and dosage of DMARDs. The annual cost-effectiveness calculated from them. [Results] All averages of clinical indices were decreasing constantly. The annual cost of DMARDs was about 496,000 yen / patient in 2019, 10,000 yen lower than the cost in 2018. The rate of the cost of biologics was 67.8% and decreased in 5 years. However, the usage rates of JAK inhibitors increased to about 13%. Their annual costs /patient were higher than other DMARDs in Japan. ([The rate of the number of low activity patients to that of high activity patients] / cost) were decreased in 2017, but increased in 2018 and 2019. [Conclusions] The NHI price revision leaded to the stop of increase of the DMARDs' cost in 2014. And it continued from 2015 to 2019. The usage of biologics decreased, but that of JACK inhibitors increased. Those prices are still high in Japan. So, the revision of those prices may be needed for improvement of cost-effectiveness of DMARDs.

P18-7

The clinical effect of abatacept for rheumatoid arthritis (RA) with high ESR titer

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Conflict of interest: None

[Objective] A substantial number of patients with rheumatoid arthritis (RA) have a high titer of ESR. There is a possibility that factors other than TNF related to the pathogenesis in these patients, and the T-cell function control may be useful. We evaluate the efficacy of abatacept in patients of RA with high ESR titer. [Methods] T he mean ESR (mm/hr)/CRP (mg/dl) in 407 RA patients was 25.0. We divided RA patients to 2 groups, high ESR (ESR>50) and low ESR group (the other cases). 3 patients dropped out from this study because of side effect of Abatacept within 12 weeks. 24 patients with high group and 39 patients with low group were assigned to receive abatacept. DAS28 (4ESR), C-DAI were assessed. [Results] 4 weeks after, DAS28 was significantly lower in high group compared with low group (3.15±0.80 vs 3.80±0.77, P<0.05). There was no significant difference after 12 weeks in both groups. 24 weeks after, C-DAI was significantly lower in high group compared with low group (2.96±2.13 vs 5.23± 3.23, P<0.01). [Conclusions] Our data suggests that abatacept was more effective in high ESR group in response to early effect and remission rate, and useful for treatment of RA patients with high ESR tieter.

P18-8

A case of rheumatoid arthritis with negative acute-phase proteins requiring biological agents to control progress of bone lesions during MTX treatment

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Conflict of interest: None

[Case] A 17-year-old woman had been suffering from arthralgias of her finger joints for 4 weeks and was referred on suspicion of rheumatoid arthritis (RA). The initial examination revealed swelling of 8 small joints. Her laboratory tests showed elevated rheumatoid factor 118 U/mL and anti-cyclic citrullinated peptides antibodies 451.3 U/mL. All of C-reactive protein (CRP: 0.04 mg/dL), erythrocyte sedimentation rate (ESR: 11 mm), matrix metalloproteinase-3 (17.7 ng/mL) were normal. Ultrasonographic examination of her joints revealed synovial thickening and increased blood flow. A diagnosis of RA was established and administration of 10 mg/week of methotrexate (MTX) was started. 10 months later, the dose of MTX was increased to 12 mg/week because of worsening of swelling and tenderness of the joints. After 15 months of that, she developed worsening arthralgias again and hand X-ray showed joint space narrowing. Ultrasound examination also revealed bone erosions. Treatment with certolizumab-pegol was started. CRP and ESR were consistently negative during the course. [Conclusions] There are some RA patients with negative acute-phase proteins however, the severity of symptoms are not always correlated. Ultrasonography will be useful in the diagnosis and management of rheumatoid arthritis.

P19-1

The Clinical Efficacy of Shortening the dose interval of Subcutaneous Tocilizumab (TCZ-SC) in Rheumatoid Arthritis (RA): A Single-Center Retrospective Study

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Conflict of interest: None

[Objective] We investigate efficacy and the drug survival of shortening the dose interval of TCZ-SC for RA in daily clinical practice. [Methods] We conducted a retrospective survey of the medical records of RA patients who started shortening the dose interval of TCZ-SC until Jun 2020. [Results] 18 patients (17 female) were evaluated, 9 patients received TCZ-SC every 10 days (Q10D) and 9 patients received TCZ-SC every week (QW), 6 of 9 patients received TCZ-SC Q10D switched to TCZ-SC QW. Baseline characteristics of the patients mean age 53.6 years, mean disease duration 16.3 years, MTX use 66.7%, mean MTX dosage 7.7 mg/ week, PSL use 44.4%, mean PSL dosage 4.0 mg/day, Bio-naïve 50%, DAS28-ESR 2.72±0.24, mean period until shortening TCZ injection were 2.1 years. At Week 24 and 52, DAS28 were 2.10±0.19 and 1.74±0.13, the remission rate of DAS28 were 69.2% and 100% respectively. At Week 24 and 52, the drug survival rate of TCZ-SC Q10D and TCZ-SC QW were 63.5% and 63.5%, 88.9% and 76.2% respectively. Four patients discontinued TCZ-SC for inadequate response switched to Sarilumab or TNF inhibitor. [Conclusions] The study revealed the clinical efficacy of shortening the dose interval of TCZ-SC for RA in daily clinical practice.

P19-2

Can 100mg of golimumab be reduced to 50 mg 3 months after introducing of golimumab in patients with rheumatoid arthritis?

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Conflict of interest: None

[Objective] The aim of this study was to investigate whether the dose could be reduced to 50 mg 3 months after introducing of golimumab (GLM) in patients with rheumatoid arthritis (RA) who started 100 mg of GLM. [Methods] The clinical background and the changes of disease activity score (DAS28-CRP) were analyzed for 49 patients who were treated with GLM at least 3 months. The patients were divided into two groups; who could successfully reduce from 100 mg to 50 mg at 3 months (R group) and who could not reduce to 50 mg or maintained of 100 mg after 3 months (M group). [Results] There were no significant differences between 2 group in age, sex, the rates of concomitant use of methotrexate and prednisolone, and the DAS28-CRP at baseline. The averaged difference of DAS28-CRP from baseline at 12 weeks had significant difference

between 2 groups (-0.86 in M group and -2.25 in R group). [Conclusions] From the results of this study, the dose of GLM was successfully reduced from 100 mg to 50 mg at 3 months in the cases with good response for GLM.

P19-3

Examining factors affecting eligibility for golimumab dose escalation based on T2T strategy

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Conflict of interest: Yes

[Objective] In Japan, golimumab (GOL) has been approved for use in two doses in RA treatment. We decided to conduct a retrospective analysis to clarify risk factors related to treatment optimization, including the option to escalate the dose of GOL therapy early. [Methods] Patients: We selected from RA patients who started GOL therapy at our hospital from 2012 to 2020. And, we enrolled them who had experienced 1 biologic or naïve (n=25). Statistical analysis: We compared between GOL 50 mg and 100 mg for risk factors of joint destruction, background data, and SDAI and CRP during the period, and treatment responsivity between baseline and week 4. Moreover, we performed a regression analysis on the achievement of LDA at week 12. [Results] At the time of GOL introduction, only ACPA levels was showed a significant difference among the background data. In multivariate regression analysis, only SDAI at baseline showed a statistically significant difference. [Conclusions] We were able to indicate that disease activity at the start of GOL induction affects the achievement of LDA at week 12 by this study. Introducing GOL therapy based on the T2T strategy can be expected to improve treatment efficacy by the escalation dose at week 4 with reference to SDAI at the start.

P19-4

Tocilizumab can reduce the usage of methotrexate in RA patients after remission

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Conflict of interest: None

[Objective] To investigate concomitant drugs in RA patients who maintain remission using TCZ. [Methods] 106 RA patients involved in this study. At the beginning of TCZ, the average age was 59 years old, the average duration of RA; 12 years, and the average CDAI; 16. All patients received among csDMARDs, bDMARDs and PSL, and they were used in MTX; 74%, PSL; 38%, bDMARDs; 43%. 43% were administered more than 2 kinds of csDMARDs including MTX. At the end of this study, we investigated concomitant drugs among them who maintain remission (CDAI≦2.8) using TCZ. [Results] At the end point, the average duration of TCZ was 5.9 years and 47% patients maintained remission. The background among these patient at the beginning of TCZ showed that the average age was 55 years old, the average duration of RA; 9.3 years, the average CDAI; 17, they were used in MTX; 76%, PSL; 32%, bDMARDs; 38%. 38% were administered more than 2 kinds of csDMARDs including MTX. There were no differences between 47% patients and whole patients at the beginning of TCZ. At the end point, MTX was used in only 6%, there were no patients who received PSL and 12% were administered more than 2 kinds of csDMARDs including MTX. 64% were only received TCZ. [Conclusions] TCZ can reduce the usage of MTX in RA patients after remission.

P19-5

Efficacy and safety of shortening the dosing interval of tocilizumab for patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety shortening the dosing interval of tocilizumab (TCZ) for patients with rheumatoid arthritis (RA). [Methods] We examine retrospectively patient background, persistency, efficacy, and safety of 6 RA patients with shortened the dosing intervals of TCZ. [Results] Patient background: 2 cases of intravenous drip infusion every 4 to 3 weeks, 4 cases of subcutaneous injection every 2 weeks to a week, 1 male, 5 females, average age 62.8 years, disease duration 8.0 years, RF positive 100%, RF 834.8±1146 IU/ml, ACPA positive 100%, ACPA 849.6, use of MTX 2 cases, MTX dosage 2.7 mg, use of PSL 3 cases, and PSL dose 0.8 mg, CRP 0.5 mg/dl. DAS28-CRP improved significantly from 3.72 (0 week), to 1.84 (12 weeks), to 1.84 (24 weeks) and to 1.44 (52 weeks). SDAI improved significantly from 20.6 (0 week), to 8.2 (12 weeks), to 5.4 (24 weeks) and to 4.7 (52 weeks). MMP-3 improved significantly from 142.2 (0 week), to 96.0 (12 weeks), to 70.5 (24 weeks) and to 66.3 (52 weeks). At 52 weeks, all patients continued to shorten the dosing interval. The adverse event was laryngeal edema in a case. [Conclusions] Shortening the dosing interval of TCZ for patients with rheumatoid arthritis was effective. No adverse events leading to discontinuation of TCZ were observed.

P19-6

Possibility of Celtorizumab pegol (CZP) dose reduction and prolongation

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Conflict of interest: Yes

[Objective] To evaluate the safety and efficacy of patients receiving reduced and prolonged CZP use in clinical practice. [Methods] A retrospective analysis of 38 Rheumatoid Arthritis patients (9 in the Normal (N) group and 29 in the Reduced/Prolonged (RP) group) who were administered CZP between April 2015 and April 2020 at our institution was performed. [Results] The mean age at CZP initiation was 59.5±14.5, 71.1% female, 64.9% anti-CCP antibody positive, disease duration 7.0±6.7 years, DAS28-CRP 3.36±1.16, 97.4% and 11.0±2.8 mg/w of MTX use, the duration was 124.3±75.2 weeks with 86.8% continuation of CZP as of October 2020. In the N group, except one patient (400 mg q4w), the mean dose and interval was CZP 200 mg q2w, in the RP group that was 200 mg q6.5±2.2w, and the mean transition time to reduction or prolongation was 32.9±22.6 weeks with DAS28-CRP 1.59±0.32 at the transition point. As of October 2020, there was a trend for greater reduction of MTX in the RP group (MTX 8.4±2.6 mg/w, N group MTX 10.2±2.2 mg/w) and also a trend for lower disease activity in the RP group (DAS28-CRP 1.44±0.37) than the N group (2.03±0.64) ($p< 0.05$). [Conclusions] When deep remission is maintained, it can be possible to achieve not only a reduction and prolongation of CZP but also a reduction of MTX.

P19-7

Examination of the extension of the administration interval of Sarilumab

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Conflict of interest: None

[Objective] To investigate the extension of the administration interval in patients using sarilumab. [Methods] Of the 20 patients who started using Sarilumab from March 2018 through August 2020, the dosing interval was extended for the patients with stable disease activity under their consent. It was investigated. The efficacy and safety of Sarilumab were assessed in this trial. [Results] 4 in 20 patients who used Sarilumab successfully extended the dosing interval. The male-female ratio was 3:17, the average age was 73.5 years old, the average duration of the illness was 15.6 years, the distribution for Steinbrocker's Stage classification was; I:1, II:3, III:5, IV:11, and for Dysfunction Class Classification was; I:1, II:14, III:3, IV:2. There were 3 patients of 1st Bio, 6 patients of 2nd, 1 patients of 3rd, and 10 patients after 4th. Among all the patients, 10 patients were normally treated with the drug, and 4 patients successfully extended the period of the drug administration. 6 patients discontinued the treatment due to drug eruption (n=2), pneumonia (n=1), agranulocytosis (n=1), unknown (n=1) and financial reason (n=1). [Conclusions] We observed nei-

ther disease activity deterioration nor drug related complication in any cases in the trial.

P19-8

Spacing or discontinuation of Etanercept injection due to remission in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the impact of spacing or discontinuation of etanercept injection due to remission in patients with rheumatoid arthritis. [Methods] All 17 patients who started spacing of injection interval with etanercept or discontinued etanercept between April 2018 and August 2020 at our hospital were registered in the study. [Results] The median injection interval was 3.5 weeks (2-5 weeks). Five patients withdrew after gradual spacing injection interval. Sustained remission rate after starting interval extension was 94% at 6 months, 76% at 12 months and 52% at 24 months. No statistical differences were found between sustained remission group and flare group. [Conclusions] Sustained remission rate after spacing of etanercept injection was 52% at 24 months.

P20-2

Two cases of severe iatrogenic immunodeficiency-associated lymphoproliferative disorders (IID-LPD) successfully treated by steroid therapy without chemotherapy

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Conflict of interest: None

[Case 1] A 72-year-old man who diagnosed in Rheumatoid arthritis (RA) in X-11 was stable at 14 mg/week of methotrexate (MTX). In April X, fever, elevated sIL-2R, multiple lymphadenopathy, and multiple nodular shadows in chest CT scan were observed. Iatrogenic immunodeficiency-associated lymphoproliferative disorders (IID-LPD) was suspected and MTX was discontinued. Lymph node biopsy showed findings consistent with IID-LPD. However, he developed impaired consciousness and pancytopenia due to hemophagocytic syndrome. After several weeks of methylprednisolone pulse (1000 mg/day for 3 days) therapy for severe condition, consciousness and pancytopenia improved remarkedly and became a remission. [Case 2] A 78-year-old woman who diagnosed in RA in X-24 treated with MTX of 6 mg/week, tacrolimus (TAC) of 1 mg and prednisolone (PSL) of 5 mg. IID-LPD was suspected because of loss of appetite, elevated sIL-2R, multiple nodules in lung, liver, spleen and kidney in CT scan. MTX and TAC were discontinued. However, nodules increased rapidly and the respiratory condition deteriorated rapidly. After the dose of PSL was increased to 30 mg, the nodules disappeared and became a remission. [Conclusion] Two cases of severe IID-LPD who treated by steroid alone mainly without chemotherapy could become a remission.

P20-3

A case of cryptococcal meningitis developed during the treatment of abatacept in rheumatoid arthritis patient

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Conflict of interest: None

A 79-year-old woman with a 3-year history of RA was admitted with a 1-week history of fever, headache, and confusion. She received 125 mg/week abatacept subcutaneous injection for 2-year before admission. Other medications included MTX 8 mg weekly. Her past medical history is notable for type 1 diabetes. Brain MRI showed multiple white matters high-intensity lesions. Nuchal rigidity was not present. However, meningitis was clinically suspected. Lumbar puncture was performed and demonstrated that cryptococcal antigen positive, and *Cryptococcus neoformans* in the cerebrospinal fluid (CSF). Amphotericin B liposomal and flucytosine were initiated and successfully lasted for 1 month with disappearance of *Cryptococcus neoformans* in CSF and no new lesions by brain MRI. The treatment was subsequently changed to fluconazole which terminated at 3 months without flare of meningitis. Mode of action of abatacept is the inhibition of T cell-costimulation which may inhibit host defense toward Cryptococcus neoformans in the present case. Our present case was limited in signs of megingeal irritation which might also relate with the use of abatacept. To the best of our knowledge, this is the first report of cryptococcal meningitis developed during the treatment of abatacept in RA patient.

P20-4

Pyogenic liver abscess after seven years of cholecystectomy in a patient with rheumatoid arthritis

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Conflict of interest: None

[Background] Pyogenic liver abscess (PLA) is a rare disease and most patients had a history of abdominal surgery (AS). I report a case of rheumatoid arthritis (RA) with PLA long time after cholecystectomy due to gallbladder (GB) cancer. [Case] A 66-year-old woman had a 31-year-history of RA. Etanercept (ETN) with MTX and PSL made her RA activity low. She had GB cancer associated with pancreaticobiliary maljunction and underwent cholecystectomy and hepaticojejunostomy at the age of 58. At 65 she had appetite loss and fever (37.4°C). Laboratory studies showed 16,060 leukocytes/μl, elevated CRP (9.84 mg/dl), ALP (373 IU/l), and γ-GTP (35 IU/l). A computed tomography of the abdomen showed multiple low-density lesions within the left lateral segment of the liver. She was diagnosed with PLA. After cessation of ETN and MTX, she was treated with CTRX and LVFX, but had a poor response. Then she received SBT/CPZ and had a good response. [Clinical significance] The median time for the occurrence of PLA after the AS was 2.0 (IQR 0.25, 6.0) years (Zang J, 2018). One of the risk factors of PLA was hepatobiliary malignant diseases. As compromised hosts were increased susceptibility to PLA, proper screening should be performed for RA patients after AS.

P20-5

A case of methotrexate-related lymphoproliferative disorder that was confirmed by re-biopsy

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Conflict of interest: None

[case] 74 year old female. At the age of 62, she was diagnosed with Rheumatoid arthritis. Methotrexate (MTX) was started at the age of 65, and Adalimumab was started at the age of 70. She was aware of dry cough and dyspnea in June when she was 73 years old. CT showed a large amount of pleural effusion and mediastinal lymphadenopathy. For examination, ultrasound bronchoscopy did not lead to the diagnosis of malignant lymphoma. It was followed up, and it improved gradually. However, there were respiratory symptoms again, and the increase of the pleural effusion was admitted by X-ray. A biopsy was performed in the left cervical lymph nodes, leading to a diagnosis of follicular lymphoma. [examination] MTX

is anchor drag for Rheumatoid arthritis. Long-term MTX use increases likely to cause lymphoproliferative disease (LPD). However, there are many reports that MTX-LPD disappears naturally after MTX is discontinued. In this case, the exacerbation of lymphoma was observed after MTX discontinuation. MTX-LPD often develops DLBCL. However, this time, it becomes a diagnosis of follicular lymphoma by biopsy, and the frequency is not high. In patients who re-emerge after MTX discontinuation, it is necessary to consider the start of chemotherapy in line with the biopsy results.

P20-6

Seven cases of leukopenia associated with methotrexate in a suburban general hospital

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Conflict of interest: None

[Objective] All physicians treating rheumatoid arthritis (RA) are familiar with adverse effects of methotrexate (MTX) and prescribe it with caution. However, adverse effects are not rare. We studied the clinical manifestations of patients who presented with leukopenia while taking MTX. [Methods] Retrospective case series study in single hospital. Patients with Grade 2 or higher leukopenia associated MTX were included. [Results] Five women; six cases and a man. The median age at the onset of leukopenia was 81 years (range; 69-92). In four cases, the leukopenia was found at the emergency hospitalization for fever and/or impaired consciousness. One case was founded leukopenia at the hospitalization because of pain in her mouth. The other two cases were detected during the routine outpatient consultation and during hospitalization for hypopharyngeal cancer. The MTX dosage was 4 mg/week in 3 patients, 6 mg/week in 1, and 8 mg/week or more in 3. The eGFR before the onset of the leukopenia was above 60 in all cases. [Conclusions] All cases had more than one risk factor of MTX-induced myelotoxicity. Myelotoxicity was sudden and unexpected. It is important to ensure that patients are encouraged to visit the outpatient clinic as soon as symptoms such as fever and oral erosions appear.

P20-7

Three cases with rheumatoid arthritis (RA) and airway diseases including mycobacterium avium complex (MAC) infection who has been effectively and safely treated with administration of abatacept (ABT)

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Conflict of interest: None

In rheumatoid arthritis (RA), patients with airway diseases (e.g. bronchiolitis and bronchiectasis) are difficult to treat, and their prognosis are poorer than those without airway diseases. We administered abatacept (ABT) to three RA patients with the diseases, including mycobacterium avium complex (MAC) infection. The administration has enabled improvements of their disease activity and their dose reduction of prednisolone, while it has not been involved in flare of airway diseases or MAC infection. Additionally, ABT has been continued over several years in them. In conclusion, we assume that administration of ABT could be proportionally effective and secure among disease-modifying anti-rheumatic drugs in treatment of RA patients with airway diseases.

P21-1

Treatment of patients with rheumatoid arthritis through cooperation between hospitals and local clinics

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Conflict of interest: Yes

[Objective] We actively refer patients with rheumatoid arthritis to local clinics for treatment. Here, we examined whether these patients had continued to receive appropriate medical care. [Methods] From 2015 to 2020, 210 patients were referred to local clinics. The course of treatment after referral was investigated, and problems after referral were analyzed. [Results] Forty-two patients were referred to rheumatologists, 106 were referred to non-specialists with experience in rheumatism treatment, and 62 were referred to family doctors. The treatments consisted of methotrexate in 126 cases, biologics in 17 cases, and other treatments in 67 cases. Circulating patients who regularly visit our hospital are 176 cases, 100 patients are stable, and 34 patients had variance and returned to our hospital. The average SDAI of stable patients was 4.0 at referral and 4.5 at survey. The variance consited of deterioration of disease activity in 27 cases, occurrence of adverse events in four cases, and inadequate medical care at the referral clinic in three cases. [Conclusions] Stable patients with remission or low disease activity can receive appropriate rheumatism treatment in cooperation with local clinics.

P21-2

The effect of isoflavone aglycone (Heber star) on joint pain after exclusion of rheumatoid arthritis

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Conflict of interest: None

[Objective] Many women have menopausal joint pain (MJP), and the age of onset overlaps with rheumatoid arthritis (RA). Hormone replacement therapy (HRT) is effective, but it is difficult for rheumatologists to handle. On the other hand, soy-derived isoflavone metabolite supplements have few adverse events and are also recommended in the gynecological field. We investigated the effects of isoflavone aglycone (Iso-A) in women with MJP after RA exclusion. [Methods] The subjects were women who were tested for RA. Iso-A was used at 30 mg (Heber star) daily, and equol was used at 10 mg (Equol) daily. We compared the results of DASH and SMI after 3 months. [Results] Of the 1187 patients, 86% were female and 88% did not have a diagnosis of RA. 409 patients purchased supplements (equol 153, Iso-A 256). Results were obtained from 50 of 135 patients who took Iso-A and reached 3 months. Improvements of DASH 29% and SMI 16% were observed. No difference in efficacy was observed in 11 patients who switched from equol to Iso-A. [Conclusions] Iso-A iso significantly improved menopausal symptoms and upper limb disorders after RA exclusion. There was no difference in the effect even when switching from equol. A-iso is cheaper, beneficial to patients, and effective for MJP after RA exclusion.

P21-3

Cohort study of MTX Adherence Survey in RA special clinicians -Second Report-

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Conflict of interest: None

[Objective] We already reported at JCR in 2017 that the adherence of taking MTX was good for patients on our group facilities. We analyzed the poor adherence factors. [Methods] The survey was carried out RA patients at 20 facilities and the 2832 patients answered about the adherence question. We divided 4 group, almost (A), 80% (B), half (C), and hardly (D) of taking MTX. We analyzed among 4 group that patient background, disease awareness, MTX awareness, and reasons for forgetting to take it. [Results] As the analysis into group A (2500 cases) and group BCD (332 cases), there was no difference in gender ratio, duration, disease awareness or MTX administration, but the low rate of group A in younger patients. The same analysis was performed by dividing into the AB group (2773 cases) and the CD group (59 cases), the MTX administration (78%) and side effects (37%) was lower in the CD group. The biggest reason for poor adherence on CD group was forgetting to take the drug (51%), and side effects (36%) were also frequent. There was no difference in the rate of poor ad-

herence between institutions. [Conclusions] Although the MTX adherence for the patients with RA among clinicians is high. But some patients need assistance for missed to take the drugs and taking care for side effects.

P21-4

Clinical characteristicstudy of elderly rheumatoid arthritis patients (RA) at Ogawa Red Cross Hospital

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Conflict of interest: None

(Purpose) To compare treatments and complications between elderly onset RA patients and young patients. (Patients and methods) The study involved 165 patients (113 female, average age 70 years old) in Jul 2020. They were surveyed their characteristics, therapeutic agents, renal function by eGFR and complications by medical records. The components were evaluated among three groups (Group A; under 65 years old, 65 years old <Group B <75 years old, Group C; more than 75 years old). (Results) A:25% (74%women), B:33% (57%women), C:41% (66%women). As a treatment, MTX use (55%, average 6.3 mg/w) (A:21%, 7.3 mg, B;19%, 6.5 mg. C:16%, 4.7 mg). PSL use (28%, average 5.3 mg) (A:7%, 5.1 mg, B;7%, 4.4 mg, C:15%, 5.9 mg). AntiTNF inhibitors (ETN, IFX, GLM) (11%) (A:4%, B:5%, C:2%). Anti-IL6 inhibitors (SAR, TCZ) (12%) (A:1%, B;7%, C:4%). ABT (5%) (A:1%, C:4%). JAK inhibitors (7%). SASP (40%) (A:6%, B:9%, C:25%). TAC8% (A:1%, B:2%, C:5%). MZB1% (B:1%). Renal dysfunction 18% (A:1%, B:4%, C:13%), Malignancies; 1 case. (Conclusion) The number of elderly RA patients has been increasing in our hospital, and the ratio of women was high in any generation. As the generation rose, the number and the amount of MTX use decreased, ABT, SASP, and PSL were used frequently by the elderly. Renal dysfunction was often observed in group C.

P21-5

Study for adherence of patients with rheumatoid arthritis (RA) treated with Golimumab (GOL) in our hospital under the COVID-19 pandemic world

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Conflict of interest: None

[Objective] Study for adherence of RA patients with Golimumab (GOL) in our hospital under COVID-19 pandemic. [Methods] Sixteen RA patients were treated with continuous GOL during from Sep. 2019 to Aug. 2020. This is a single center, non-interventional, retrospective study. We measure MPR (Medication Possession Ratio): The ratio of effective dose to the total planned dose, MPR ≦ 80% is considered as not achieving adherence. The verification drugs are GOL and Methotrexate (MTX) of the same patient. Regardless of changes in the dose of GOL and MTX, we will consider the number of effective doses. We measure disease activity with DAS28 (4) CRP. In TOKYO, COVID-19 Pandemic announced on 2020/3/2. So, we compared MPR from GOL, MTX, DAS28CRP between pre-pandemic a half year and post-pandemic a half year. [Results] Pre-pandemic, MPR ≦ 80% is 1, 100% is 15. Post-pandemic, MPR ≦ 80% is 2, 100% is 12, 83% is 2 cases. MTX combined with 12 cases, pre-pandemic, MPR ≦ 80% is 1. MPR> 80% is 11. Post-pandemic, MPR ≦ 80% is 2. MPR> 80% is 10 cases. DAS28CRP changes pre-pandemic to post-pandemic, remission (<2.3) 10 to 9, LDA (2.3-2.7) 1 to 2, MDA (2.7-4.1) 4 to 3, high. HDA (4.1-) 1 to 2 cases. [Conclusions] In our hospital under the COVID-19 pandemic, MPR for GOL is good enough, disease activity is controlled.

P22-1

5 cases of undifferentiated inflammatory mono-arthritis treated with arthroscopic synovectomy and medication

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Conflict of interest: None

[Objective] The purpose of this study was to review the 5 patients of undifferentiated inflammatory mono-arthritis treated with arthroscopic synovectomy and medication. [Methods] 5 cases of undifferentiated inflammatory mono-arthritis (52 to 76 years, 2 men and 3 women, 4 knee joint and 1 ankle joint) were enrolled in this study. In every cases, CRP was positive and RF and ANCA was negative on blood test and crystal test and bacterial culture test were negative on joint fluid test. [Results] Arthroscopic synovectomy was performed and pathological findings reported multilayered synovial cell, increased neutrophil, lymphocyte, lymphocyte, and capillary vessel which resemble RA synovitis in 4 cases and inflammatory synovium including mature adiposed tissue in deep layer which match lipoma arboscens in one case. Synovitis in other joints was observed in 2 cases after synovectomy. In every cases, joint pain and synovitis continued and treatment by DMARDs was started. Mild radiographic joint damage was observed in three patients whose symptoms lasted more than 6 months before the synovectomy. [Discussion] Early treatment of undifferentiated inflammatory mono-arthritis, with pathological examination of synovium may also be of benefit by prevention of disease persistence, joint damage.

P22-2

Mid-term results of reverse shoulder arthroplasty

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Conflict of interest: None

[Objective] Reverse total arthroplasty (RSA), which is useful for patients with pseudoparalysis of the shoulder, but its long-term results remain unclear. [Methods] We retrospectively reviewed 9 shoulders in 9 patients, including 6 females and 3 males, at least 54 months of follow-up. Pseudoparalysis was caused by cuff tear arthropathy in four shoulders, by massive rotator cuff tear in three and by rotator cuff retear in two. One of the two patients with rotator cuff retear was a patient with rheumatoid arthritis (RA). All patients had received TM Reverse Shoulder prosthesis (Zimmer, Inc, Warsaw, IN). The age at the time of RSA ranged from 71 to 80 years. The follow up duration ranged from 54 to 66 months. Range of motion (ROM) of the shoulder was measured and clinical evaluation was made using a Japan Orthopedic Association (JOA) shoulder score system. [Results] Flexion, abduction and external rotation of the shoulder ROM were improved postoperatively, but internal rotation was impaired. Postoperative JOA score was significantly higher than preoperative one. A minor revision surgery for recurrent dislocation was performed in a RA patient. [Conclusions] RSA for pseudoparalysis, except RA patients, may be a useful intervention in order to restore the function of the shoulder.

P22-3

A case performed total knee arthroplasty for rapidly destructive osteonecrosis of the left femoral medial condyle diagnosed with undifferentiated arthritis

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Conflict of interest: None

[Introduction] Rapidly destructive arthropathy is a disease that causes rapid joint destruction in several months. We report a case of rapidly destructive osteonecrosis of left knee diagnosed with undifferentiated arthritis. [Case] In January 2020 a 71-year-old man developed left gonalgia after falling. MRI revealed medial meniscus injury with damage of articular cartilage and subchondral bone. Lab. data: CRP 11.63 mg/dL, ESR 84 mm, RF 3 U/mL, ACPA 1.3 U/mL, MMP-3 291 ng/mL. Although PSL has been administered in diagnosis of UA, due to rapid destruction on imaging TKA was performed on June 2020. [Discussion] Recently, it has been reported lord concentration resulted from meniscus tears/extrusion causes subchondral insufficient fractures, however the mechanism of rapid destruction remains unknown. It is speculated in RDC local production of

MIF and MMPs accelerates joint destruction after insufficient femoral head fracture. In our case inflammatory reaction and MMP-3 were high, therefore synovitis was expected to be involved, suggesting possibility of local immune disorders as in the case of RDC. [Clinical significance] We reported local immune disorders might be associated with rapid destruction of knee joint. We believe further elucidation will lead to the establishment of treatment.

P22-4

Survey of perioperative instructions for patients with rheumatoid arthritis on biologics and/or methotrexate who underwent non-orthopedic surgeries

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Conflict of interest: None

[Objective] For patients with rheumatoid arthritis (RA) on biologics (BIO) and/or methotrexate (MTX) undergoing non-orthopedic surgeries, the perioperative management of the drugs in various guidelines is not clearly described. To establish a protocol, we investigated the current perioperative instructions in non-orthopedic surgeries. [Methods] The perioperative instructions for patients with RA on BIO and/or MTX who underwent scheduled non-orthopedic surgeries under general anesthesia at our hospital in the past six years were retrospectively investigated. [Results] In 87 operations involving 77 patients, 33 operations received preoperative instructions regarding the continuation or withdrawal of the drug, while the remaining 54 operations had no prior instructions or the final administration day was unknown, as in eight of 24 patients on BIO. [Conclusions] In some cases without instructions, it is suggested that instructions were not given because the risk of the drugs were not recognized or information on the operation was not shared among clinical departments. Prior confirmation of drug history or creation of an in-hospital preoperative RA drug protocol should be considered in establishing a more appropriate preoperative drug management.

P22-5

A case of reconstruction for severe finger deformity due to Jaccoud arthropathy

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Conflict of interest: None

[Case] A 54-year-old woman was suspected of having scleroderma and started steroid treatment around the age of 40. She visited to our hospital for the purpose of treating severe finger deformity. No joint destruction was observed in the MP joints from the right index finger to the little finger, but palmo-ulnar dislocation and shortening accompanied by flexion contracture of about 120 degrees and the swan-neck deformity were observed. The palmar skin crease was deeply digging into the skin and was soggy. Due to severely deformed hand, she could not grasp a large object. [Treatment] Finger joint replacement was performed on the index finger MP joint, but in the middle, ring, and little finger MP joints, myostatic contracture and shortening of the finger flexor muscle was extremely severe, so sufficient space for the implant could not be secured, and fusion was performed with the little finger PIP joint [Results] After the operation, appearance of the hand as well as hand function improved. She could grasp the steering wheel of the car that the patient wanted. [Discussion] Jaccoud arthropathy is characterized by no joint destruction or contracture. But in this particular case, severe joint contracture due to contracture of the finger flexor muscles was observed.

P22-6

a case of total knee arthroplasty (TKA) for arthritis caused by hypertrophic osteoarthritis secondary to refractory liver cirrhosis

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Conflict of interest: None

[Objective] The purpose of this study is to report clinical outcome for a case of total knee arthroplasty (TKA) for arthritis caused by hypertrophic osteoarthritis secondary to refractory liver cirrhosis. [Case] A 59 years old woman [Medical history] She had been attending our department for liver cirrhosis due to primary sclerosing cholangitis (Child-Pugh: Grade B). Her roentgenographics showed subperiosteal bone formation with periosteal reactions in both femurs and tibias, and the diagnosis of secondary hypertrophic osteoarthritis due to liver cirrhosis was made. Since she was waiting for liver transplantation for cirrhosis, it was difficult to treat the primary disease at an early stage, and her ADL dropped significantly, therefore, we performed TKA. Her pain was immediately relieved after surgery and she was discharged home on her own. [Clinical significance and discussion] The treatment of primary desease is the first priority in the treatment of arthritis in hypertrophic osteoarthritis. In this case, the primary disease was difficult to treat and she developed bone degeneration, which led to TKA even though she was young. We need to decide on a treatment strategy that takes into account the treatment status, prognosis and ADL of the primary disease.

P22-7

A Chronic Nonspecific Monoarthritis Case with Low MMP-3 Value and Inflammation Marker after Total Knee Arthroplasty

Hitoshi Imamura
Takagi Hospital

Conflict of interest: None

[Introduction] Chronic nonspecific monoarthritis is being considered similar to monoarticular rheumatoid arthritis conceptually that does not meet with the 2010 ACR/EULAR Classification Criteria for rheumatoid arthritis (RA). [Case Study] A 65-year-old women without specific medical history. She has been suffering from joint pain on her left knee for three month without particular cause. Joint edema was found in her left knee but not any other joints. Hematological examination before the surgery showed CRP 1.00 mg/dl, ESR1h 48 mm, MMP-3 101.1 ng/ml, Anti-CCP antibody 481.2 U/ml, rheumatoid arthritis factor 120 U/ml. It scored 5 in the classification criteria so it doesn't meet with the RA diagnosis criteria. TKA was implemented. Inflammation marker and MMP-3 value were significantly lowered and no RA happened in two years after the surgery. [Finding] Chronic nonspecific monoarthritis usually develops to polyarthritis and RA. Long-term observation is considered necessary in this case while synovium excision may defer the development of polyarthritis and RA.

P22-8

Efficacy and safety of sarilumab after 52 weeks

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Conflict of interest: None

[Objective] Sarilumab is a new drug, therefore, its efficacy and safety after 52 weeks are insufficient. [Methods] In 50 patients with RA who started administration of salilumab after September 2018, therapeutic effect, continuation rate, and safety were examined in 24, 52 weeks. [Results] 36 patients were female, average age was 65.3 years, average dis-

ease duration was 4.8 years. There were 23 patients with MTX (7.8 mg/w), 24 patients with PSL (6.6 mg/d). The continuation rate of 24 weeks was 90%, it of 52 weeks was 74%. The reasons for discontinuation within 24 weeks (5 cases) were cytopenia in 2 cases, insufficient effect in 1 case, and other 2 cases. That of after 24 weeks (8 cases) were cytopenia in 2 cases, insufficient effect in 4 cases, and others in 2 cases. The HDA/MDA rate before treatment was 42%/48% for CDAI. After treatment, the CDAI remission rate was 36% at 24 weeks and 66% at 52 weeks. Regardless of the background, MTX-/+ and naïve / switch cases showed significant improvement after 24 and 52 weeks. The average of MTX at 52 weeks was 5.5 mg/w, and that of PSL was 2.0 mg/d, suggesting the effect of reducing the dose of MTX and PSL. [Conclusion] It was confirmed that the continuation rate and efficacy after 52 weeks were high, and that the safety was also high.

P22-9

Evaluation of multifocal osteonecrosis in patients with osteonecrosis of femoral head using whole-body MRI and bone scintigraphy

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Conflict of interest: None

[Objective] This study aimed to compare the detection rate of osteonecrosis (ON) by whole-body magnetic resonance imaging (WB-MRI) vs whole-body bone scintigraphy (WB-BS). We also aimed to clarify the characteristics of patients with multifocal ON among patients with ON of the femoral head (ONFH). [Methods] Forty patients who had symptomatic ONFH and underwent surgery as well as WB-MRI and WB-BS in our hospital were included in the study. Data on patient demographics were collected from their medical records. [Results] The accuracy in the detection of ON in the hip joints by WB-MRI vs WB-BS was moderate, while that in other joints was low. Among 131 joints with ON detected by WB-MRI, 80 were symptomatic, and 51 were asymptomatic. On the other hand, while WB-BS could detect symptomatic ON in more than 80% of the joints, it could detect asymptomatic ON in less than 30% of the joints. Eleven out of the 40 patients had multifoca ON. All patients with multifocal ON had a history of steroid therapy. [Conclusions] Compared to WB-MRI, WB-BS has a lower sensitivity for detecting asymptomatic ON. Considering the cost, examination time, and radiation exposure, WB-MRI is a more sensitive and powerful tool for evaluating multifocal ON.

P22-10

A case of membranoproliferative glomerulonephritis with IgA-dominant deposition accompanied by rheumatoid arthritis treated with etanercept

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Conflict of interest: None

A 87-year-old woman diagnosed with rheumatoid arthritis in 1982. Treatment with etanercept 500 mg/week was started in 2015 resulted in remission of rheumatoid arthritis. She was seen as an outpatient with limb edema, which had been gradually worsening for four months. Blood tests showed Cr 0.59 mg/dL and albumin 2.0 g/dL, and urinalysis showed urine occult blood 2+, urine protein 3+, and urine protein/Cr ratio 11 g/gCr. She was diagnosed with nephrotic syndrome and was admitted to our hospital for further examination. Antinuclear antibody, MPO-/PR3-ANCA and cryoglobulin were negative. Hyper-IgA and hypocomplementemia were observed. Kidney biopsy performed on Day 10 of hospitalization revealed membranoproliferative glomerulonephritis with IgA-dominant deposition. Oral prednisolone 20 mg/day was started and urine protein/Cr ratio improved to 1.4 g/gCr on Day 20 of hospitalization. A case of IgA nephropathy with a form of membranous proliferative glomerulonephritis has been reported and our case was considered a subtype of IgA nephropathy as well. Reports of IgA nephropathy during the use of biologics used in patients with rheumatoid arthritis are rare.

P22-11

A case of RA patient with insufficient fracture of the second cuneiform bone of the foot, which caused atraumatic foot pain

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Conflict of interest: None

[Objective] In patients with rheumatoid arthritis, foot pain may interfere with daily activities. We report a case of RA patient with insufficient fracture of the second cuneiform bone of the foot, which caused atraumatic foot pain. [Case] A 61-year-old woman. A patient with rheumatoid arthritis who was diagnosed at the age of 46 was treated at another hospital. She has been treated at our hospital from June 2017. She complained of left foot pain that occurred without traumatic mechanism, and mild swelling and tenderness were observed around the midfoot. X-ray image showed neither narrowing of the joint space nor erosion of the bone. Blood examination showed CRP 0.05 mg / dl and ESR 6 mm / Hr. There were no swelling or tender joints except her left midfoot. DAS28 (3CRP) score was 1.15, and DAS28 (3ESR) 1.51. MRI imaging revealed a fracture in the second cuneiform bone. She was allowed to walk under load within her pain range, with arch support, and medication for osteoporosis was changed from bisphosphonate to PTH. After that, her foot pain disappeared in 4 months, and the pain in the same area has not recurred until now. [Conclusions] It is necessary to keep in mind the possibility of insufficient fracture as the cause of foot pain that occurs without trauma.

P22-12

A Case of elbow periprosthetic fracture with regional thickening of the bone cortex in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We experienced a case of mild dislocation due to a fracture around the elbow joint in a patient with rheumatoid arthritis. Regional cortical thickening is associated with the fractured part at the time of injury, and the pathophysiology and the effect of fracture treatment will be investigated. [Case] The case is a woman in her 70s, a patient with rheumatoid arthritis, and corresponds to Steinbrocker stage IV / class 2, medications containing etanercept, and had been receiving denosumab for 1.5 years. The injury was due to forced hyperextension. Mayo classification ulnar class 2, and the bone cortex of fractured part showed regional thickening. Splint for 8 weeks, and PTH preparation was started. There is a tendency for X-ray bone fusion at half year. The range of motion of the elbow joint decreased, and it was improved by range of motion. [discussion] Proximal ulnar fractures, which tend to be relatively unstable in periprosthetic elbow fractures, and regional cortical thickening may tend to prolong bone union, but conservative treatment due to mild dislocation was selected and it was effective. Generally different from the site of atypical fractures of the ulna. One of the causes was that the mechanical load was changed by the artificial elbow joint.

P22-13

The investigation of patients treated with Infliximab (IFX) in Akita Registry in 201

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Conflict of interest: None

[Objective] To investigate the patients treated with IFX who registered with the Akita Orthopedic group on Rheumatoid Arthritis (AORA). [Methods] Two thousand, one hundred and fifty-nine patients were registered with AORA in 2019. Of these, 125 patients were treated with IFX who comprised the subjects of this study. [Results] The patient character-

istics were follows: there were 22 males and 103 females, the mean age was 58 year and the mean disease duration was 129 months. The DAS 28ESR could be calculated in 93 patients, and the mean was 4.87 (REM: 2.1%, LDA: 10.8%, MDA: 11.8%, HDA: 75.3%). The mean CRP was 2.28 mg/dl, and the mean MMP3 was 263.9 ng/ml. One hundred and nineteen patients had been prescribed methotrexate (MTX) with a mean dose of 7.1 mg, and 94 patients had been prescribed prednisolone (PSL) with a mean dose of 5.7 mg. Fore patients were administrated IFX as a second biologics. The mean duration of IFX administration was 46 months. Thirty-three patients could continue IFX treatment during the investigation.

P23-1

Comparison of sustained clinical remission and/or low disease activity rate between rapidly discontinued and gradually de-escalation of baricitinib in rheumatoid arthritis

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Conflict of interest: None

[Objective] We analyze predictors of sustained REM/LDA in rheumatoid arthritis (RA) patients treated with baricitinib. [Methods] Cases were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2015 and 2019 (n=3,674). Patients were included baricitinib started with 2 mg/day (n=108). In 108 (Male 18, Female 90 cases, RA duration 13.3+/-12.8 years) cases. CDAI and patient clinical parameters were analyzed. In gradually de-escalation methods, baricitinib were decreased to 50%, 42%, 28%, 14% in order with stable REM/LDA over 12 weeks. [Results] (1) "Predictors to detect who can achive REM/LDA" Patients who achieved to REM/LDA showed b/tsDMARD naïve (p=0.0020) and non- difficult to treat RA (p=0.0072). (2) "Comparison of sustained REM/LDA rate between two de-escalation methods" 12 cases were tapered baricitinib with rapidly discontinued method and 47 patients were with gradually de-escalation. Gradually de-escalation method showed higher sustained REM/LDA rate compared with rapidly discontinued method after tapered baricitinib at 40 weeks (97.9% vs. 33.3%, p<0.0001). [Conclusions] A combination of history of DMARDs and tapering baricitinib using gradually de-escalation methods may help to predict successful baricitinib deduction in RA patients with sustained clinical REM/LDA.

P23-2

Efficacy and safety of baricitinib in rheumatoid arthritis at 24 weeks

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Conflict of interest: None

[Background] Baricitinib (BAR) was approved as a targeted synthetic DMARDs (tsDMARDs) for rheumatoid arthritis (RA) in September 2017 but there are only a few reports on its clinical use. [Objective] We report the efficacy and safety of BAR in 25 RA patients in our hospital. [Methods] From September 2017 to December 2019, BAR was introduced in our hospital, and 25 RA patients who were able to observe the progress by the time of 24 weeks afterwards were made to be an analysis object. Therapeutic effects and safety using CDAI were analyzed retrospectively, and the background factors contributing to each analysis were examined. [Results] Of the 25 RA patients, 80.0% were female, with a mean age of 65.2 years at the start of BAR and a mean duration of illness of 12.2 years. The methotrexate (MTX) combined use rate was 44.0%, and 20.0% was the biologics non-use example. The mean CDAI at the start of BAR was 21.9 and the mean CDAI at 24 weeks was 16.3. Especially, the improvement was mainly observed in the MTX combined use and biological preparation non-use group. By 24 weeks, 6 patients discontinued Bari because of primary failure in 3, secondary failure in 1, pneumonia in 1, and breast cancer in 1. [Conclusions] The efficacy and safety of BAR in clinical practice were demonstrated.

P23-3

Efficacy and safety of one-half dose Baricitinib in patient with rheumatoid arthritis in a routine care

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Conflict of interest: None

[Objectives] Baricitinib (BAR) is a JAK inhibitor that has been prescribed in a routine care in Japan since 2017. There are a few studies that have examined the efficacy of BAR begun at one-half dose (2 mg) in RA patients in a routine care. In this study, we investigated the efficacy of BAR in RA patients. [Methods] RA patients treated with BAR for longer than 12 weeks were included in this study. We retrospectively reviewed the efficacy (DAS28-CRP), discontinuation of BAR therapy and adverse event in one-half dose (2 mg group) and typical dose (4 mg group), respectively. [Results] Fourteen (2 mg group) and fifteen (4 mg group) patients were included in this study. Mean age was both 66 years old and concomitant methotrexate rates are 76% and 93% (2 mg and 4 mg groups, respectively). Mean DAS28-CRP was 3.7 and 3.6 at baseline, and 1.7 and 1.8 at 12 weeks (2 mg and 4 mg groups, respectively). The number of patients who withdrew from BAR owing to insufficient efficacy was two (2 mg group) and four (4 mg group). Serious adverse event is two in 2 mg group. [Conclusion] One-half dose (2 mg) as well as Typical dose (4 mg) of BAR was effective in RA patients in a routine care. This study provides support for the possible use of one-half dose of BAR in RA patients.

P23-4

Clinical results of baricitinib in our hospital (Comparison of Effectiveness and Adverse Events by Doses)

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Conflict of interest: None

[Objective] Baricitinib (Bari) is an effective treatment for rheumatoid arthritis. The standard dose is 4 mg, but it can be reduceed to 2 mg depending on the patients. In the RA-BUILD study, there was no difference in ACR improvement between doses at 24 weeks, however, clinical outcomes are unknown. We compared treatment effects and side effects between doses at 52 weeks of bari use. [Methods] We studied 46 patients with rheumatoid arthritis, who had used bari for more than 52 weeks. [Results] 46 patients were included. 48% of patients in the 2 mg continuous group, 11% in the 4 mg continuous group, 24% in the 2 mg to 4 mg group, and 17% in the discontinuation group. DAS28-CRP at 52 weeks was improved in both groups (2 mg group: 3.25±1.32→1.50±0.63; 4 mg group: 3.30±0.86→1.99±0.69), and MMP-3 was reduced (2 mg group: 218±188 ng/mL→86.3±44.9 ng/mL, 4 mg group: 249±230 ng/mL→126±63.6 mg/mL). Dose of PSL decreased in both groups (2 mg continuous group: 4.3±2.7 mg→3.2±2.2 mg, 4 mg group: 7.7±5.2 mg→3.2±2.3 mg). Bari was discontinued in 8 patients and there was no obvious difference between doses. [Conclusions] Bari improved DAS28-CRP and reduced MMP-3 at 52 weeks in both the 2 mg and 4 mg groups, and had a steroid spacing effect. In this analysis, there was no difference in the incidence of adverse effects between doses.

P23-5

Efficacy of disease activity and safty in old rheumatoid arthritis patients treated with low dose baricitinib

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Conflict of interest: None

[Objective] The JAK1/2 inhibitor baricitinib is a targeted synthetic disease modifying antirheumatic drugs with few contraindicated drugs. The therapeutic effect of low-dose baricitinib on elderly rheumatoid arthritis (RA) patients was investigated. [Methods] Six RA patients aged 70 years or older who had insufficient MTX effect and started treatment with

baricitinib 2 mg/day and were able to follow up until 52 weeks later were included. The continuation rate, therapeutic effect and adverse effects up to 52 weeks of treatment were evaluated. [Results] The patients were 4 females and 2 males, with a mean duration of RA disease of 16.4 years and an average age at the start of baricitinib treatment of 74 years. The disease activity of DAS-CRP/SDAI/CDAI before treatment was 3.72/14.6/13.9, and improved to 2.44/7.3/6.7 at 24 weeks of treatment, and maintained at 2.42/6.5/5.7 at 52 weeks. All patients were combined with MTX. Hepatic function increased, leukocyte depletion, cold, ingrown toenail, and dizziness were observed during the administration period, requiring temporary suspension of medication in some cases. But all patients continued to treat with baricitinib 2 mg/day until 52 weeks. [Conclusions] Low-dose baricitinib for elderly RA patients may be an efficacy and safety option.

P23-6

Efficacy of half-dose baricitinib for the elderly and continuation of 3 years

Tamami Kikuchi
Joetsusougoubyouin

Conflict of interest: None

[Objective] There are few reports on the long-term results of JAK inhibitors in clinical practice. Previously, we reported the effectiveness of half-dose BAR administration for the elderly under the title of 'Experience of administration of baricitinib to elderly RA patients including the very elderly'. Since more than 3 years have passed, we will report the clinical course. [Methods] Six cases were selected, who were 75 years old or older and had high disease activity, and it was judged that treatment enhancement was necessary at an early stage. For efficacy, disease activity was evaluated by SDAI and compared before administration, 4 weeks and 3 years after administration. The presence or absence of adverse events and the continuation rate (5 months and 3 years later) were examined. [Results] SDAI averaged 23.8 before the start, 7.0 after 4 weeks, and low after 3 years. The continuation rate was 83% after 5 months and 100% after 3 years. No new adverse events were observed other than CK elevation and thrombophlebitis observed in short-term observation. [Conclusions] The efficacy and continuation rate of half-dose BAR in the elderly after 3 years was as high as after 5 months.

P23-7

Efficacy of Baricitinib in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] To investigate the efficacy of baricitinib in rheumatoid arthritis patients. [Methods] 18 Rheumatoid arthritis patients who were treated with baricitinib from September 2017 and could follow more than 52 weeks were recruited. Efficacy in disease activity scores and adverse events were investigated. [Results] There were 4 men and 17 women. Mean age was 62.0±17.7 years old, and mean disease duration 8.8±9.8 years. Mean DAS28-CRP were, baseline: 3.63±1.13, after 4 weeks: 2.68±1.20, after 12 weeks: 2.65±1.24, after 24 weeks: 1.89±1.09, after 52 weeks: 2.01±0.72, which improved from baseline. One patient had herpes zoster, though resumed baricitinib treatment. Two patients canceled baricitinib treatment for upper respiratory tract infection. [Conclusions] Baricitinib was effective in rheumatoid arthritis treatment.

P24-1

Efficacy of JAK inhibitors in refractory rheumatoid arthritis

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Conflict of interest: None

[Objective] We investigated the efficacy and continuation factors of JAK inhibitors for refractory rheumatoid arthritis. [Methods] The continuation rate were investigated by the Kaplan-Meier method. Among them, RA patients who switched to Tofacitinib (TOF) or Baricitinib (BAR) after using 3 or more bDMARDs with different targets but discontinuing due to insufficient effect were considered refractory. As a statistical method for predicting the continuation of 6 months or more, we used various test methods using the patient background as explanatory variables. [Results] By September 2020, a total of 897 bDMARDs had been administered to 397 RA patients. The continuation rate was 64.1% in 63 TOF patients and 80.9% in 66 BAR patients, with no significant difference (P = 0.124). Among them, the continuation rate in refractory RA cases was 56.1% in 21 cases of TOF and 66.2% in 18 cases of BAR, and there was no significant difference (P = 0.796). In the TOF cases, there was a significant difference between the disease duration (P = 0.035) and the PSL combined dose (P = 0.045). [Conclusions] Although it was a retrospective and short-term study, JAKi was effective even for refractory RA in which bDMARDs were inadequately effective. Long-term follow-up is desired in the future.

P24-2

Clinical results of two JAK inhibitors in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] Targeted synthetic disease modifying antirheumatic drugs, JAK inhibitors, have been shown to have some effect as a treatment for rheumatoid arthritis (RA). However, there are few reports comparing their effectiveness. We investigated the clinical results of tofacitinib (TOF) and baricitinib (BAR). [METHODS] 51 RA patients who received JAK inhibitors were enrolled in this study and the clinical course of RA was regularly evaluated. The age at dosing, RA duration, eGFR, the treatment rate of MTX and PSL, the dose of MTX and PSL, the difference of DAS28-CRP (ΔDAS28-CRP), and the survival rate at the final follow up were investigated. [Results] 29 patients were registered in the TOF group and 22 patients were enrolled in the BAR group. The average age at the start of administration was 67.5 years in the TOF group and 64.1 years in the BAR group, and the duration of RA was 14.8 years/16 years (TOF/BAR), eGFR 76.5/82.5 (mL/min), and MTX dose 6.9/8.4 (mg/Week), MTX dose rate was 68.2/59.1%, PSL dose was 5.4/2.5 (mg), and PSL dose rate was 36.4/27.2%. ΔDAS28-CRP was not significantly different between the two groups. There were no difference in the survival rate of TOF and BAR. (P=0.57) [Conclusion] There were no difference in the efficacy and survival rate between the two grops.

P24-3

Study on the safety of JAK inhibitors in the treatment of rheumatoid arthritis in our hospital

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Conflict of interest: None

Objectives: The efficacy of JAK inhibitors in the treatment of RA has been established. Their long-term safety, however, remains unclear in Japan. We studied the safety issues of JAK inhibitors experienced in our hospital. **Methods:** We retrospectively reviewed the medical charts of all the RA patients who were treated with either tofacitinib (TOF) or baricitinib (BAR) from January, 2016 to January, 2020. **Results:** Total 55 patients were treated with JAK inhibitor (20 with TOF, 35 BAR). Their mean age was 68, mean RA duration was 11 years and mean observation period was 14 months. Nine (16%) were treated with MTX (mean 7.1 mg/week), 14 (25%) with PSL (mean 3.5 mg/day) and 47 (85%) had experienced bDMARDs. Kaplan-Meyer survival analysis estimated 1 year treatment success ratio of 61%. There was neither serious infection, Herpes zoster nor venous thrombosis. Two patients with TOF developed malignancy

(3.8 per 100 PY). **Conclusions:** Post-marketing surveillance of TOF and BAR in Japan reported that IR/100 PY of serious infections at 6 months was 6.81 in TOF and 3.75 in BAR. It is suggested that our dose adjustment of JAK inhibitors according to patients age, renal function and comorbidity was important for the prevention of serious infections.

P24-4

Clinical results of JAK inhibitors in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] he purpose of this study was to investigate the clinical results of JAK inhibitors (tofacitinib (TOF), baricitinib (BAR)) in elderly patients with rheumatoid arthritis (RA). [Methods] Of the 52 patients who received JAK inhibitors, 31 patients (20 TOF, 11 BAR) whose age at the start of administration was 65 years or older (average 74 years) were investigated in this study. We followed the clinical course (eGFR, administration of DMARDs, PSL, DAS28-CRP, and adverse events). [Results] Mean eGFR was 74.2 mL/min. Twenty cases (65%) were switch cases from bDMARDs, and MTX and PSL were administered to 15 cases (48%) and 9 cases (29%), respectively. Mean DAS28-CRP was 4.52 at the start of administration, which showed a significant decrease of 2.42 and 2.18 at 12 and 24 weeks after administration ($p < 0.01$). By final follow up, 8 patients (25%) had been discontinued. Discontinuation due to adverse events were observed in 6 cases, of which 2 cases had elevated creatine kinase and 1 case each had anemia, herpes zoster, gastrointestinal symptoms, and foot callus infection. PSL and csDMARD could be withdrawn or reduced in 6 or 12 patients, respectively. [Conclusions] JAK inhibitors are also effective for elderly RA patients, suggesting that PSL and DMARDs may be reduced or discontinued.

P24-5

Comparative study of tofacitinib and baricitinib cases at our hospital

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Conflict of interest: None

[Objective] To compare the efficacy and safety of tofacitinib and baricitinib among JAK inhibitors in the treatment of rheumatoid arthritis. [Methods] We compared the patient background at the time of introduction and 24-week efficacy and serious adverse events in 63 patients with tofacitinib and 35 patients with baricitinib who were introduced at our hospital from December 2013 to January 2020. [Results] In the baseline patient background, there was a significant difference in duration of illness between the two groups. In both medicines, the efficacy at 24-weeks have improved significantly and tended to be more effective when used in combination with MTX, but no significant difference was observed. Serious adverse events were herpes zoster, pneumonia, and malignant neoplasms in 7 cases, 4 cases, and 3 cases with tofacitinib, and 6 cases, 3 cases, and 1 case with baricitinib. [Conclusions] Both tofacitinib and baricitinib showed significant improvement in disease disease 24 weeks after the start of administration, and there was no difference in efficacy. Serious infections were similar for both medicines. In the clinical practice, there was no difference in the efficacy and safety of the two medicines.

P24-6

A short-term study of the therapeutic effect of switching from biologics to baricitinib in patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy of treatment of rheumatoid arthritis (RA) patients who have been switched from biologics to baricitinib (BAR) with inadequate response. [Methods] Overall indices such as DAS-28CRP, DAS28ESR, and CDAI, as well as changes in MMP-3 and adverse events were studied, in 2 male and 6 female patients who switched to BAR. [Results] At BAR induction, mean age and disease duration of patients were 74.1 years and 14.1 years. Mean follow-up term was 6.6 months after switching. The patients had been treated with an average of 2.4 biologics before switching. DAS28CRP decreased from a mean of 2.89 before the change to 2.40 at last observation, DAS28ESR decreased from 3.39 to 3.10, CDAI decreased from 12.0 to 8.94, and MMP-3 (ng/dl) decreased from 270.5 to 143.3. Adverse events had occured in one patient who got herpes zoster. [Conclusions] This study included the patients with treatment difficulties, such as those with a history of intractable to multiple biologic therapies, long disease duration, and inability to use methotrexate, DAS28CRP of the patients showed remission in 5 patients and low disease activity in 1 patient at the last observation. BAR would be a useful option in patients with RA who are intractable to multiple biologic therapies.

P24-7

Remission-induction therapy of steroids and half-dose baricitinib for seronegative rheumatoid arthritis with over 80 years old onset

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Conflict of interest: Yes

[Purpose] To investigate the efficacy of remission-induction therapy using prednisolone (PSL) and half dosage of baricitinib (BAR) for seronegative rheumatoid arthritis (RA) with over 80 years old onset. [Method] Five patients aged 80 years or older, diagnosed with seronegative RA at Niigata Rinko Hospital after April 2019, were treated for remission-induction with PSL and BAR 2 mg/day, and followed up to 12 weeks after the initiation of the therapy. [Results] DAS28 (3)-CRP at RA diagnosis averaged 3.9±0.77, the mean mHAQ was 2.04±0.92, the mean serum CRP was 10.4±5.7 mg/dl, and the mean dosage of PSL was 9.6±6.7 mg/day, respectively. Two weeks after the start of BAR, data were improved dramatically as the mean DAS28 (3)-CRP 1.27±0.51, the mean mHAQ 0.44±0.11, and the mean serum CRP 0.09±0.11 mg/dl. The mean dosage of PSL was also reduced to 5.5±3.5 mg / day. Furthermore, 12 weeks after the start of BAR, the improved state was maintained and the mean dosage of PSL was decreased to 3.6 ±3.1 mg/day. No adverse events were observed during the observation period. [Conclusion] Remission-induction therapy with PSL and BAR half dose can improve RA disease activity immediately, reduce the dosage of PSL, and perhaps prevent the onset of frailty in patients with super-aged rheumatoid arthritis.

P25-1

Clinical characteristics of NinJa 2019 RA patients treated with JAK inhibitors in each CKD stage

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Conflict of interest: None

[Objective] To clarify the characteristics of NinJa2019 RA patients treated with CKD treated with JAK inhibitors (JAKis). [Methods] Data of 12155 patients registered to NinJa2019 with serum creatinine level (N19Cr) were used, and patients treated with tofacitinib (TOF), baricitinib (BAR), peficitinib (PEF) or upadacitinib (UPA) were extracted. HAQ-DI, DAS28 and treatment were compared between N19Cr and each JAKi in total, or in three CKD stage groups, G1,2, G3, and G4,5. [Results] Patient numbers were TOF: 268, BAR: 204, PEF: 15 and UPA: 14. There was no difference in age and eGFR among N19Cr/TOF/BAR/PEF/UPA. Case number of CKD groups, G1,2 -G3- G4,5 were 8869-3106-180/183-81-

4/157-46-1/10-5-0/11-3-0. HAQ-DI of TOF was significantly higher than N19Cr in total and in G1,2. DAS28 of TOF and BAR were significantly higher than N19Cr in total and G1,2, and that of TOF was significantly higher than N19Cr in G3. Steroid and NSAIDs were more prescribed in patients treated with JAKis than N19Cr, except for steroid in TOF-G1, 2 and BAR-G3. [Conclusions] eGFR was less than 60 mL/min/1.73 m^2 in 21.4% to 33.3% of patients treated with each JAKi. Part of patients treated with JAKi have significantly higher HAQ-DI and DAS28, and they were treated more frequently with steroid and NSAIDs than N19Cr.

P25-2

Evaluation of MTX tapering in the patients with rheumatoid arthritis for treatment with JAK inhibitor

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Conflict of interest: None

Objective: If a patient with rheumatoid arthritis (RA) is in persistent remission, tapering the csDMARD could be considered. The aim of this study is to consider about MTX tapering in the patients with RA for treatment with JAK inhibitor (JAKi). Method: In this retrospective study, we evaluated 22 RA patients (77.3% of women, average age 60.5 years old, and disease duration 6.7 years) for treatment with JAKi (tofacitinib (n=7), baricitinib (n=11), peficitinib (n=4)) about MTX dose, background, and clinical course. Result: We classified to MTX tapering group (T group, n=11) and non-tapering group (N-T group, n=11). In T group, the dose of MTX at starting time of JAKi was 11.3 mg/w (8.2 mg/w at 24w). Significant difference did not detect to N-T group (10.7 mg/w) (p=0.678). SDAI at starting time and 24w did not detect significant difference with T and N-T group (22.23 to 3.30 (T) vs 22.85 to 4.29 (N-T)), p=0.558). RA patients after treatment of bDMARDs were 54.5% in T and 72.7% in N-T group. PSL combination rate at stating time of JAKi was 90.9% in T and 54.5% in N-T group. PSL discontinuation rate at 24w was 50% in T and 0% in N-T group. Conclusion: MTX tapering is possible in RA patients inducted remission with JAKi and MTX. But tapering MTX was difficult for RA patients continuing PSL.

P25-3

Clinical study of the efficacy and safety of upadacitinib for 10 patients with multidrug-resistant, refractory and highly active rheumatoid arthritis at our clinic for a short period of 12 weeks

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Conflict of interest: None

[Objective] To verify the efficacy and safety of the novel JAK inhibitor Upadacitinib (Upa) for high-active RA that is resistant to multiple biologics and JAK-Is. [Method] From April to July 2020, all 10 patients with refractory RA in our clinic Female age (mean below) 65.6y Illness 7.8y Stage average 2.7 Class1.5 ACPA202.4 RF79.2 DAS28-CRP5.58 J-HAQ 1.35 MMP334.7 Bio Average usage 3.5 JAK1.9 MTX combination rate 40% (average 7.5 mg) PSL combination rate 20% (average 2 mg). Upa 15 mg was administered these patient and the improvement of GSUS (mean 2.58) and PDUS (mean 2.38) in DAS28CRP J-HAQ MMP3 is evaluated from 2w to 12w. [Results] DAS28 was Significant improvement 2w3.32 (P<0.01) and 4w1.91 (P<0.002) after administration. MMP3 was 79.75 (P<0.005) after 4w, GSUS1.86 (P<0.05) PDUS1.2 (P<0.005) after 2w, GSUS1.32 (P<0.03) PDUS0.31 (P<0.002) after 4w Significant improvement in a short period. 12w after administration, 8 patients were in remission, 1 patient was LDA, and 1 patient was IR.1 patient had mild liver dysfunction as a side effect. [Conclusions] Significant improvement was observed in a short period of time for drug-resistant refractory pathology, and remission was obtained with a high frequency of 80%. We hope that Upa will have a long-term effect on more refractory RA patients in the future.

P25-4

Is Responsiveness to IL-6 Inhibitors Related to Responsiveness to JAK Inhibitors?

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Conflict of interest: Yes

[Objective] We focused on IL-6, a cytokine that utilizes JAK, among the cytokines suppressed by existing biologics, and investigated whether there was a relationship between response to IL-6 inhibitors and that of JAK inhibitors in RA patients. [Methods] RA patients who had a history of treatment with both types of drugs were selected and analyzed for efficacy in a retrospective manner. Efficacy was assessed by continuous use for at least 1 year, or SDAI improvement of at least 20%. Patients who had received more than one drug for each drug were evaluated for the first drug. [Results] There were 28 RA patients who had a history of treatment with both drugs. 22 patients were evaluable for drug efficacy. IL-6 inhibitors were tocilizumab in all cases, and JAK inhibitors were tofacitinib in 16 cases, baricitinib in 5 cases, and peficitinib in 1 case. IL-6 inhibitors were effective in 68% (15/22 cases), of which 80% (12/15 cases) were effective with JAK inhibitors. On the other hand, of the cases in which IL-6 inhibitors were not effective, 57% (4 cases / 7 cases) of the JAK inhibitors were effective. [Conclusions] Patients who were responsive to IL-6 inhibitors may have a higher rate of response to JAK inhibitors, but this was a small sample size and further data accumulation is desired.

P25-5

Outcomes of RA patients treated with JAK inhibitors at our facility

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Conflict of interest: None

[Objective] The JAK inhibitor (JAKi), which was comparable to the biologic (BIO) in EULAR recommendation 2019, has been launched for 7 years. Since the increase in switching from JAKi to a different JAKi, we analyzed the outcomes of RA patients treated with JAKi. [Methods] We investigated patient background, pretreatment drugs, and adverse events in 63 RA patients treated with JAKi at our hospital. We also investigated the retention rate of JAKi about pretreatment drug from 2013 to 2020. [Results] The average of age, duration and gender were 67 (y), 16 (y), and 78% female. Twenty patients haven't used BIO and 43 patients had used BIO. The persistence rate was 94% on no usage experience of BIO. However, its rate of anti-IL-6R antibody failure, anti-TNF failure and abatacept failure were is 60%, 89% and 67%. There were 6 cases who used 2 or 3 JAKi, the reason was ineffectiveness in 5 cases. 65% of patients continued some kind of JAKi, but 16% of patients were changed to BIO. Herpes zoster appeared in 7 cases, of which 2 cases were discontinued and in 5 cases were re-administered [Conclusions] Some patients exhibited resistance for multiple JAKi or intolerance. It is necessary to identify the optimal JAKi patients who seem to be a different type in the case of BIO.

P25-6

Short-term use experience of upadacitinib in patients with RA in clinical practice

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Conflict of interest: None

[Purpose] We report the short-term report use results of RA patients who used the JAK inhibitor upadacitinib (UPA), which became available from April 2020. [Subjects and methods] Since July 2020, 10 RA patients who used UPA at our clinic were targeted. The average age is 61.1 years,

The average RA morbidity is 15.2 years, and there are 4 cases of change from biologics (tocilizumab 1, adalimumab 1, abatacept 1, certolizumab pegol 1) and 5 cases were changed from other JAK inhibitors (tofacitinib 1 and baricitinib 4) The starting dose of UPA was 7.5 mg in 1 case and 15 mg in 9 cases, MTX was used in 5 cases at the start, and UPA single was 5 cases. The continuation status and efficacy were investigated. [Results] Stomatitis (2 cases), herpes zoster (1 case), and sore throat (1 case) were observed as adverse events, but none of them were serious. Patients satisfaction was high in all cases 4 weeks after the start of administration, and change in the mean DAS28-CRP value improved to 2.45 before administration and 2.17 4 weeks after administration. [Discussion] Although it has been used for a short period of the time, the use of UPA is useful for RA patients who use biologics for oral use, or for patients with diminished efficacy or decreased renal function with other JAK inhibitors.

P25-7

Filgotinib inhibits monocyte differentiation via pro inflammatoly cytokine production in osteoblasts

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Conflict of interest: None

[Objective] Filgotinib is a selective small molecule inhibitor of JAK 1 enzymes, and is currently in clinical development for the treatment of rheumatoid arthritis (RA). Here, we examined filgotinib inhibited monocyte differentiation and proinflammatoly cytokine production in osteoblasts. [Methods] To determine whether filgotinib was involved in proinflammatoly cytokine production, cytokines in filgotinib treated IL-6 and IL-6R stimulated MG63 (human osteosarcoma cell line) conditioned medium was measured using ELISA. Finally, to confirm if monocyte was differentiated with filgotinib, THP-1 was cultured with filgotinib treated MG63 conditioned medium. [Results] MCP-1/CCL2 and CXCL16 in filgotinib treated MG63 conditioned medium was significantly decreased compared with in nontreated MG63 conditioned medium. Additionally, THP-1 with IL-6 and IL-6R treated MG63 conditioned medium differentiated into multinuclear cells. On the other hand, THP-1 with filgotinib treated MG63 conditioned medium did not differentiate into multinuclear cells. [Conclusions] Filgotinib inhibited proinflammatory cytokine production. These data indicate that filgotinib acts on bone metabolism, suggesting that filgotinib may prevent bone destruction.

P26-1

Examination of 19 cancellation possibility examples of 35 MTX combination examples during 54 RA patients treated with TOF in our hospital for three years

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Conflict of interest: None

[Purpose] As we experienced a combination cancellation example of MTX in a continuation example this time at our hospital for TOF dosage three years, I report a background and the progress of the case. [Method] As for the dosage start MTX combination example during 54 continuation examples, MTX weight loss possibility example, 19 of 54.3% were MTX cancellation examples 31 of 88.6% of those with 35 for TOF dosage three years of our hospital. The average age at the time of the TOF dosage start of 19 MTX cancellation examples is 8.2 years during 63.8 years old, the mean contraction of a disease period. The quantity of mean MTX combination is 6.5 mg/week. DAS28ESR mean at a TOF start: 4.6, mean DAS-28CRP: 4.2. Result] The change (start/dosage three years later) of the disease activity after the TOF dosage of 19 MTX cancellation examples is DAS28ESR: It was good with 4.6/2.5. The reason of the MTX cancellation was gastrointestinal dysfunction, hepatic dysfunction such as good other stomatitis, a decrease in number of the lymphocytes, stroma-related pneumonia in progress. [Consideration, Conclusion] In this examination, maintenance of the effectiveness was able to experience a possible example after the cancellation of combination MTX of TOF for a long term.

P26-2

3 cases of rheumatoid arthritis in combination with JAK inhibitor and immunosuppressive medicine other than MTX

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Conflict of interest: None

There are quite a few cases that require biologics in the treatment of rheumatoid arthritis, and there are also cases in which the biologics have become ineffective. We experienced three cases of RA patients who were ineffective with biologics, who were in remission with the combined use of JAK inhibitors and immunosuppressants. The first case was a 71-year-old man who had difficulty using MTX due to problems with his cognitive function. TAC was used in combination with MTX, and BAR led to remission. The second case was a 64-year-old woman who was temporarily in remission with MTX, TAC, and BAR. After remission, TAC was discontinued and follow-up is underway. The third case was a 71-year-old man who had difficulty in introducing MTX due to BAR and interstitial pneumonia. AZA was used in combination with MTX, leading to remission. Although the observation period was short in all three cases, no obvious adverse events were observed with the combined use of BAR and TAC or AZA. It was considered desirable to use some immunosuppressive drug in combination with patients who have difficulty using MTX. It is estimated that there will be more cases in which it is difficult to continue to use MTX due to problems with renal function, lung condition, and cognitive function in the elderly society.

P26-3

JAK Failure in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Although there have been many reports on the efficacy of JAK inhibitors in rheumatoid arthritis, there have been few reports on subsequent drug selection in patients with inadequate response to JAK inhibitors. Drug use and treatment response afterwards were examined on the JAK inhibitor use stop example. [Methods] The subjects were 16 RA patients who discontinued use of JAK inhibitors. The cause of drug discontinuation, treatment to which the drug was changed, and response to the change were examined at Week 24 with DAS -28 CRP. [Results] JAK inhibitor was changed due to insufficient response in 5 patients, and the drug was changed due to decreased response in 2 patients. There were 7 adverse events. After discontinuation of the JAK inhibitor, 75% of the cases which changed to other JAK inhibitor achieved the remission. [Conclusions] Adverse events were the most common cause of discontinuation of JAK inhibitors. It was considered that the security of further symptom example number was necessary in the effect insufficient example.

P26-4

A Case of Rheumatoid Arthritis with Multiple Bowen's Disease While Using Tofacitinib

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Conflict of interest: None

[Cases] 77-year-old woman In 1997, She developed arthralgia and was diagnosed with rheumatoid arthritis. The effect of MTX was not enough. She was prescribed infliximab, etanercept and tocilizumab, but both were discontinued due to insufficient effect or secondary failure. From August 17, 2016, she was given tofacitinib 10 mg/ day, and her arthritis became low-disease activity. From around spring 2019, brown rashes appeared in her left and right cheeks and right forearm. She underwent biopsy from the three lesions, and all were diagnosed Bowen's disease, and completely removed. Tofacitinib has been discontinued and has not observed new Bowens disease. [Consideration] Bowen's disease is a squamous cell car-

cinoma limited to the epidermis, and multiple ones are rare if there are no factors such as the intake of arsenic. The use of Ruxolitinib (JAK 1, 2 inhibitors), cases of multiple skin cancer has been reported. In this case, there is no history of arsenic intake, it has developed after the start of JAK inhibitors, and it is considered undeniable that JAK inhibitors may have been involved in Bowen's disease. It is necessary to be careful to malignancy of skin, during JAK inhibitor administration.

P26-5

A case of intestinal Bechet's disease-like symptoms associated with chronic myelomonocytic leukemia with JAK2 V617 gene mutation was improved by ruxolitinib, a JAK inhibitor

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Conflict of interest: None

[Case] A 74-year-old man was treated with colchicine for nodular erythema and oral ulcers and diagnosed with Bechet's disease (BD). One year ago, he was hospitalized for bloody stool and treated with 20 mg/day of prednisolone (PSL) as ulcers were found at the terminal ileum. From the same period, the monocyte level was high (1000/uL or more), the platelet level rose to about 500,000/uL, there was a der (1; 7) (q10; p10) translocation, and the gene mutation of JAK2 (V617F) was observed in the peripheral blood. Therefore, we diagnosed the patient with BD-like symptoms associated with chronic myelomonocytic leukemia (CMML), started a treatment with azacitidine, and tapered off the PSL prescription. However, bloody stool appeared two months ago, and multiple ulcers were observed at the terminal ileum again. We then administered 30 mg/day of PSL and ruxolitinib. After that we tapered off the PSL, and there were no flares of BD-like symptoms. [Conclusions] Patients with CMML sometimes show BD-like symptoms. However, only a few reports demonstrated the association of JAK2 (V617) gene mutation and BD-like symptoms. In this case. ruxolitinib, a JAK inhibiter improved the BD-like symptoms, suggesting a relationship between BD-like symptoms and cytokine over activation caused by the JAK2 mutation.

P26-6

Double blinded randomized controlled trial to reveal the effects of Brazilian propolis intake to rheumatoid arthritis disease activity index; BeeDAI

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Conflict of interest: Yes

[Purpose] Propolis has various physiological activities, and has been proven to suppress arthritis and IL-17 production in a mouse model. Therefore, the effect of propolis administration on patients with rheumatoid arthritis (RA) with moderate disease activity was examined in a double-blind randomized trial. [Methods] Eighty female RA patients were randomized to 40 in the propolis group (P group) and 40 in the placebo group (C group) and observed for 24 weeks. Changes in disease activity, HAQ-DI, SF-36, joint sonography, cytokines (IL-6, IL-17, IL-10), anti-CCP antibody, and MMP-3 were evaluated. [Results] The age was 61.5 years, 12% (2.0 mg / d) used glucocorticoids, 70% used MTX (12 mg / w), and 21% used bDMARDs. DAS28-ESR decreased from 3.96 [3.53, 4.32] to 3.86 [3.07, 4.46] in group P and from 3.89 [3.50, 4.31] to 3.40 [3.07, 4.46] in group C, but there was no significant difference between the groups (p = 0.427). HAQ-DI changed from 0.10 [0.00, 0.453] to 0.10 [0.00, 0.45] in group P and from 0,05 [0.00, 0.26] to 0.12 [0.00, 0.31] in group C, but there was no significant difference between the two groups. In the SF-36 subscale, there was no significant difference between the groups.

P26-7

The influence of the multi drug resistance factor MDR1 expression on the effect of Janus kinase inhibitors

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Conflict of interest: None

[Objective] Janus kinase inhibitor (JAKi) has been developed for the treatment of rheumatoid arthritis (RA). However, there are ineffective cases. We focused on multidrug resistance factor (MDR1). To the best of our knowledge, there are no reports on the association between JAKi and MDR1. In this study, we assessed whether the expression of MDR1 had any relations with JAKi. [Methods] Human Umbilical Vein Endothelial Cells (HUVECs) were exposed with rifampicin (RIF) for 72 hours to induce MDR1, followed by the treatment with JAKi (Tofacitinib, Baricitinib, and Peficitinib) for 48 hours. Then, the proliferation of HUVECs were assessed by WST assay and Hoechst stain. MDR1 expression was assessed by real time polymerase chain reaction. [Results] MDR1 expression in HUVEC was increased by RIF exposure. Treatment with JAKi decreased proliferation of HUVECs. Proliferation of HUVECs after JAKi treatment was higher under RIF pretreatment than control. MDR1 expression by RIF exposure may have increased the extracellular efflux of JAKi and attenuated its effect, leading to an increase in proliferation of the HUVECs. [Conclusions] It was demonstrated that MDR1 expression in HUVECs was increased by RIF exposure. Our results suggest that the effect of JAKi may be affected by MDR1 expression.

P27-2

trend in patients with rheumatoid arthritis undergoing total knee arthroplasty

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Conflict of interest: None

[Objective] It has been reported that the number of artificial joint replacement surgery for large joints has decreased due to advances in the treatment of rheumatoid arthritis (RA), and that the age of patients at the time of surgery is increasing year by year. The purpose of this study was to investigate the trend in the background of RA patients who underwent total knee arthroplasty (TKA). [Methods] The patient background of RA patients was compared in the first and second term, divided into two stages depending on the year of surgery (first term: 2004-2011 84 cases, second: 2012-2019 54 cases). [Results] Items with significant differences between the first and second terms were concomitant MTX (%) 34.5/57.4, age (year) 67 /71, and CRP (mg/dl) 1.82/0.99. The concomitant of biologics, PSL, csDMARD other than MTX, serum MMP-3 and ESR did not show a difference in the first and second terms. In the knee X-ray, there was no difference between FTA (°) 179/177, but osteophyte was more found 72.2% in the second term (51.2% in first term). [Conclusions] Compared to the first term, in the second term, patients were older, but more concomitant MTX, lower CRP, and more have osteophytes, so it seems to be the disease activity is relatively low.

P27-3

Joint orientation angle of lower limb in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study was to evaluate joint orientation angle of lower limb in patients with rheumatoid arthritis (RA). [Methods] A total of 75 patients (93 knees) scheduled to undergo total knee arthroplasty (TKA) for RA were enrolled. Hip-knee-ankle (HKA) angle, mechanical lateral distal femoral angle (mLDFA), mechanical medial proximal tibial angle (mMPTA) and joint line convergence angle (JLCA) were measured on preoperative anteroposterior whole-leg radiographs in standing position. Positive value in HKA angle and JLCA was defined as valgus and varus alignment, respectively. [Results] The mean value ± standard deviation of HKA angle, mLDFA, mMPTA and JLCA were -3.2±9.3° (range, -20°-24.4°), 86.5±3.7° (78.8°-96.2°), 86.0±4.0° (73.6°-97.0°) and 2.6±4.2° (-8.6°-13.0°), respectively. HKA angle<-3° was 55.9% and HKA angle>3° was 22.6%. In knees with HKA angle<-3°, mLDFA>90° was 28.8% and mMPTA<85° was 67.3%. In knees with HKA angle>3°, mLDFA<85° was 71.4% and mMPTA>90° was 47.6%. HKA angle was correlated with mLDFA (r=-0.69, P<0.05), mMPTA (r=0.75, P<0.05) and JLCA (r=-0.81, P<0.05), respectively. mLDFA was correlated with mMPTA (r=-0.31, P<0.05). [Conclusions] Knees with RA showed a diversity in femoral and tibial coronal alignment.

P27-4

Total Knee Arthroplasty without Patellar Resurfacing for Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We investigated the outcome of total knee arthroplasty (TKA) without patellar resurfacing in patients with rheumatoid arthritis (RA). [Methods] The subjects were 86 patients with 113 knees. The mean follow-up period was 9 years and 5 months. The items investigated were clinical and plain X-ray findings. [Results] Knee ROM before surgery/at assessment was -12.8/-1° of extension and 119.6/119.6° of flexion, while the JOA score was 42.4/90.2. At assessment, the incidence of anterior knee pain or discomfort was 7.1%, respectively. There were no significant differences of knee flexion at assessment 124.3/118.2° (p=0.048), follow-up period, age, use of biological agents, type of TKA, ROM, JOA score, and FTA between the patients with patellar findings (23.9%) and those without patellar findings. However, the incidence of discomfort was significantly higher in the patients with patellar findings. Patellar resurfacing was not performed in any of the patients. [Conclusion] The clinical outcome of without patellar resurfacing TKA was generally favorable and was similar between the patients with and without patellar findings. We concluded that without patellar resurfacing TKA was an acceptable procedure in patients with RA.

P27-5

Changes in the background characteristics of rheumatoid arthritis patients who undergone total knee arthroplasty

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Conflict of interest: None

[Objectives] We investigated the background characteristics of RA patients who had undergone TKA in our hospital. [Methods] Subjects were 234 RA patients (294 joints) who underwent primary TKA from 2000-2019. Changes in the number of surgeries, patient background characteristics, drug treatment history and preoperative X-ray images were investigated. 2000-2009 was the first period, and 2010-2019 was the second period. [Results] The total number of RA-TKAs was 294 (8.1%), compared to the total number of primary TKAs of 3650 during the survey period at our hospital. The proportion of RA-TKA decreased significantly in 137/1266 cases (10.8%) in the first perio and 157/2384 cases (6.6%) in the second period (p<0.001). There were no significant differences in age at surgery, disease duration between the two periods. There was no significant difference in the proportion of patients who were on corticosteroids, while those on methotrexate and biological agents were increased from 14.4% to 52.3% and from 1.9% to 20.0%. Preoperative Hb and Alb were significantly increased (p=0.003, p=0.011), and preoperative CRP was significantly decreased (p<0.001). [Conclusion] The proportion of RA-TKA decreased, anemia and albumin levels were significantly improved, and disease activity control was better.

P27-6

Total knee arthroplasty for tibia plateau fracture in a patient with rheumatoid deformity of the knee: a case report

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Conflict of interest: None

Case: Female patient with rheumatoid arthritis (RA), 79 years old. The onset of RA was 59 years old. She had been treated with etanercept 25 mg/w and prednisolone 4 mg/d for RA, and alendronate 35 mg/w for osteoporosis. Lateral joint space narrowing in the right knee had previously been found. She fell down and was transported to our hospital. Tibia plateau fracture was found on the deformed knee. Total knee arthroplasty (TKA) was scheduled, after bone union in the epiphyseal area was gotten, using teriparatide and casting. Range of motion exercise was started after six weeks after the injury, and TKA was performed 12 weeks after the injury. Nexgen-LCCK was used for the arthroplasty, but metal augmentation was not needed. The tibial rotation was defined with reference to the medial tangent of the proximal tibia. Two years after the operation, the range of motion is 0-135 °, the JOA score (RA) is 91 points, and the course was good. Summary: Total knee arthroplasty was performed, after bone union in tibia plateau fracture on the knee with rheumatoid deformity, using teriparatide and casting. The course was good.

P28-1

Comparison of the resection arthroplasty and joint-preserving arthroplasty for rheumatoid forefoot deformity

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Conflict of interest: None

Purpose: To compare the short-term clinical outcomes of joint-preserving arthroplasty and resection arthroplasty for forefoot deformity in patients with rheumatoid arthritis (RA), and to clarify the advantages of resection arthroplasty. **Methods:** 29 patients (1 male and 28 female) of which 38 feet underwent forefoot surgery in the period since 2006. This retrospective study was divided into two groups; Group 1 included 13 feet in joint resection arthroplasty (mean age 62.8 ± 10.3); Group 2 included 25 feet in joint-preserving arthroplasty (62.3 ± 10.3). Survey items included; patients' backgrounds, surgical outcomes, other items. **Results:** Surgery time Group 1 was 162.4 ± 53 and Group 2 was 241.5 ± 84.3 minutes and hospitalization days was 27.5 ± 13 and 47.6 ± 22.8 days respectively. Noted both results were significantly shorter for Group 1 than Group 2. Noted both JSSF RA and foot scale and SAFE-Q were higher in Group 2, but improvement was more gradual. **Conclusions:** The surgical outcomes were better in joint-preserving arthroplasty, but those of resection arthroplasty were also good. Furthermore, resection arthroplasty has the advantage of a shorter operation time, shorter hospital stay. Resection arthroplasty is recommended for patients at high risk of anesthesia such as the elderly.

P28-2

Short-term clinical results of joint preserving surgery for rheumatoid forefoot deformity

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Conflict of interest: None

[Objective] To investigate short-term clinical results of joint preserving surgery for rheumatoid forefoot deformity. [Methods] Sixteen foot of 9 patients, of which surgery was performed at our hospital between 2015 and 2018, were included in this study. The modified Scarf method was performed for the hallux valgus and the distal shortening oblique osteotomy for the claw toes. Their mean follow-up period was 37.6 months. Postoperatively, the HVA, the M1M2 angle, and M1M5 angle were measured on the standing anteroposterior radiographs for the forefoot. JSSF-RA scale, SAFE-Q were also recorded. [Results] Postoperatively, the HVA, M1M2 angle, and M1M5 angle significantly improved compared to those preoperatively (mean HVA: 51.2→28.9, M1-M2: 16.7→11.2, M1-M5: 34.6→24.9). The postoperative mean JSSF-RA scale showed pain: 30, deformity: 18, ROM: 13.3, walking ability: 14.8, ADL: 7.2, and total: 84 points. The postoperative mean SAFE-Q showed pain: 85, physical functioning: 75.4, social living: 84, shoe-related: 85, general health: 70 points. [Conclusions] Short-term results of joint preserving surgery for rheumatoid forefoot were generally good, especially in the pain scale. Mid- to long-term follow-up will be necessary to evaluate this surgical method for the rheumatoid forefoot deformity.

P28-3

Short-term surgical results for hallux valgus; comparing RA and non-RA patients

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Conflict of interest: Yes

[Objective] The purpose of this study was to evaluate the short-term radiographic results of patients who underwent osteotomy for hallux valgus. [Methods] The present study was based on 27 feet that underwent osteotomy for hallux valgus. In 18 of the feet hallux valgus was attributed to rheumatoid arthritis (RA), and 9 were due to other causes (non-RA). The hallux valgus angle (HVA) was measured pre-, post-, and 1 year after surgery, and we investigated the factors that could influence the results. [Results] The mean preoperative HVAs were 46° and 43° in the RA and non-RA groups, respectively (P=0.26), and after surgery they improved to 11°/9° (P=0.20). One year after surgery the HVAs had again deteriorated to 23° and 13° (P=0.06), respectively. In the RA group K-wires were used for fixation in 14 feet, while only 4 feet were fixed with locking plates. Among the non-RA group 1 foot was fixed with K-wire, 7 with plates, and 1 with a plate and k-wire. Recurrence was observed in 10 feet from the RA group and only 1 foot from the non-RA group (P<0.05). Feet in the RA group that were treated with K-wire showed a significantly higher recurrence rate (P<0.05). [Conclusions] The results of this study would suggest that rigid fixation with a locking plate should be used for RA patients.

P28-4

Two cases of rheumatoid arthritis who had total ankle replacement through a lateral transfibular approach (Trabecular Metal Total Ankle; TM ankle)

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Conflict of interest: None

[Objective] The purpose of this study is to report clinical outcomes for two cases of rheumatoid arthritis (RA) who had total ankle replacement through a lateral transfibular approach (TM ankle). [Case 1] A 44 years old woman [Medical History] She had RA at 17 years old, has been treated with infliximab and methotrexate. The arthralgia in her right ankle joint occurred at 42 years old, and developed gradually, and so she had TM ankle. Currently 19 months after surgery, the course is good. [Case 2] A 76 years old woman [Medical History] She had RA at 45 years old, has been treated with Etanercept and Iguratimod. The arthralgia in her left ankle joint occurred at 75 years old, and developed gradually, she had received orthosis therapy, but less effective, and so she had TM ankle. Two months after surgery, she had the ankle lateral malleolus plate removed due to the infection, and the infection subsided. Currently 11 months after surgery, her walking condition is good. [Clinical significance and discussion] Good surgical results of TM ankle have been reported although a small number. Even in RA cases, it has been actively performed overseas and good results have been reported. Even in RA, if a case is selected, it seems that there is an advantage in performing this surgical procedure.

P28-5

A case of rheumatoid arthritis with bilateral medial malleolus stress fractures due to severe varus knee deformity

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Conflict of interest: None

[Introduction] There are few reports of tibial stress fractures associated with varus knee deformity due to knee osteoarthritis (KOA). And most of the sites of occurrence are the proximal tibia. In this study, we experienced the medial malleolus stress fractures which is thought to be caused by varus knee deformity due to KOA in a patient with rheumatoid arthritis (RA). [Case] A 70-year-old woman with RA and osteoporosis. The patient presented bilateral knee pain without ankle pain. Severe varus knee deformity was observed. First, TKA on the right side was performed. Two months after the operation, swelling and pain of the left ankle joint appeared and fractures of the bilateral medial malleolus were observed. There was no pain in the right ankle joint and TKA on the left side and osteosynthesis of the left ankle were performed. After the operation, the course is good. [Discussion] In this case, it is considered that fractures occurred which caused by mechanical stress due to varus knee deformity and, fragile bone due to RA and osteoposis. It is cosidered the patient had no symptom on the right ankle, because the FTA was corrected by TKA. [Conclusion] We experienced a case of RA with ankle fracture due to bilateral varus knee deformity. After the operation, the course was good.

P29-1

Long-term results of Sauve-Kapandji procedure using poly-L-lactic acid-containing hydroxyapatite screw for wrist disorder in rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study was to investigate long-term results of Sauve-Kapandji (SK) procedure using poly-L-lactic acid with hydroxyapatite (HA-PLLA) screw for wrist disorder in rheumatoid arthritis. [Methods] From March 2004 to November 2006, 12 joints of 11 patients with rheumatoid arthritis who underwent SK procedure using the HA-PLLA screw were included in this study. The average age at surgery was 51.8 years (29-70), and the average observation period was 14.3 years (12.7-15.3). [Results] Bone fusion was observed in all joints. Screw breakage was observed in one joint, and there were no cases of marked bone resorption around screws. [Conclusions] No marked bone resorption around screws was observed, and bone fusion was observed in all cases by SK procedure using HA-PLLA screws.

P29-2

Clinical Results of Finger Extensor Rupture at the Wrist

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Conflict of interest: None

[Objective] Extensor tendon rupture is often seen in RA patients. We report the clinical results of extensor tendon reconstruction. [Methods] Five hands of 5 patients with extensor tendon rupture that was surgically treated in our hospital from 2019 were included in this study. We reconstructed the ruptured extensor by using several procedures in combination with one of the several procedures for wrist arthroplasty. Clinical results was evaluated by finger range of motion and according to the evaluation criterion for the wrist. [Results] Extension lag of the MP joint was distributed 0 to 60 at the final follow-up. The average arc of wrist dorsi-/volar-flexion slightly decreased, but that of forearm rotation increased after the treatment. In a case of poor result, wrist pain persisted mainly due to pseudogout, which further resulted in lack of postoperative tendon gliding exercise. In other cases, no wrist pain reported, good scores for activities of daily living were obtained, and then extension lags were small. [Conclusion] For treatment of extensor tendon rupture, early tendon gliding exercise should be promoted with a care for re-rupture, and painless and stable wrist joint should be achieved.

P29-3

Impact of accumulation of disease activity 10 years after rheumatoid wrist surgery on postoperative assessment

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Conflict of interest: None

[Purpose] The relationship between the accumulation of RA disease activity for ten years and postoperative evaluation of wrist surgery in Bio era were investigated. [Methods] We investigated 55 wrists in 50 patients with rheumatoid wrist who were performed wrist surgery between 2006 and 2009. The mean age at surgery was 57.5 years (25-80 years) and the average RA duration was 8.9 years (0-34 years). The mean DAS28-ESR taken every 3-4 months for 10 years after surgery was determined and divided into REM+LDA group and MDA+HDA group. The Bio use rate, changes of grip power and ROM and changes in Larsen grade score of radioscaphoid joint and midcarpal joint were investigated. [Results] The Bio use rate was 34.1% in REM+LDA group and 45.5% in MDA+HDA group. There were no significant differences in grip strength and ROM between the two groups, and the total change in Larsen grade of the radioscaphoid joint and midcarpal joint showed significant differences between the two groups. [Conclusion] The accumulation of disease activity for 10 years after RA wrist surgery may affect the total Larsen grade change in the radioscahpoid joint and midcarpal joint.

P29-4

Report of surgical treatment of 2 patients with RA with wrist joint dysfunction

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Conflict of interest: Yes

[Introduction] Wrist dysfunction is an important issue in the treatment of RA. Therefore, early functional improvement is required. Here we report two RA patients with wrist destruction who required partial wrist fusion early after drug intervention. [Case 1] A 38-year-old woman was referred to our hospital for left wrist joint pain. At the time of examination, swelling and tenderness of the left wrist joint were observed. After 6 months of medication, no improvement in symptoms was observed, so partial wrist fusion was performed. [Case 2] A 38-year-old woman was referred to our hospital for right wrist joint pain. A plain X-ray image showed fusion of the carpal bones. We described drug treatment, but she herself chose wrist arthrodesis. The postoperative course was good in both cases, and the pain improved. [Conclusion] In the case of monoarthritis type RA, synovitis and bone destruction are observed in the patient, but blood biochemical tests show no abnormal findings, and there are some cases in which drug treatment is ineffective. For these cases, aggressive surgical treatment should be considered rather than continuing conservative treatment.

P29-5

Clinical outcome of the PROSNAP linked total elbow prosthesis for rheumatoid elbows with periarticular fracture

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Conflict of interest: None

[Objective] We investigated the clinical results of total elbow arthroplasty (TEA) using the linked elbow prosthesis (PROSNAP) for rheumatoid elbows with periarticular fracture. [Patients and Methods] We investigated 6 elbows of 6 rheumatoid arthritis (RA) patients. The mean follow-up period was 44.8 (range 6-96) months. Fracture site were olecranon in two, medial humeral condyle in two, distal humerus fracture in one, supracondylar in one. The clinical condition was assessed according to range of motion (ROM), Japanese Orthopaedic Association-Japan Elbow Society Elbow Function Score (JOA score), and Mayo Elbow Performance score (MEPS), and postoperative complications. [Results] The mean postoperative ROM in extension and flexion were -19.2 degrees and 143.3 degrees, respectively. The mean postoperative JOA score and MEPS were 92.5 points and 95.0 points, respectively. In all cases, bone union or fibrous union were achieved at the final follow-up. No patient showed evidence of infection or implant loosening. [Conclusions] The reconstruction of PROSNAP for rheumatoid elbows with periarticular fracture by PROSNAP TEA was safe procedure with satisfactory clinical results.

P30-1

Risk factors for postoperative complications in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study is to investigate the risk factors of postoperative complications of rheumatoid arthritis (RA), especially in surgical site infection (SSI). [Methods] we reviewed 525 orthopaedic surgeries that were performed in two institutes from January 2015 to December 2018. The mean age was 67.3 years old. The mean of RA disease duration was 21.5 years. [Results] SSI were identified 22 cases (4.2%). Total SSI involved five cases of superficial SSI and 17 cases of deep SSI. SSI were happened most in Foot and ankle surgeries (10/103 cases: 9.9%). Multivariate logistic regression analysis revealed that the risk factors of SSI were sex (male), lower BMI, surgery time (P=0.0013) and foot and ankle surgeries ($p<0.001$). Corticosteroid was used for 65.7% patients, MTX and bioDMARDs were used 62% and 30.4%, respectively. The medical treatment content was not an independent risk factor for SSI. [Conclusions] We should pay close attention to surgery time and foot surgeries to prevent postoperative infection.

P30-2

The efficiency of reconstructive surgery in rheumatoid hand and foot from a viewpoint of patients' daily livings

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Conflict of interest: Yes

[Objective] To elucidate the efficiency of surgical reconstruction in rheumatoid hand and foot from patients' viewpoint through QOL, body composition, and physical activity. [Methods] The authors subjected thirteen patients (male 1, female 12) among sixteen patients who underwent functional reconstructive surgery in hand and foot. The subjects were evaluated before the surgeries, three months later, and six months later. Health assessment questionnaire (HAQ), euro-QOL (EQ-5D), body composition, and physical activity were adopted as indicators and compared with each surgical location. [Results] The average age was 66.2 years and the average disease duration was 26.0 years. The number of cases with hand surgery was six, foot surgery was two, and hand and foot simultaneous surgery were five. The HAQ score improved among cases with hand surgery. The EQ-5D was unchanged among cases with hand surgery and foot surgery but improved significantly among cases with hand and foot simultaneous surgery. [Conclusions] We introduce hand and foot simultaneous surgery dependent on cases because of the windows of opportunity among exacerbated cases. QOL improved significantly then multiple location surgeries would have noteworthy therapeutic values from the viewpoint of patients' daily livings.

P30-3

Perioperative complications for the cervical spine lesions of rheumatoid arthritis

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Conflict of interest: None

[Objective] The rheumatoid cervical disorders are often found in the upper cervical spine represented by subluxation of the atlantoaxial vertebral spine. We investigated the characteristics of perioperative complications of RA cervical spine lesions. [Methods] The subjects were 92 RA cervical spine surgeries performed at our hospital between 2010 and 2020. Perioperative complications were compared between the upper cervical spine surgery group and the middle and lower. [Results] The pathological conditions were AAS in 38 cases, AAS + subluxation of the axis in 1 case, rheumatoid myelopathy in 50 cases, ossification of the posterior longitudinal ligament of the cervical spine in 2 cases, and central cervical spinal cord injury in 1 case. For the middle and lower cervical lesion the same surgery as for normal degenerative diseases was selected, with laminoplasty in 47 cases and laminectomy in 6 cases. There were 18 perioperative complications. By surgical site, upper cervical spine surgery was performed in 11 cases including 2 deaths, and middle and lower cervical spine surgery was performed in 7 cases, and perioperative complications were higher in upper cervical spine surgery. [Conclusions] More careful perioperative management was needed in surgery on the upper cervical spine.

P30-4

Prevalence of rotator cuff tear on MRI in the patients with rheumatoid arthritis having shoulder pain

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Conflict of interest: None

[Objective] The diagnosis of shoulder pain in RA patients achieved remission is difficult to distinguish synovitis with RA from rotator cuff tear (RCT). The purpose of this study was to investigate the prevalence of RCT on MRI in the patients with RA having shoulder pain. [Methods] Twenty-nine shoulders in 19 patients (average 64.9 years old, 6 males, 13 females) with shoulder pain investigated by MRI were included in this study. The average duration of the illness was 6.3 years. MTX was used in 14 cases (average 6.6 mg/ week) and PSL was used in 6 cases (average 2.7 mg/ day). Biologics were used in 6 cases. The prevalence of RCT and the associated lesions was investigated on MRI. [Results] Twelve shoulders in 29 patients (41.4%) had RCT. Bone erosion in the area rotator cuff attached in 16 cases, subacromial synovitis in 14 cases, arthritis of the glenohumeral joint in 9 cases were detected. The patients with RCT tended to be older and had longer duration of the illness compared with the patients without RCT. [Conclusions] This study suggested that RCT was commonly observed in the patients with RA. To diagnose the cause of the shoulder pain, detailed examination should be carried out.

P30-5

Long-term clinical results of a case of 12 joints reconstruction for mutilans type psoriatic arthritis

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Conflict of interest: None

[Purpose] We report a case of mutilans type psoriatic arthritis with generalized skin erythema and desquamation. 15 years have passed since 12 joints were reconstructed. [case] A 31 year-old man (He is now 46 years old.) was admitted to our hospital in 2005. At the age of 17, he was diagnosed with psoriatic arthritis and was treated with immunosuppressant Cys (50 ~ 75 mg) mainly at the dermatology department of another hospital. Since 2 years ago, he had difficulty walking due to knee and ankle pain, and visited the presenter for surgery. Both knees showed end-stage joint destruction of X-P. Bilateral TKA were performed in one stage while Cys was continuously administered. It became possible to walk independently in postoperative 4 weeks. After that, while continuing the administration of Cys, 12 joints of the whole body were reconstructed sequentially. He is currently working as a long-distance truck driver. [conclusions] A case of mutilans type psoriatic arthritis in a bedridden patient who had to undergo joint reconstruction of 12 joints of the whole body was presented. Surgery is risky and requires continuous follow-up, but quality of life has improved dramatically.

P31-1

Direct anterior approach for hip arthroplasty in spondyloarthritis

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Conflict of interest: None

[Objective] The purpose of this study was to report the clinical experience of total hip arthroplasty (THA) via a direct anterior approach (DAA) in spondyloarthritis. [Methods] We studied five patients with spondyloarthritis who underwent THA via a DAA using fluoroscopy. The preoperative template was performed according to spinopelvic alignment and stiffness. We investigated the JOA score, alignment of the acetabular component, and cumulative incidence of dislocation. [Results] Preoperative PI - LL was 18 - 65°, and ΔLL was -4 - 30°. The average radiographic inclination was 40.5°, and anteversion was 17°. The average JOA score was improved from 45.7 to 80.5. No dislocation occurred. [Conclusions] This study has shown that the THA via a DAA based on spinopelvic alignment and stiffness can be helpful in spondyloarthritis.

P31-2

HLA-B 54, 61showed significantly higher frequency in patients with spondyloarthritis (SpA) and pustulotic arthro-osteitis (PAO) with axial lesions

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Conflict of interest: None

[Objective] We investigated the HLA class I gene of patients with axial lesions classified into SpA and PAO at our hospital. [Method] HLA-B typing was performed using the PCR-rSSO method for 140 patients with axial lesions classified as SpA or PAO at our hospital. [Results] Of the 140 cases, alleles that were positive in 10 or more cases were B61 in 45 cases, B54 in 36 cases, B51 in 27 cases, B7 and B35 in 20 cases each, B60 and B62 in 19 cases each, and B46 in 18 cases, B52 in 12 cases, and B55 in 10 cases. As a result of testing the positive rate of allele with that of a general Japanese person at HLA Research Institute using the chi-square test, B54 and B61 showed a high frequency with a significant difference. (B54: $p = 0.0002$, B61: $p = 0.0354$). In addition, of the 140 cases, these allyls were more frequent in 20 patients with advanced spinal lesions in which ankylosing was observed more than three consecutive vertebral bodies on spinal radiographs. [Conclusions] HLA is significantly more involved in disease development than other genes, and specific HLA class I alleles are thought to be associated with seronegative arthritis, including SpA. Our findings suggest that HLA-B 54, 61 may be a risk factor in the development of axial lesions in SpA and PAO.

P31-3

Clinical characteristic of SAPHO syndrome/pustulotic arthro-osteitis (PAO) in the real-life clinical setting -single-center analysis

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Conflict of interest: None

[Objective] To clarify the clinical characteristic of SAPHO syndrome/PAO in the real-life clinical setting. [Methods] Patients with SAPHO syndrome/PAO patients, who visited outpatient clinic in Fujita Health University between 2012 and 2019 and who met the criteria proposed by Benhamou, were included. Clinical information was retrospectively collected. Clinical features, the transition of the treatment, duration of continuation of the drugs, and drug survival rate were examined. [Results] 17 cases were included. Mean age and disease duration were 46.2 and 12.4 years, respectively. Of these, 23% were male, 41% on prednisolone. All were bio-naïve. Fourteen had cutaneous manifestations as an initial symptom. Of 17 cases, 76% had sternoclavicular joints, 47% axial joint, 29% peripheral joints, respectively. As a treatment, the number of a IL-23p19 inhibitor was immediately increased after the market launch. Mean durations of drug survival (months) were 27 for TNF inhibitors, 9 for a IL-23p19 inhibitor. Continuation rate at 1 year was 44% for TNF inhibitors, 80% for a IL-23p19 inhibitor. The main reason for cessation was inadequate response to joint involvement. [Conclusions] Our real-life data suggest that IL-23p19 inhibitor were frequently used and had relatively better continuous rate.

P31-4

Tietze's syndrome: significance of differential diagnosis in rheumatic diseases

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Conflict of interest: None

[Objective] To realize again the importance of Tietze's syndrome in the differential diagnosis of chest pain, taking into account knowledge on rheumatic diseases affecting the anterior chest wall, especially spondyloarthritis. [Methods] Retrospective reviews on both literatures concerning Tietze's syndrome and 14 patients with the disease, who were excluded infection and neoplasm. [Results] (1) Six males and 8 females were with younger than 50 years old except a 70-year-old-female. (2) Severe acnes and pustules were observed in 7 patients, and one with psoriatic skin lesion was diagnosed on psoriatic arthritis in his clinical course. (3) Two patients with HLA-B27 have no feature of ankylosing spondylitis. (4) No particular features were in X-ray and CT scanning findings. (5) Sacroiliac joint changes were seen in 2 patients and enthesopathy in sole of the foot and Achilles' area in 6 patients. (6) Treatments with NSAID, SASP, MTX, LEF, and TAC were done. (7) Serological tests were negative or low-titers in general. (8) Ten patients were followed-up over 4 years, and 4 lost. [Conclusions] We should differentiate Tietze's syndrome from spondyloarthritis, addressing between sternoclavicular hyperostosis and various rheumatic diseases.

P31-5

Effectiveness of IL-17 inhibitors in the treatment of psoriatic arthritis compared to TNF inhibitors

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Conflict of interest: None

(Objectives) Biologics such as TNF inhibitors (TNFi) and IL-17 inhibitors (IL-17i) are currently approved for the treatment of psoriatic arthritis (PsA). We evaluated the effectiveness of TNFi and IL-17i, which are central to PsA treatment. (Methods) We examined 28 patients who were diagnosed as PsA from August 2006 to October 2020 in our hospital and treated with TNFi or IL-17i. We analyzed DAS28-CRP and MDA achievement. (Results) TNFi and IL-17i were given as the first biologics to 19 patients and 8 patients. Mean DAS28-CRP of each group after 12 weeks was 2.1±0.8 and 1.9±0.8 (P=0.71) and MDA achievement ratio was 70.6% and 87.5% (P=0.62). 14 patients changed their first biologics to the second biologics after 66.5±53.0 months because of inadequate response. 4 patients treated with TNFi before were given other TNFi and 10 patients, of whom 8 were treated with TNFi, 1 with IL-17i and 1 with IL-12/23i before, were given IL-17i as the second biologics. Mean DAS28-CRP of each group after 12 weeks was 2.2±0.4 and 1.7±0.4 (P=0.07) and MDA achievement ratio was 70.6% and 87.5% (P=0.62). (Conclusions) IL-17i were effective both as the first biologics and as the second biologics for PsA and their effectiveness was equivalent to that of TNFi. IL-17i can be a key for the treatment of PsA.

P31-6

Collagen Turnover Markers are Associated with Active Psoriatic Arthritis and Decrease with Guselkumab Treatment in a Phase-3 Clinical Trial

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Conflict of interest: Yes

[Objective] To evaluate tissue-derived extracellular matrix (ECM) products in serum of active psoriatic arthritis (PsA) patients (pts) in the DISCOVER (D) 2 study & their relationship with radiographic damage and clinical response of guselkumab (GUS) treatment. [Methods] In D2, pts were treated with GUS 100 mg at Week (w) 0, 4, then every 8w; GUS 100 mg q4w; or placebo (PBO). 11 serum biomarkers of ECM collagen formation (PRO-C1, -C2, -C3, -C4, & -C6) & degradation (C1M, C2M, C3M, C4M, C6M, & COL10) were measured in 260 pts at w0, 4, 24, & 52 and in 76 healthy controls (HC). [Results] At baseline (BL), C1M, C3M, C4M, C6M and PRO-C3 & PRO-C6 were significantly higher in PsA pts vs HC. BL C3M, C4M, & C6M were positively correlated to BL skin & joint disease; BL C1M, C3M, C4M, C6M, & PRO-C1 were positively correlated to BL radiographic damage. In pts treated with GUS or PBO, there were no significant differences in BL expression levels of C1M in responders vs non-responders. However, responders in GUS group had a significantly greater reduction in C1M levels compared to non-responders. [Conclusion] C1M serves as a biomarker that tracks with joint response. C1M reduction in responders was observed, providing insight into how

GUS may work to protect bone degradation in PsA.

P31-7

Efficacy of Guselkumab, a Monoclonal Antibody that Specifically Binds to the p19 Subunit of IL-23, on Axial-Related Endpoints in Patients with Active PsA with Imaging-Confirmed Sacroiliitis: Week-52 Results from Two Phase-3, Randomized, Double-blind, Placebo-controlled Studies

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Conflict of interest: Yes

[Objective] To assess guselkumab (GUS) efficacy through 1 year in active psoriatic arthritis (PsA) patients (pts) with imaging-confirmed sacroiliitis in DISCOVER (DISC)-1&2. [Methods] In DISC-1 (n=381) & DISC-2 (n=739), pts with active PsA despite standard therapies were randomized 1:1:1 to GUS 100 mg Q4 W, GUS 100 mg Q8W, or placebo (PBO). PBO pts crossed over to GUS Q4W (PBO→GUS) at W24. Only pts with sacroiliitis at baseline (BL) were included in this analysis. [Results] 312 pts presented with imaging confirmed sacroiliitis (Q4W n=103; Q8W n=91; PBO n=118). Improvements in PsA axial symptoms were greater with GUS vs PBO through W24. The LS mean changes from BL in BASDAI, spinal pain, mBASDAI, & ASDAS were maintained from W24 to W52 in GUS groups; improvements from BL to W52 in PBO→GUS were similar to GUS groups. Similar trends were observed for the proportions of pts achieving BASDAI50 & ASDAS responses of inactive disease, major improvement, and clinically important improvement at W52. Efficacy at W52 trended similarly between HLA-B27+ and HLA-B27- pts. [Conclusions] Improvements in axial symptoms were maintained through W52 in GUS-treated pts with active PsA who had imaging-confirmed sacroiliitis.

P31-8

Guselkumab Provides Domain-Specific and Comprehensive Efficacy as Assessed Using Composite Endpoints in Patients with Active Psoriatic Arthritis

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Conflict of interest: Yes

[Objective] To assess guselkumab (GUS) efficacy in active psoriatic arthritis (PsA) patients (pts) through Week (W) 24 in DISCOVER (DISC)-1&2 studies using composite indices. [Methods] In DISC-1 (n=381), 31% pts received 1-2 prior anti-TNFs, while pts were biologic-naïve in DISC-2 (n=739). Pts were randomized 1:1:1 to GUS 100 mg every 4W (Q4W), GUS 100 mg at W0, W4, then every 8W (Q8W) or placebo (PBO). Composite endpoints included: Psoriasis Disease Activity Score (PASDAS), Minimal Disease Activity (MDA), Very Low Disease Activity (VLDA), Modified PsA Responder Criteria (mPsARC; based on evaluation of 68 joints for tenderness and 66 for swelling), Disease Activity Index for PsA (DAPSA), and clinical DAPSA (cDAPSA; determined by excluding CRP). [Results] Across studies, differences between GUS Q4W or Q8W & PBO were observed as early as W8 & continued to increase when response was assessed using the joint-focused mPsARC, DAPSA LDA/Remission composite endpoints. Response rates of cDAPSA were similar to DAPSA in DISC-1&2. Higher proportions of GUS Q4W- & Q8W-treated vs PBO-treated pts achieved PASDAS, MDA, VLDA, and remission with DAPSA or cDAPSA. [Conclusions] GUS 100 mg Q4W & Q8W had robust benefits in active PsA pts across domains regardless of composite index/study population.

P31-9

Clinical features of 13 patients with inflammatory bowel disease-related arthritis

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Conflict of interest: None

[Objective] We examined the clinical characteristics of patients with inflammatory bowel disease (IBD)-related arthritis. [Methods] We retrospectively collected and analyzed the medical records of 13 IBD patients having joint symptoms, in our hospital between March 2015 and September 2020. [Results] The mean age of the patients was 51 years; 7 were men, 9 had ulcerative colitis (UC), and 4 had Crohn's disease (CD). The types of joint symptoms were axial arthritis (3 patients) and peripheral arthritis involving small joints only (10 patients), large joints only (3 patients), and both joints (4 patients). The medications used at the onset of the arthritis included infliximab (3 patients), prednisone 10 mg or more (1 patient), and 5-ASA (3 patients). Bowel disease had improved in 3 patients. Arthralgia preceded the onset of IBD in 2 patients. Among the 8 patients in whom IBD preceded arthralgia, the mean time from the onset of IBD to the development of arthralgia was 9.9 years, with no significant difference between UC and CD (8.75 years vs. 12.9 years). [Conclusions] The mean time from the onset of IBD to the start of joint pain was 9.9 years, which is consistent with previous reports. Joint symptoms may be present even when the condition of bowel disease is improving.

P31-10

Clinical features of inflammatory bowel disease in our hospital

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Conflict of interest: None

[Objective] Patients with ulcerative colitis (UC) and Crohn's disease (CD) often have extraintestinal complications. In the present study, we analyzed the clinical profile of our patients in collaboration with the Department of Gastroenterology. [Methods] A retrospective analysis was performed to determine the clinical features of 86 patients with UC and 32 with CD, including the prevalence of antinuclear antibodies (ANA) and ANCA, joint symptoms, autoimmune diseases and dermatological complications. [Results] (1) In use of biologics. UC7%; CD72% (2) ANA 40 times or more/160 times or more. UC50%/9%; CD47%/17% (3) MPO-ANCA/PR3-ANCA positive rate. UC11%/76%; CD0%/50% (4) With Joint symptoms. UC8%; CD19% (5) With autoimmune disease. UC10% (Interstitial pneumonia 2, Hashimoto disease 2, Sjogren's syndrome 1, PBC1, PSC1, optic neuritis 1, myocarditis 1); CD0% (6) With Dermatological disease. UC14%; CD19% [Conclusions] (1) Autoantibodies: ANA titers were often negative or low, while PR3-ANCA positive rates were high. (2) Extraintestinal complications: Less than 20% of patients had

joint symptoms, and no classical collagen disease was observed. On the other hand, dermatological complications such as psoriasis, palmoplantar pustulosis, chronic folliculitis, and pyoderma gangrenosum were found.

P31-11

A study of calcification in peripheral enthesis by using ultrasonography

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Conflict of interest: None

[Objective] In rheumatic disease, evaluation of the enthesis by ultrasonography may be useful, and it is important to examine calcification in enthesis. [Methods] Articular ultrasound examinations were made at Ohsaki Clinic between January 2019 and August 2020, in 495 patients (88 males and 407 females) with an average age of 59.2 years who were suspected or confirmed to have rheumatic disease. Madrid Sonographic Enthesis Index (MASEI) is used to identify calcified lesions at the 12 sites in total on the left and right side by site and age. [Results] Calcification was found at a rate of 14.1% for the triceps tendon, 7.0% for the tibial tubercle, 0.3% for the inferior pole of the patellar tendon, 45.3% for the quadriceps tendon, 63.1% for the Achilles tendon, and 2.6% for the plantar fascia. In the enthesis of the Achilles tendon and the patellar quadriceps tendon, the proportion of calsification increased with age. In the enthesis of the Achilles tendon, the latter was found to be 7.0 times on the right side and 6.5 times on the left side in comparison between those under 30 years old and those over 70 years old. [Conclusions] When assessing enthesitis, considering age is required for calcification in the enthesis of the Achilles tendon, patellar quadriceps tendon.

P32-1

A Case report: Reactive arthritis after COVID-19 infection

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Conflict of interest: None

Background: Reactive arthritis is typically preceded by sexual transmitted disease or gastrointestinal infection. Herein, we report the case of “reactive arthritis” after SARS-CoV-2 infection. Case: This patient is a 51-year-old male with a past medical history of steatohepatitis who was admitted for COVID-19 pneumonia. Despite starting standard dose of favipiravir, his respiratory condition deteriorated during hospitalization. On the fourth hospital day, he was intubated. On day 11, he was successfully extubated. On day 21, one day after starting physical therapy, he developed acute bilateral arthritis in his ankles, with mild enthesitis in his right achilles tendon. Arthrocentesis of his left ankle revealed mild inflammatory fluid without crystals. Culture of synovial fluid was negative. Exams for syphilis, HIV, ASO, antinuclear antibody, rheumatoid factor, and anti-cyclic citrullinated peptide antibody were negative. Gonococcal and Chlamydia trachomatis urine PCR were also negative. He was diagnosed with reactive arthritis. NSAIDs and intra-articular corticosteroid injection resulted in moderate improvement. Clinical significance: SARS-CoV-2 infection may cause ‘ReA’. In patients with acute arthritis after COVID-19 infections, ‘ReA’ should be considered.

P32-2

A case of late-onset spondyloarthritis (LOSpA) with a onset mode similar to Polymyalgia rheumatica

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Conflict of interest: None

[Case] 76-years-old woman [Clinical history] From April X, shoulder joint pain, thigh pain, and lower leg edema appeared. Blood tests showed CRP of 13.6 mg/dl and negative for RF and anti-CCP antibody. Ultrasonography showed synovial thickening of the long-head biceps tendon sheath. Polymyalgia rheumatica (PMR) was diagnosed because of acute onset. After administration of prednisolone (PSL) at a dose of 15 mg/day, the subjective symptoms improved rapidly. However, CRP did not improve below 4 mg/dl despite the administration for 4 weeks. PET-CT showed accumulation around the shoulder, ischial tuberosity, greater trochanters, lumbar spinous processes and sacroiliac joints. MRI showed bone marrow edema in the sacroiliac joint bilaterally, and X-ray of the right sacroiliac joint showed grade 2 sacroiliitis. Based on these findings, the definitive diagnosis was changed to axial spondyloarthritis (SpA). After discontinuing of PSL, secukinumab was administered. It resulted in remission of disease activity. [Discussion] Late-onset SpA may have an onset pattern similar to PMR, which can lead to misdiagnosis. It is considered important that listing LOSpA as a differential disease for elderly onset arthritis helps in not only a correct diagnosis but also avoiding unnecessary medication.

P32-3

Thrombotic Microangiopathy in psoriatic arthritis: a case report

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Conflict of interest: None

A 70-year-old woman with psoriatic arthritis was hospitalized for the evaluation of myalgia and elevated serum CK and LDH. Physical examination showed skin sclerosis of fingers and hypertension. ANA titer was 1:640, but no autoantibody was detected by commercial-based measurement. CT scan showed pleural effusion and systemic lymphadenopathy. The pathological examination of the biopsied lymph node and muscle tissue revealed non-specific inflammation. After admission, the development of hemolytic anemia with schistocytes, thrombocytopenia and decreased renal function lead to the suspicion of thrombotic microangiopathy (TMA). Based on the tentative diagnosis of scleroderma renal crisis with TMA, captopril was administered and then plasma exchange was added. Her renal tissue was biopsied for the evaluation of renal dysfunction and urinary casts. The pathological findings suggested lupus nephritis. The addition of high-dose prednisolone, intravenous cyclophosphamide and warfarin gradually improved her diseases and plasma exchange was discontinued two months later. TMA in this case was difficult to diagnose because of rare complication with psoriasis. Renal pathology lead to the final diagnosis. We report this case with literature review.

P32-4

A case of reactive arthritis induced by intravesical BCG therapy for bladder cancer whose lesion could be evaluated by ultrasound imaging

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Conflict of interest: None

[Case] A 68-year-old man was admitted to our hospital because of fever, developed right knee joint pain, and hyperemia of conjunctiva following the 5th intravesical instillation of BCG in the treatment of pT1N0M0. His right knee joint had redness, automatic and passive pain. Acute phase reactants were increased and synovial fluid from his right knee showed increased cell number, low glucose level and negative Gram stain. Although reactive arthritis following BCG therapy was suspected, we started antimicrobial treatment in consideration of the possibility of septic arthritis and disseminated BCG infection. Doppler Ultrasound detected signs of synovitis of right knee and enthesitis of tendon of the quadriceps femoris and fibular collateral ligament. Joint pain improved after naproxen, and we discontinued antibiotics receiving negative culture results. After discharge from the hospital, negative mycobacterial culture results were reported about the joint fluid. [Clinical significance] In spondyloarthritis, it is considered that intra-articular synovitis may occur secondary to enthesitis, we report the case in which enthesitis and synovitis could be evaluated by ultrasonography.

P32-5

A case in which an IL-17A inhibitor was administered as first biologic DMARD and was effective for ankylosing spondylitis

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Conflict of interest: Yes

[Case] A 69-year-old man developed right buttock pain and low back pain around the age of 24. At the age of 32, he became aware of his back stiffness and went to the hospital. Ankylosis of the sacroiliac joint was confirmed by X-ray, diagnosed ankylosing spondylitis (AS) and a nonsteroidal anti-inflammatory drug (NSAID) was administered. At the age of 36, he developed iritis in the left eye. From January 2019, lower back pain increased, and he was referred to our hospital for treatment. He had inflammatory back pain and tenderness at the plantar fasciitis enthesiits, but no peripheral arthritis, dactylitis, or skin or nail abnormalities. A laboratory test showed CRP increased to 2.22 mg / dl and HLA-B27 was positive. In the radiograph, bilateral sacroiliac joint was totally ankylosis (Grade 4). We diagnosed ankylosing spondylitis. Despite the administration of NSAIDs, BASDAI was 6.5, and ASDAS (CRP) 3.04, showing high disease activity. When secukinumab was started at the request of the patient, both symptoms and data improved. [Discussion] Secukinumab was administered to 6 uncontrolled AS patients including this case, and good efficacy was observed not only with First Bio but also with a switch from a TNF inhibitor and a switch from an IL-17 inhibitor.

P32-7

A case report of ankylosing spondylitis in which ankylosis of the elbow joint was the chief complaint at the first visit

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Conflict of interest: None

[Objective] We report a case of AS in which ankylosis of the elbow joint was the chief complaint at the first visit. [Case] A 26-year-old man had right elbow joint pain for several years, and his range of motion was gradually restricted. The range of flexion and extension of the right elbow was about 15°. Xp-ray of the right elbow showed bone erosion and prominent bone proliferative changes in the elbow joint. Lumbar Xp-ray showed an tonic image of the right sacroiliac joint. HLA B Locus is positive for B7 / B40. The patient was diagnosed with AS and underwent right elbow arthroplasty, resulting in a full arc. Infliximab (IFX) was introduced postoperatively. Even after that, good elbow joint function can be maintained. [Discussion] The complication of AS lower limb joint symptoms is said to be about 70%, but reports of complications of elbow joint symptoms are not within the scope of our hunting, and the chief complaint at the first visit as in this case is elbow joint toughness. Cases were considered to be rare. [Results] We experienced a case in which ankylosis of the elbow joint was the chief complaint at the first visit.

P32-8

A case of ankylosing spondylitis (AS) diagnosed after the development of pyoderma gangrenosum (PD) who underwent aortic valve replacement finally

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Conflict of interest: None

[Objective] We present a 75 years-old woman. She was admitted to dermatology because of ulceration of lower extremities. Skin biopsy made the diagnosis of PD and PSL was started. We were consulted whether there are underlying diseases or not. She had back and cervical pain which started before 40. At the first visit, cervical rotation was markedly restricted, and thoracic expansion test was positive. Because PD is reported to be a complication of Takayasu arteritis, we took PET-CT, which revealed bamboo spine and abnormality of sacroiliac joints, resulting in the diagnosis of AS. Because inflammatory markers were positive, we suggested the introduction of biologics, but she refused. In 2018, diastolic murmur of L4/6 developed, which was revealed to be aortic regurgitation. Overwork triggered the development of heart failure, and aortic valve replacement was done. Because inflammatory cells were found in the removed valve, AS was thought to be a cause of valve trouble. Finally, adalimumab was introduced and inflammatory markers turned negative. Valve replacement became needed due to several reasons: very long duration from the onset to the diagnosis of AS, and refusal of introduction of biologics. This is the first case of the combination of AS, PD and valve replacement.

P32-9

A case of axial spondylitis diagnosed by ultrasound-guided sacroiliac joint injections

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Conflict of interest: None

[Case] A 26-year old female patient presented with 18 months history of low back pain which could not be controlled with analgesics or physiotherapy. Six months ago, she began experiencing joint pain and was diagnosed with rheumatoid arthritis. She received methotrexate, but her symptoms did not improve. Her low back pain worsened at night and improved with exercise. Physical examination revealed tenderness on the enthesis of the lateral humeral epicondyle, medial femoral condyle and plantar fascia. She was positive for Patrick's test, Gaenslen's test and modified Schober's test. She was suspected of having axial spondylitis, but sacroiliitis was not observed on X ray or MRI. Bilateral ultrasound-guided sacroiliac joint injections with lidocaine was performed and her low back pain improved from seven to two in NRS score and finger-to-floor distance changed from -24 cm to 13 cm. After the commencement of adalimumab, her symptoms ameliorated (from 6.2 to 2.3 in BASDAI and from 2.7 to 0.9 in ASDAS). [Clinical significance] Patients with early stage of axial spondylitis can have a normal MRI of the sacroiliac joints. However, in our case, ultrasound-guided joint injections assisted the diagnosis by confirming sacroiliac joints as the source of low back pain.

P32-10

Post-streptococcal reactive arthritis followed by streptococcal sepsis: a case report

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Conflict of interest: None

[Introduction] Post-streptococcal reactive arthritis (PSRA) is a nonpurulent arthritis that develops after prior infection with streptococcus. Here we report a case who presented PSRA after systemic abscess caused by streptococcus. [Case] 88 -year-old man. He fell down 3 days ago. The patient was followed up at rest, but he was referred to our hospital because of severe inflammation. The image findings showed the lumbar burst fracture, purulent discitis, iliopsoas abscess, and pyogenic arthritis of left knee and left wrist. Emergency debridement and irrigation were performed followed by spine stabilization surgery. Joint fluid, abscess from iliopsoas and blood cultures detected Streptococcus dysgalactiae. He was treated with the antibiotic treatment, although left knee arthritis was prolonged. It was judged to be arthritis associated with streptococcal infection due to no respose to antibacterial agents. Systemic administration of a small amount of prednisolone rapidly improved the symptoms of arthritis. [Clinical significance] It is challenging to distinguish PSRA from RA, and if antibacterial agents or NSAIDs treatment is ineffective for arthritis observed after streptococcal infection, and if the serologic reaction is negative, this disease should be considered.

P33-1

Long-term outcomes of treatment with denosumab in patients with osteoporosis

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Conflict of interest: None

[Objective] To investigate the long-term outcome of denosumab (Dmab) treatment in patients with osteoporosis (OP). [Methods] Of 289 patients who were initiated with Dmab in Hokuto Hospital, 143 patients who had been naïve to OP treatment and who had at least one outpatient follow-up after the first dose were included. Baseline data, changes (Δ-) in lumbar spine (L-) and femoral neck (H-) bone mineral density (BMD) were assessed by Wilcoxon's signed-rank test, and treatment retention rates (TRR) were assessed by the Kaplan-Meier method. Missing data were supplemented by LOCF method. [Results] Mean age 79.8 years, 86.7% female, BMI 22.1 kg/m², L-T score -2.4 and H-T score -2.7 at baseline. ΔL-BMD, ΔH-BMD and TRR were 7.5%, 2.6% and 92.6% (n=129) at 12 months (-m), 10.1%, 3.8% and 82.1% (n=112) at 24m, 13.8%, 3.7% and 71.3% (n=61) at 36m, 16.4%, 3.6% and 57.1% (n=41) at 48m, 18.2%, 6.5% and 57.1% (n=20) at 60m, 16.4%, 6.6% at 72m and 57.1% (n=15), and 16.2%, 5.7% and 47.1% (n=11) at 84m. The reasons for discontinuation were following; 16 dropout, 16 change of medication, 7 transfer or institutionalization, 4 non-drug related death, and 1 osteonecrosis of the jaw. [Conclusions] Long-term Dmab treatment will be an effective strategy for treatment of OP patients.

P33-2

The two years efficacy of anti-RANKL monoclonal antibody (Denosumab) under the treatment of connective tissue disease (CTD)

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Conflict of interest: None

[Objective] We evaluated the two years efficacy of Denosumab (Dmab) by using BMD and serum TRACP-5b and BAP. [Methods] Twenty-two CTD patients under the treatment of Dmab were included. The patients were retrospectively analyzed for 24 months by measuring BMD of lumbar vertebra (L), femoral neck (FN) and the serum TRACP-5b and BAP. [Results] Baseline patient characteristics (n=22) was as follows; Mean age: 74 years old, ratio of male to female (M:4 F:18), RA (n=16), SLE (n=6). After the treatment in all patients, BMD of L was 97.0% vs 99.4%, 101% (pre. vs post one year, two years.) (*p=n.s.*). PSL 6.8±13.0 mg/day vs 1.0±2.2 mg/day, 0.0±1.1 mg/day. Those of FN was 81.0% vs 82.1%, 83.0% (*p=n.s.*), TRACP-5b was 481.0 mU/dL vs 382.6 mU/dL, 306.5 mU/dL (*p=0.0001*), BAP was 13.0 μg/L vs 10.0 μg/L, 10.0 μg/L (*p=0.048*). In RA, BMD of L was 95.0% vs 97.3%, 98.2% (*p=n.s.*). Those of FN was 78.0% vs 78.4%, 79.3% (*p=n.s.*), TRACP-5b was 485.0 mU/dL vs 442.9 mU/dL, 352.0 mU/dL (*p=0.034*), BAP was 12.0 μg/L vs 11.0 μg/L, 11.0 μg/L (*p=n.s.*). In SLE, BMD of L was 131.0% vs 133.0%, 133.0% (*p=n.s.*). Those of FN was 91.5% vs 92.2%, 93.0% (*p=n.s.*), TRACP-5b was 469.8 mU/dL vs 222.0 mU/dL, 183.3 mU/dL (*p=0.003*), BAP was 15.7 μg/L vs 9.1 μg/L, 8.8 μg/L (*p=n.s.*). [Conclusions] The patients under the treatment of Dmab for 2 years had the statistical improvement of serum TRACP-5b.

P33-3

A case of hypercalcemia due to prolongation of denosumab administration interval

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Conflict of interest: None

[Introduction] Hypocalcemia is a common side effect of denosumab. However, hypercalcemia after discontinuation of denosumab treatment. We report a case of hypercalcemia due to prolongation of denosumab administration interval. [Case] A 22-year-old male admitted to our hospital because of abdominal pain and nausea. He developed systemic juvenile idiopathic arthritis 13 years before, and had received denosumab 7 years before due to osteoporosis. The interval between the doses was shortened from 6 to 3 month to suppress bone erosion, and the interval was prolonged to 6 months because of the improvement of arthritis. Laboratory tests showed serum Ca 13.4 mg/dL, Cre 1.88 mg/dL, P 2.2 mg/dL, intact PTH 19 pg/mL, PTHrP <1.1 pmol/L, 25 (OH) D 9.9 ng/mL, 1, 25 (OH) 2D 11 pg/mL, and TRACP-5b 993 mU/dL, BAP 18.7 μg/L, urinary Ca/Cre ratio 0.93, %TRP 42%. Bone scintigraphy, head MRI, and ultrasonography showed no evidence of malignancy. The patient was refractory to treatment despite discontinuation of oral activated vitamin D and administration of bisphosphonates and calcitonin. The patient's hypercalcemia improved when denosumab was administered, and has not worsened since. [Discussion] Monitoring serum Ca is required after prolongation of the interval of denosumab administration.

P33-4

Effects of initial treatment of osteoporosis by bisphosphonates or denosumab on bone mineral density with abatacept or golimumab 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) or abatacept (ABT) 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 golimumab and abatacept from 2017, which are relatively common among bDMARDs at our hospital. There was a total of 18 patients whose BMD were measured. Patients were divided into GLM and BP treated (GLM-BP group; 6 cases), ABT and BP treated (ABT-BP groups; 4 cases), ABT-DMAB treated (ABT-DMAB group; 8 cases) groups. 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 3 groups. The highest percent change was L-BMD in ABT-DMAB (107%), and the lowest percent change was H-BMD in ABT-DMAB (100%). [Conclusions] GLM and ABT are said to have an effect on osteoclasts. BP and DMAB are thought to increase BMD similarly even under that influence.

P34-1

Romosozumab Treatment in Patients with Osteoporosis: Results after 6 Months and Predictors of Efficacy

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Conflict of interest: None

[Objective] We investigated the efficacy of 6-month romosozumab (ROMO) treatment in osteoporosis (OP) patients. [Methods] The patients' baseline (BL) characteristics, time course of lumbar spine BMD, total hip BMD, BTM, and predictors of efficacy were investigated in 38 ROMO-treated OP patients. [Results] The mean age was 73 years. Past insufficiency fractures were experienced by 78.9% of cases, and 26.3% of cases were treated with concomitant PSL. Cases were categorized as postmenopausal OP (n=14), RA (n=14), GIOP (n=8), and others (n=2). OP pretreatments included bisphosphonate (n=24), none (n=5), SERM (n=4), DMB (n=2), and vitamin D (n=2). LSBMD and THBMD significantly increased by +7.8% and +2.2%, respectively. BTM was mostly changed after 1 month. BAP and P1NP were increased, and NTX and TRACP-5b were decreased. Height, past fracture, BL-P1NP, BL-NTX, and BL-TRACP-5b were significantly correlated with the change in LSBMD (after 6 months) by Spearman's correlation analysis. FRAX, BL-THBMD, and the change in P1NP after 1 month were significantly correlated with the change in THBMD after 6 months. [Conclusions] ROMO quickly increased BMD, especially LSBMD, and changed BTM after 1 month. The factors correlated with increased BMD may be different between LSBMD and THBMD.

P34-2

Cliniclal efficacy of romosozumab in patients with rheumatoid arthritis complicated with osteoporosis

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Conflict of interest: None

[Objectives] We investigated the cliniclal efficacy of romosozumab (ROMO) for 12 months in patients with rheumatoid arthritis complicated with osteoporosis. [Methods] 12 patients received continuous ROMO therapy more than 6 months. We reviewed the results about the increase and decrease of bone mineral density (BMD) of lumbar spine (LS) and total hip (TH) by DEXA for 6 and 12 months and bone turnover markers, PINP, TRACP-5b and corrected serum calcium level at 1, 3, 6 and 12 months. [Results] Gender of patients are all female. The mean age was 73.2±7.9 years old; disease duration was 21.9±16.8 years; LS-BMD was 0.828±0.149 g/cm^2; TH-BMD was 0.534±0.084 g/cm^2. The change of PINP, TRAC-5b and corrected serum calcium level from baseline to 1, 3, 6, 12 months were each 60.8→129.6→125.6→114.6→87.9 μg/l, 450→353→432→482→473 U/dL and 9.5→9.2→9.1→9.4→9.4 mg/dl. The rate of increased LS-BMD from baseline to 6, 12 months were 9.0±8.2%, 13.0±11.5% and TH-BMD were 4.8±5.0%, 7.4±6.9%. [Conclusion] The changes in bone turnover markers after the start of ROMO showed a so-called dual effect. Clinical efficacy of ROMO for RA-OP was extremely effective and ROMO was regarded to have the high potential to be an important option in the treatment of osteoporosis.

P34-3

Effects of prior osteoporosis treatment on treatment response of romosozumab, and the predictors of treatment response

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Conflict of interest: None

[Objective] To investigate the effects of prior treatment to romosozumab (ROMO). [Methods] Patients comprised 87 patients with an average age of 78 years. We investigated the rate of change in bone mineral density (BMD) and serum bone metabolism markers (TRACP-5b, P1NP) at baseline, half-year, and one year. Patients were treated previously with naive- (N, n=38), bisphosphonates (BP, n=24), PTH (P, n=15), and Denosumab (D, n=10). We used Statistical methods by repeated measures of ANOVA. [Results] There were no differences between groups in age, BMI, Alb, and BMD at baseline. The rate of change in P1NP and TRACP-5b increased only in group D, and interaction was observed ($p < 0.01$). Half-year and 1 year after administration, the rate of change in the lumbar spine (LS) BMD was 10.8 / 13.5% in the N group, 5.2 / 6.7% in the BP group, 9.0 / 9.9% in the P group, and 2.6 / 7.3% in the D group respectively, and the BP group ($P < 0.01$).), D group ($p = 0.02$) showed an interaction. there were no significant statistical differences in the femoral neck BMD. [Conclusions] LS-BMD was a remarkable increased in the N group, and it was confirmed difficult to increase in the BP group and the D group. Changes in bone metabolism markers differed only in group D, suggesting that they may affect ROMO treatment.

P34-4

The efficacy and safety of romosozumab for glucocorticoid induced osteoporosis in patients with rheumatic diseases

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Conflict of interest: None

[Objective] To reveal the efficacy and safety of romosozumab (ROM) for glucocorticoid induced osteoporosis (GIOP) in patients with systemic rheumatic diseases. [Methods] The median age was 70 years old, 6 patients had pre-existing vertebral fractures. Background rheumatic diseases were as follows; SLE 3, RA 3, PMR1, systemic scleroderma 1, dermatomyositis 1, and GPA 1. The median dose of PSL was 3.5 (1-20 mg/day). Bone mineral density (BMD) of lumbar spine and femoral neck at the baseline were as follows (mean±SD); BMD score (0.64±0.17, 0.50±0.06 g/cm^2), T-score (-2.85±1.23, -2.78±0.78), YAM (64.0±15.5, 62.9±7.8) (%). After 1-year treatment course of ROM, BMD, T score and YAM of lumbar spine and femoral neck were as follows: 0.77±0.16, 0.47±0.05 (g/cm^2), -2.11±1.35, -2.93±0.50, 74.3±15.7, 59.1±7.4 (%). There were statistical significant increase of lumber vertebral bone density (Wilcoxon t-test $P<0.05$). During the observation period, there were 2 adverse events (one vertebral fracture and one femoral neck bone fracture accompanied by fall) and one cancellation of ROM treatment. [Conclusions] Romosozumab significantly improved lumbar vertebral bone density in GIOP patients with systemic rheumatic diseases.

P34-5

Efficacy of romosozumab in RA patients with osteoporosis for whom conventional drugs were ineffective

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Conflict of interest: None

[Objective] Efficacy of romosozumab in RA patients with osteoporosis for whom conventional drugs were ineffective was investigated. [Methods] A total of 14 RA patients with osteoporosis for whom conventional drugs were ineffective was enrolled in this study. These patients were treated with romosozumab and were observed for more than 6 months. Changes of bone mineral density in lumbar spine and femoral neck, and serum bone turnover markers, TRACP-5b and P1NP, were evaluated. [Results] Mean age was 73 years, and 12 patients were completed treatment with romosozumab for 6 months. Change of bone mineral density from baseline was +7.4% in lumbar spine and +4.1% femoral neck. Change of serum turnover markers from baseline was -26% in TRACP-5b and +66% in P1NP. There was no serious adverse event in all patients. [Conclusions] Romosozumab was effective in RA patients with osteoporosis for whom conventional drugs were ineffective.

P34-6

Examination of clinical effects of Romosozumab and its effect on disease activity in combination with biologics

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Conflict of interest: None

[Objective] We investigated the possible effects on bone mineral density (BMD) and disease activity by inhibiting sclerostin for osteoporosis with rheumatoid arthritis (RA) using Romosozumab (Rmab). [Methods] Of RA patients who used biologics, 32 patients who received Rmab (2 males and 30 females). The effects on BMD and RA disease activity (DAS28-CRP, SDAI) in the TNF-α inhibitor use group and the nonTNF-α inhibitor use group were investigated. [Results] The average age is 68.7 years. The biologics used in combination were 13 patients in group ***1*** (IFX2, ETN2, GLM8, CZP1) and 19 patients in group ***2*** (ABT11, TCZ5, SAR3). Changes in DAS28 in group ***1*** were 2.50 before administration and 2.37 one year later. SDAI was 9.75 before administration and 7.61 one year later. Changes in DAS28 in group ***2*** were 2.58 before administration and 2.08 one year later. SDAI was 11.46 before administration and 7.18

one year later. On the other hand, the effects of BMD were +10.74% for the lumbar spine YAM, -1.56% for the total hip in group ***1***, and +7.23% and +0.66% for group ***2***. [Conclusions] Rmab in RA patients using biologics did not affect disease activity. It also increases lumbar BMD but requires regular monitoring in patients taking TNF-α inhibitors as BMD near the joints may decrease.

P34-7

Therapeutic effect of romosozumab of RA using bDMARDs treatments

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Conflict of interest: None

[Objective] It becomes able to be accepted by introduction of various bDMARDs for bone weakness of RA after 2003. We investigated BMD of the RA patients of csDMARDs and bDMARDs during use of ROMO, BP and RL. [Methods] We investigate LBMD and THBMD of six patients with bDMARDs who received ROMO, and five patients with csDMARDs who received ROMO. Furthermore, we investigate LBMD and THBMD of six patients with bDMARDs who received BP or RL, and eight patients with csDMARDs who received BP or RL. [Results] The BMD rate of change (LBMD/THBMD) was that bDMARDs group (-0.008/-0.032) who received ROMO and that csDMARDs group (0.05/-0.01) who received ROMO. The BMD rate of change was that bDMARDs group (0.023/0.122) who received BP or RL, and that csDMARDs group (0.035/0.03) who received BP or RL. [Conclusions] When we cured to RA patients in bDMARDs or csDMARDs, as for us, it was thought that there was the need that receive osteoporosis treatment.

P35-1

Prescription status of osteoporosis treatment for patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] To examine the prescription status of osteoporosis (OP) therapeutic drugs for rheumatoid arthritis (RA) patients from the point of bone mineral density. [Method] From YAM value (%), we classified RA patients into OP group, bone loss (BL) group, and normal (N) group, and investigated the prescription status of OP therapeutic agents. [Results] The target cases were 191 cases, of which 36 were male and 155 were female, and the age ranged from 31 to 91 years, with an average of 64.3 years. The YAM value was 32% to 146%, with an average of 88.3%. There were 26 cases (13.6%) in the OP group, 32 cases (16.8%) in the BL group, and 133 cases (69.6%) in the N group. OP treatment drugs (including duplication) were vitamin D preparations in 61 cases, bisphosphonate preparations in 22 cases, denosumab preparations in 7 cases, teriparatide preparations in 2 cases, and elcatonin in 1 case, and 108 cases (56.5) were not treated with drugs. The prescription rate for OP treatment was 21/26 cases, 80.8% in the OP group, 16 cases / 32 cases, 50.0% in the BL group, and 46 cases / 133 cases, 34.6% in the N group. [Discussion] It was considered necessary to properly evaluate the bone mineral density in RA cases and take measures against OP for the purpose of preventing fractures.

P35-2

Fracture incidence rate and fracture risk in patients with rheumatoid arthritis in our department

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Conflict of interest: None

[Objective] We investigated the fracture incidence rate in patients with rheumatoid arthritis (RA) in our hospital and examined background factors to identify fracture-preventive measures. [Methods] We included 133 patients with RA who were continuously followed up for ≧12 months as outpatients at the Department of Orthopedic Surgery, Shirakawa Kosei General Hospital between April 1, 2016 and September 30, 2020. We determined the fracture incidence rate and statistically analyzed the background differences between the fracture and non-fracture groups. [Results] During follow-up, 30 fractures occurred in 26 patients, and the fracture incidence rate was 6.24 per 100 person-years. Falls were the most frequent cause of injury (17 fractures). At study inception, the mean HAQ score and rate of anti-osteoporosis drug use were significantly higher in the fracture group than in the non-fracture group (1.308 and 65.4% vs. 0.535 and 33.6%, respectively). [Conclusions] The fracture incidence rate in patients with RA in our hospital was 6.24 per 100 person-years. Falls accounted for more than half of the injuries. A high HAQ score indicated a fracture risk. Thus, maintaining physical function and taking proactive measures for reducing fall accidents may prevent fractures in patients with RA.

P35-3

A case of SLE patient could be treated with teriparatide fot articular calcification and osteoporosis

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Conflict of interest: None

[Background] Systemic lupus erythematosus (SLE) is an autoimmune disease. More than 10 mg of predonisolon (PSL) are frequently used for treatment and prophylaxis against osteoporosis including bisphosphonate (Bis) are recommended. Patients with SLE may have periarticular ectopic calcification. Here, we report the prevention of osteoporosis and the improvement of periarticular calcification by changing Bis use to teriparatide (rhPTH). [Case] A 58-year-old woman [Progress] At 39 years old, she developed erythema butterfly and polyarthritis. She was diagnosed with SLE and treated with PSL 30 mg/d. Alendronate 35 mg/w was administered to prevent osteoporosis. Introduced to our hospital at 50yo for the purpose of treatment for arthritis. We treated her with PSL 1 mg/kg and MMF. She had multiple periarticular calcification and required opioid for pain management. We switched from Bis to rhPTH for osteoprosis management. Three months after switching rtPTH, calcification improved. After continuing for one year, rhPTH was changed to Bis again. No relapse of calcification was observed 5 years after. [Clinical significance] This case suggests that rhPTH can be safely used in osteoporotic cases with ectopic calcification and may improve ectopic calcification.

P35-4

One-year Denosumab and Romosozumab treatment in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy of Denosumab and Romosozumab treatment for 1 year to osteoporosis in patients with rheumatoid arthritis (RA). [Methods] Patients with RA received subcutaneous injection of Denosumab 60 mg (n = 12) at baseline, 6 months and 12 months and monthly Romosozumab 210 mg (n = 25) were enrolled. We examined mineral density (BMD) of the lumbar spine and femoral neck, Disease Activity

Score-28 with ESR (DAS28-ESR), modified Health Assessment Questionnaire (mHAQ), methotrexate (MTX), Non-Steroidal Anti-Inflammatory Drugs (NSAID), prednisolone (PSL), Rheumatoid Factor (RF), Anti-Cyclic Citrullinated Peptide Antibody (ACPA), and Matrix Metalloproteinase (MMP)-3 before and one year after administration. [Results] Denosumab and bisphosphonate showed no significant difference in almost all parameters of disease activity. In patients treated with denosumab, mean changes in lumbar and femoral neck BMD at 12 months were +6.9% ($p < 0.01$) and +5.3% ($p < 0.05$), respectively. While mean changes with Romosozumab were +9.5% ($p < 0.05$) and +4.1% ($p < 0.05$), respectively. There were no significant differences between Denosumab and Romosozumab. [Conclusions] In patients with RA, both Denosumab and Romosozumab treatment for 1 year provided favorable benefits.

P35-5

Analysis of affecting factor of rheumatoid arthritis to osteoporosis

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Conflict of interest: None

[Objective] We, the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) report on the analysis of factors affecting osteoporosis. [Subjects] The subjects were 463 patients with all the evaluation items from 2234 Registry in 2018. They were 70 males, 393 females, and an average age of 67.8 years. Bisphosphonate (BP) was used in 132 cases 28.5% and SERM 18 cases 3.89%, bDMARDs 142 cases 30.1%, PSL 216 cases 46.7%. [Methods] DAS28CRP/DAS28ESR-induced disease activity, BP, SERM, bDMARDs, and PSL were evaluated between the TRACP-5b high level group (men 591 or more, women 421 or more, postmenopausal women 760 or more) and normal group, Chi-square test was performed. [Results] DAS28CRP and DAS28ESR were found to have significantly less disease activity or less in the normal group ($p>0.01$, $p=0.002$). The use of BP ($p=0.594$), SERM ($p=0.402$), bDMARDs ($p=0.7633$), PSL ($p=0.707$) showed no significant difference. [Conclusions] The 2010 ACR Steroid Osteoporosis Treatment Guideline recommends the treatment of BP and PTH, there was no significant difference in the use of BP in this study. As for a significant difference in disease activity, it was speculated that good disease control affected physical activity and systemic osteoporosis, indicating the importance of T2T in daily treatment.

P36-1

Relationship between calcium pyrophosphate dihydrate crystal and operated osteoarthritis of the knee

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Conflict of interest: None

[Objective] To investigate the relationship between CPPD crystal and operated knee OA. [Methods] Seven hundred forty-three TKAs or HTOs were performed for over KL grade III OA of knees (average age 72.8: male 147: female 596). At the operation, joint fluids were collected and elucidated the CPPD crystal. We evaluated the relationship between CPPD crystals and age (years), height (cm), weight (kg), BMI, CRP, ESR (mm/h), MMP-3, degree of osteophyte formation and alignment. [Results] CPPD crystals were detected from 213 OA knees (29%). There were significant differences between CPPD (+/-) groups about age (71/77), height (154/150), weight (63/57), BMI (26/25), and ESR (24/27). CPPD (+) rate in female (31%) was significantly higher than that in male (18%). The more severe osteophyte formation became, the higher CPPD (+) rate was, significantly. Although CPPD (+) rate in valgus knees (57%) was higher than that in varus knees (29%). The risk factors (odds ratio) of CPPD (+) by logistic regression analysis were age (1.078), valgus knee (5.740), osteophyte (2.077), and BMI (0.934). [Conclusions] Severe osteophyte and valgus knee were risk factors of CPPD (+). However, severe osteophyte was not usually seen in valgus knee. It may suggest that there are different mechanisms between these two risk factors.

P36-2

Sequential changes of arthropathy and pain-related behavior in a rat surgical osteoarthritis model

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Conflict of interest: None

[Objective] Animal models of osteoarthritis are being applied to improve our understanding of the condition and to develop more disease-specific treatments. There are two types of models: chemical models and surgical models. In the past, we have used surgical models to remove the anterior cruciate ligament and meniscus in the knee joint. We investigated whether it is possible to create a surgical model of the hip joint as well. [Methods] Six-week-old male SD rats (n=10) were used. The right hip was designated as the instability group and the left hip as the stability group, and imaging, histological and pain behavior was evaluated at 1, 2, 4, 8, and 12 weeks after the model was created. [Results] In the radiographic evaluation of the instability group, we found osteotomy collapse from 4 weeks after the creation of the model. Histological evaluation showed superficial synovial detachment and cartilage degeneration at the same time. Imaging and tissue degeneration progressed over time, but at 12 weeks, the patient did not present with end-stage arthropathy. Pain behavioral assessment showed a decrease in ground pressure and ground contact time of the affected limb over time. [Conclusions] It was found that osteoarthritis was induced by inducing instability in the hip joint.

P36-3

Association of locomotive stage, frailty, and sarcopenia in patients just prior to knee arthroplasty

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Conflict of interest: None

[Objective] We assessed locomotive syndrome (LS), frailty and sarcopenia in patients with knee disorders immediately before arthroplasty, and investigated the relationship. [Methods] All patients scheduled to undergo knee arthroplasty at our hospital after July 2020 were assessed for basic attributes, clinical assessment, blood tests, radiography, whole-body mode DXA, knee muscle strength by dynamometer. LS tests, Japanese Cardiovascular Health Study criteria, and sarcopenia by AWGS 2019 criteria were evaluated. [Results] Among 30 patients (27 women, mean age 74 years) the overall distribution in LS was (0: 0%, 1: 3.4%, 2: 10.3, 3: 86.2), in frailty (no: 14.3%, pre-frailty: 57.4, frailty: 28.6) and in sarcopenia (no: 93.3%, yes: 3.3, severe: 3.3). More than 86% had LS degree 3, mainly due to the locomotive 25 questionnaire. The rate of LS incidence due to knee disorders was high, but sarcopenia and frailty, low. In other words, as in the previous report, LS was able to adequately screen for knee dysfunction. [Conclusions] In the group of patients with knee disorders immediately before arthroplasty, LS3 exceeded 86%, but it was not necessarily accompanied by sarcopenia and frailty. The study limitation was the small number of cases.

P36-4

Investigation of locomotive syndrome in patients who received Total Knee Arthroplasty

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Conflict of interest: None

[Objective] Knee-joint disorders are one of the diseases that can cause locomotive syndrome. The purpose of this study was to investigate the degree of locomotive syndrome in patients who underwent TKA for knee-joint disorders. [Methods] Before TKA, locomo tests (Stand-up test and Two-step test Locomo-25) were performed. The muscle mass of the lower

extremities was measured by DXA (Dual Energy X-ray Absorptiometry). [Results] Thirty patients were included (3 males and 27 females), mean age was 74.0±10.3 years, disease duration was 8.0 [1.0, 38.0] years. The mean operative side lower extremity lean mass was 5.7±1.3 kg and the mean extension force was 0.24±0.08 kgf/kg. The results of the locomo test were grade 1: 3.4%, grade 2: 10.3% and grade 3: 86.7%. There was a significant negative correlation between pain VAS and extensibility (r=-0.40, p=0.003). The grade 3 group had significantly higher pain VAS than the grade 2 in the 2-step test (p=0.014). [Conclusions] A preoperative locomotive survey was performed in patients with knee-joint disorders who required TKA. The majority (86.7%) were grade 3 and had significant loss of mobility. Pain affected the 2-step test, and if the pain was reduced by surgery, there was a possibility of improvement in locomotive function.

P36-5

Investigation of factors that determine the type of hip fracture using finite element analysis

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Conflict of interest: None

[Objective] To verify the fall situation that can reproduce the fracture type of the proximal femur fracture caused by the fall using finite element analysis. [Methods] For 20 cases of proximal femur fractures (10 cases of cervical fracture, 10 cases of trochanteric fracture) injured by the fall, finite element analysis using CT data of the intact side was performed. In the analysis, the fall from the lateral side to the posterior side was reproduced, and the fracture type that occurred was verified. [Results/Conclusions] It was suggested that more trochanteric fractures occurred in the posterior fall, and the reproducibility of the fractures was higher in the lateral fall model.

P36-6

An effect on medication adherence of osteoporotic injection-treated patients by the outbreak of COVID-19 in our medical institutions designated for type II infectious diseases

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Conflict of interest: None

[Objective] We evaluated the treatment effect and medication adherence of osteoporotic injection-treated patients by the outbreak of COVID-19 in our medical institutions designated for type II infectious diseases. [Methods] During the outbreak of COVID-19, from January to June 2020, 238 osteoporotic injection-treated patients had consulted to orthopedic surgery departments in our hospital. [Results] We had used denosumab (group D 82 cases), romosozumab (group R 77 cases), and teriparatide (group T 79 cases). Rheumatoid arthritis patients were 5.5% of them. The new induction cases of osteoporotic injection therapy were group D 28, group R 58, and group T 62 cases, and those cases during the outbreak were group D 10, group R 27, and group T 13 cases. The number of visits to our hospital during the outbreak were mean group D 2.3, group R 3.9, and group T 2.8 times, respectively. All rheumatoid arthritis patients could visit to our hospital on schedule. 86% of them had medical examinations for their reservations on schedule, but 9.7% had stopped their treatments or changed hospitals under the influence of COVID-19 outbreak. [Conclusions] Osteoporotic injection-treated patients had been necessay to enlightenment about the importance of their treatment continuations.

P36-7

Evaluation of the value of serum 25-hydroxy vitamin D in the patients affected osteoporosis

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Conflict of interest: None

[Objective] To evaluate the sufficiency of vitamin D (VD), serum 25-hydroxy vitamin D (25 (OH) D) is examined. In current study, we aimed to reveal the correlations among the value of serum 25 (OH) D and the clinical course, physical conditions in the patients affected osteoporosis. [Methods] In the 69 female patients over 65 years receiving the treatment due to osteoporosis, the value of serum 25 (OH) D and intact PTH (iPTH) were examined, and Geriatric Locomotive Function Scale (GFLS-25) was done. [Results] In the patients receiving the treatment with active VD (Group A, 47 cases), the value of serum iPTH was 16.0 ng/mL, and in other (Group B, 22) 16.2 ng/mL (P=0.89). The value of serum iPTH was 32.7 pg/mL in Group A, and 51.5 pg/mL in Group B (P=0.10). All 69 cases were divided two groups, in whom the value of serum 25 (OH) D was higher than 15 ng/mL (Group X, 40) and another (Group Y, 29). GFLS-25 was 18.8 points in Group X and 21.3 points in Group Y (P=0.57). The value of serum iPTH was 33.7 pg/mL in Group X and 45.5 pg/mL in Group Y (P=0.10). [Conclusions] There was no correlation among the administration of active VD and the value of serum 25 (OH) D, thus it was considered to be impossible determining the sufficiency of VD in the patients receiving the treatment with active VD.

P37-1

Is the amount of physical activity an outcome for treatment of sarcopenia in patients with rheumatoid arthritis?

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Conflict of interest: None

[Objective] Pain-related physical inactivity causes sarcopenia secondary to rheumatoid arthritis (RA). Various guidelines recommend at least 150 minutes/ week of moderate-to-vigorous physical activity (MVPA), however it is not an indicator for treatment of sarcopenia. The present study investigated reference value of physical activity associated with development of sarcopenia in patients with RA. [Methods] Twenty-three patients with RA was measured for physical activity by wearing accelerometer (Actigraph GT3X BT monitor). Physical activity parameter was compared between sarcopenia group and non-sarcopenia group, and cut-off values calculated using receive operating characteristic curve. [Results] The mean values for MVPA in sarcopenia group and non-sarcopenia group were 38.2 minutes / week and 160.4 minutes / week ($p < 0.05$). The cut-off values of MVPA was 92.0 minutes / week (sensitivity=78.0%, specificity=100%, and Area Under the Curve=0.91). [Conclusions] Although many reports have used skeletal muscle mass as an outcome in treatment of sarcopenia, there is no established method to increase skeletal muscle mass in patients with RA sarcopenia. Therefore, we hypothesized that the reference value of MVPA could be an indicator for the prevention and treatment of RA sarcopenia.

P37-2

An attempt of online music therapy for patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] We previously reported that active music therapy improves general health (GH) condition and moods of patients with RA.

However, currently music therapy on site cannot be performed under COVID-19 pandemic. Therefore, in this study, we investigated the effects of on-line music therapy. [Methods] Zoom online meeting system was recruited. Eight songs were sung with a piano accompaniment and 4 were played with CUPS. GH condition was evaluated by 0-10 NRS, pain by face scale, positive and negative moods by honcho, and emotional relaxation were surveyed by self-rating questionnaire including 10 cm GH-VAS, face pain rating scale, PANAS, and ERS. [Results] Nine female patients were participated. mHAQ was 0.68±0.53 (0-1.75). The sound was occasionally delayed on line and the synchronization of music was not very easy. The results of 7 patients were; GH 2.1/2.1, pain 5.7/4.4, positive affect of PANAS 23.6/25.0, Negative affect of PANAS was not changed. Four subscales of ERS were 9.4, 10, 9.6, 9.6 respectively. [Conclusions] On line active music therapy can be applied for patients with RA even under COVID-19 pandemic.

P37-3

The effect of lomosozumab treatment on skeletal muscle in patients with rheumatoid arthritis

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Conflict of interest: None

[Introduction] Drugs for treatment of osteoporosis reduce the risk of falls. Some reports suggest that the mechanism is related to skeletal muscle. [Purpose] We investigated the efficacy of Romosozumab treatment in patients with rheumatoid arthritis (RA). [Method] Patients with RA administered monthly Romosozumab 210 mg (n=10, Group R) and not-administered (n=25, Group C) were enrolled. We examined Skeletal Muscle Mass Index (SMI) measured by using Inbody770, body mass index, gender, age, RA disease duration, predonisolone, methotrexate, biologic agent, Disease Activity Score 28 with CRP (DAC28-CRP), Health Assessment Questionnaire Disability Index (HAQ-DI) before and one year after administration. Both Group R and C showed no significant difference in all parameters of patient characteristics. [Result] The mean DAS28-CRP before administration was 1.97/2.18 in Group R/C respectively, and changed to 1.52/1.90 one year later (p=0.01). The mean HAQ-DI and SMI before administration was 0.92/0.81 and 5.30/5.69 in Group R/C respectively, and showed no change one year later. There were no significant differences in DAS28-CRP, HAQ-DI and SMI between Group R and C. [Discussion] It is considered that Romosozumab treatment has no negative effect on disease activity and musculoskeletal system.

P37-4

Report on a survey on the satisfaction with the operation of the Sarilumab auto-injector

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Conflict of interest: None

[Objective] Biologic autoinjections can be challenging due to upper extremity function and device geometry. We report the relationship between operational satisfaction and physical function of the sarilumab auto-injector (SRM AI). [Methods] The subjects were 51 rheumatoid arthritis patients admitted to our hospital who could use SRM AI. We divided the SRM AI operation into three actions, “removing the cap”, “holding” and “pushing”, and surveyed patient satisfaction with a questionnaire. Patient satisfaction was divided into three categories: age, years of illness, pain, HAQ, deformity, grip strength, ROM, Hand20, and FIM. [Results] Spearman’s rank correlation coefficients and multiple linear regression analysis were used to identify the items related to the satisfaction level. Satisfaction was correlated with Hand20 and age for “removing”, grip strength, forearm rotation and internal rotation of the shoulder for “holding”, and Hand20, shoulder flexion, grip strength and forearm rotation for “pushing”. [Conclusion] Satisfaction was shown to be related to upper limb function. Although self-injection itself is possible, there is a concern that it may lead to hand misuse during the process. It seems important to provide patient guidance as part of occupational therapy to prevent misuse.

P37-5

“Frail” in the elderly rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] To investigate clinical data of the elderly rheumatoid arthritis (RA) patients with frailty. [Patients and Methods] There were 58 patients (7 males, 51 females) with an average age of 81.4 years and an average duration of RA of 16.8 years. Clinical data were collected upon “Frail” hospitalization. [Results] The average DAS-28 was 3.29, with 41 (71%) having moderate disease activity or higher. Skeletal muscle index (SMI) decreased in 51 patients (88%), gait speed averaged 0.86 m/s, and locomotive degree 2 or higher was observed in 51 patients (88%), showing marked decline in lower limb muscle strength. The average grip strength was 21.6 kg for men and 11.9 kg for women, and a positive correlation (r = 0.58) was noted between SMI and grip strength. EQ-5D (QOL) averaged 0.622, BDI-II (depression) 14 points or higher in 37 cases (64%), MMSE suspected dementia in 7 cases (12.1%), CONUT (nutrition) with poor nutrition in 51 cases (88%), bone mineral density % YAM in the femoral neck was 70% or less in 33 cases (57%). [Conclusion] “Frail” in the elderly RA patients, age-related weakness appeared to be influenced by RA-related negative factors. In addition to controlling disease activity, a further physical and psychological approach is needed.

P37-6

Exercise habits in patients with rheumatic disease and the changes in Covid-19 pandemic

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Conflict of interest: None

[Objective] To investigate about exercise habits in patients with rheumatic disease. We enlightened exercise habits, reinvestigated about the effects in COVID-19 pandemic. [Methods] Outpatients filled out questionnaires before consultation at first. Questionnaires included whether they exercise usually, what kind of exercise do and what is barriers to exercise mainly. At the same time, we encouraged home exercise, and reinvestigated exercise habits and the changes after ten months. [Results] 603 patients were enrolled, 38.0% of patients exercise usually at first. Performed exercises were radio/TV gymnastics and walking in many patients. Most common barriers to exercise were lack of time (48%), those were more than pain (42%). 597 patients were enrolled in second questionnaires, 36.7% of patients enforced exercise usually. 128 patients responded the opportunity to exercise have disappeared or decreased in COVID-19 pandemic. [Conclusions] Less than 40% of patients with rheumatic disease exercised usually. In order to perform exercises habits continuously, in addition to disease control, how to incorporate exercise into a part of life is key point. There is concern that a decrease exercise habits will reduce not only physical activity but also social participation in COVID-19 pandemic.

P37-7

Questionnaire survey of a physical activity in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To design early intervention for rheumatoid arthritis (RA) health care system, we collected an information of activity of daily life (ADL) and physical activity (PA) in RA patients. [Methods] Two hundred twenty outpatients with RA in our hospital were participated in cross-sectional study. They were asked to complete self-report questionnaires assessing PA, ADL, rehabilitation experience and quality of life (QOL). Data were statistically evaluated using Mann-Whitney U test. [Results] One hundred twenty-six eligible RA patients were assigned to this study. The age was 64.4 years with 70.6% of women. They were divided into 2 groups according to the degree of PA. The score of RAQOL in active group was significantly lower than that in inactive group, and they could continue working and their hobbies. Furthermore, they were divided into another two groups according to the experience of rehabilitation. Rehabilitation group has significant higher self-efficacy for exercise than that of non-rehabilitation group. [Conclusions] Regular physical activity was related to persistence of their jobs and hobbies with improvement of their QOL in RA patients. Regarding to the self- efficacy, it is necessary to manage health care system to provide RA patients with early rehabilitation.

P37-8

Needs of rehabilitation in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The rheumatoid arthritis (RA) team was established in our hospital last year, and we investigated the current situation of RA patients and their wishes for rehabilitation. [Methods] Two hundred twenty outpatients were carried out a questionnaire survey regarding their current ADLs, exercise status, future expectations and details, and sources of RA information. [Results] Within the survey period, valid responses were obtained from 176 patients. 55% of the subjects were independent of ADLs and 55% continued to exercise after the onset of the disease. 51% of the respondents haven't any experiences in rehabilitation. They neither feel the necessity of rehabilitation, nor recognize whether they were the objects of rehabilitation. 51% patients hoped to be provided rehabilitation, 64% for exercise therapy and 45% for lifestyle guidance. Among the 124 respondents, 37% obtained information from medical staffs and 17% from the pamphlets of our hospital. [Conclusions] Although the needs for rehabilitation were constant from ADL-independent stage, many patients did not have useful information about rehabilitation outside of the hospital. It is necessary to establish a rehabilitation system that provides activity-based exercise at an early stage.

P38-1

Analysis of Systemic Lupus Erythematosus Patients' Serum to Determine Disease-specific Autoantibodies for Lupus Nephritis

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Conflict of interest: Yes

[Objective] To determine disease-specific autoantibodies in SLE patients with LN and without LN, and in proliferative LN patients and membranous LN patients. [Methods] 166 SLE patients, who were treated from August 2012 to March 2020 at Juntendo University Hospital, were recruited in the study. Reactivity to 16 autoantibodies was detected by EUROLINE ANA profile (IgG) kit. Kidney biopsies were examined by pathologists, and patients were assigned to proliferative LN group (n=36) and membranous LN group (n=19) according to the results. [Results] Positivity of anti-dsDNA antibody and anti-Histone antibody was prevalent in SLE patients with LN compared to SLE patients without LN. Also, positivity of anti-nucleosome antibody was prevalent in proliferative LN group, while the positivity of anti-RNP-A antibody and anti-RNP-70 antibody was prevalent in membranous LN group. [Conclusions] These data suggest that several autoantibodies are associated with the onset and phenotypes of LN.

P38-2

Treatment results by lupus nephritis remission induction therapy at our hospital

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Conflict of interest: None

[Objective] The efficacy and side effects of various immunosuppressive drugs in induction therapy will be compared and examined in a single institution where the initial administration method of steroid drugs is unified. [Method] It is used as induction therapy among 41 patients who underwent renal biopsy in our department for 10 years from April 2009 to March 2019 and were diagnosed with LN III and IV type. IVCY in 15 cases, tacrolimus TAC in 7 cases, MMF in 6 cases, multi-target (MT) therapy in MZB + TAC in 3 cases, MMF + TAC in 7 cases. The patient background of each county, complete remission (CR) rate at intervals of 3 months, 6 months, 12 months, adverse events, presence or absence of relapse, and steroid dose are compared retrospectively. [Result] There were no significant differences in patient background at the start of treatment. Complete remission achievement rate (%) 3 and 12 months after the start of treatment was 60 and 80 in the IVCY group, 71.4 and 71.4 in the TAC group, 66.7 and 66.7 in the MMF group, 66.7 and 100 in the MZB + TAC group, 42.9 and 85.7 in the MMF + TAC group. [Conclusion] The CR rate increased over time with IVCY and MT therapy, but the CR rate at 3 and 12 months remained unchanged in the TAC and MMF groups.

P38-3

5-year outcomes of 1st-line combination therapy for 36 patients with lupus nephritis

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Conflict of interest: None

[Objective] To evaluated the impact of 1st-line combination therapy on 5-year outcomes for patients with lupus nephritis. [Methods] The subjects were 36 patients who received induction therapy with glucocorticoids, mizoribine, and tacrolimus according to our protocol. We examined the following items: (1) overall efficacy, (2) tapering in the number of immunosuppressants, (3) comparison of MZB and TAC, and (4) cases moved on to 2nd-line therapy (switching MZB to MMF). [Results] (1) At 5 years, 88% achieved proteinuria remission (≦0.2 g/day). (2) We compared 20 cases in Group A who were able to reduce their immunosuppressants to one MZB or TAC, and 14 in Group B who could not. There was no difference in patient background and 5-year renal outcomes. Group A could be identified by early complement improvement. (3) No difference in renal outcomes and PSL dosage at 5 years was observed. (4) Complete remission was achieved in 2 cases, while 1 developed end-stage renal disease in 5th year. [Conclusions] 91% were able to continue 1st-line therapy throughout 5-year. Although maintenance therapy with two immunosuppressants was often required (41%), 5-year renal outcomes and safety were as good and acceptable as those in Group A. The efficacy of MZB and TAC in Group A was equivalent.

P38-4

A study of 98 cases of neuro-psychiatric systemic lupus erythematosus (NPSLE) in our hospital

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Conflict of interest: None

[Objective] We conducted retrospective observational study to investigate the baseline clinical features and prognosis of NPSLE at our hospital. [Methods] We conducted retrospective observational study to investigate the baseline clinical features and prognosis of NPSLE at our hospital. From April 2008 to September 2018, NPSLE was diagnosed at our hospital and 98 patients with NPSLE who had been treated were analyzed retrospectively. Their Clinical features, treatment contents, prognosis, presence or absence of lupus nephritis etc. were examined. [Results] The survival curve was not significantly different between the diffuse and focal groups with LN, but the diffuse group without LN and the diffuse and focal group without LN, and the focal group without LN and without LN. A comparison between the diffuse group without LN and the focal group without LN revealed significant differences in the items of maximum steroid use, steroid pulse, IVCY, and anticoagulant. These items were consistent with the results of analysis of NPSLE patients divided into a diffuse group and a focal group regardless of LN complications. [Conclusions] It was suggested that LN complication was not involved in prognosis or treatment in NPSLE patients.

P38-5

Examination of clinical features and treatment outcomes of 7 neuropsychiatric lupus (NPSLE) in our hospital

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Conflict of interest: None

[Objective] NPSLE is one of the prognostic factors in SLE, presents with various central nervous system symptoms, and may leave severe neuropathy. So, early diagnosis and treatment are important. We will examine the clinical picture, treatment and outcome of NPSLE in our hospital. [Methods] We investigated the patinet background, symptoms, cerebrospinal fluid (CSF) test, immunological items, MRI test, treatment and outcome of 7 NPSLE patinets who were diagnosed at our hospital from 2009 to 2020. [Results] 7cases (23~59 years old) are all females. There were 5 nervous system symptoms. Elevated CSF IL-6 was observed in 3 of 7 cases. Anti-rebosome P antibody and/or anti-phospholipid antibody were positive in some of 7 cases. MRI test showed abnormal signals in 2 of 7 cases. Treatment was high-dose steroid therapy (4 cases) and intravenous cyclophosphamide therapy (5 cases) and concomitant medications were hydroxychloroquine (5 cases), mycophenolate mofetil (2 cases) and belimumab (2 cases). 1 case left sequelae. Improvement clinical symptom was observed in 6 cases. [Conclusions] NPSLE is one of the refractory pathology of SLE and may leave serious sequelae, but symptoms are often reversible as previously reported. It's expected neurological symptoms will improve in more cases by early aggressive treatment.

P38-6

Association between drinking habits and fatigue in systemic lupus erythematosus (SLE): cross-sectional study from LUNA registry

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Conflict of interest: None

[Objective] Fatigue is one of the biggest burdens in SLE patients. Some studies reported that disease activity, glucocorticoid (GC) use and anxiety/depression are associated with fatigue, but it is still not unclear about alcohol consumption. We evaluated the association of drinking habits and fatigue. [Methods] From LUNA registry, patients between 20 and 75 years with data of LupusPRO enrolled. Exposure was frequency of drinking. The frequency devided into 3 groups, <1 day/month, ≦1 day/week and ≧2 days/week, respectively. Primary outcome was Pain Vitality domain score [0-100: high score is better] as fatigue in LupusPRO. We performed multiple regression analysis by adjusting age, sex, disease activity, disease duration, GC use and anxiety/depression as covariates. [Result] Of 542 eligible patients, female was 474 (87.5%) and mean age was 45-year-old (Interquartile range [IQR] 34-55). The frequency of drinking were <1 day/month in 326 (60.2%), ≦1 day/week in 127 (23.4%) and ≧2 days/week in 89 (16.4%), respectively. In the group of ≧2 days/week, single and multiple regression analysis showed that β coefficient was 7.29 (p=0.015) and 6.18 (p=0.034), respectively. Fatigue was less in this group. [Conclusions] Frequent drinking habit was associated with less fatigue in SLE patients.

P38-7

Effectiveness and safety of belimumab (BLM) in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] To examine the effectiveness, safety and retention rate of belimumab (BLM) in patients with SLE. [Methods] SLE patients who were prescribed subcutaneous injection of BLM in our hospital from December 2018 to October 2020 were analyzed retrospectively. Effectiveness was evaluated by change in laboratory findings, SLE disease activity index (SLEDAI) and prednisolone (PSL) dose from the start of BLM to 12 weeks. Adverse events and the reason for stopping BLM and retention rate were analyzed. [Results] Of 9 cases, 7 were female (77.8%) with median age [interquartile range] 36 [31, 55] years, SLE disease duration 21 [13.5, 157.5] months, SLEDAI 8 [4, 12.5], anti-dsDNA antibody titer 7 [2.1, 72] IU/mL and PSL 10 [4.5, 15] mg/day. BLM was continued for 20 [12, 54] weeks until October 2020 and 7 patients were continued BLM for 12 weeks. The change in SLEDAI was 4 [4, 10] and dose of PSL was 2.5 [1.0, 5.0] mg/day. No adverse events were observed during the course, and 1 case was discontinued due to pregnancy four months after administration, but no complications were found in the mother and her baby. The retention rate was 77.8% at 12 weeks. [Conclusions] Combined use of BLM was effective in reducing SLE activity and dose of PSL with safety and high retention rate.

P38-8

Impact of belimumab on clinical background and effects of systemic lupus erythematosus

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Conflict of interest: None

[Objective] There is still little information on the usefulness of belimumab (BEL) in clinical cases of systemic lupus erythematosus (SLE) in Japan. Therefore, we examined the clinical background and effects of BEL-introduced patients at our hospital. [Methods] From March 2018, we

retrospectively observed the clinical background and effects of BEL-introduced patients with less than moderate activity (SLEDAI 12 or less), excluding the active phase of lupus nephritis and central nervous system lupus. [Results] The subjects were 7 cases (7 women, age 49.3 ± 14.0 years). The data and dose of each immunosuppressant before the start of BEL to 3 months later was following; SLEDAI, 5.7 ± 2.9 to 2.3 ± 2.0 (p = 0.037); IgG, 1277 ± 316 mg/dl to 1097 ± 255 mg/dl; C3, 73.4 ± 22.4 mg/dl to 85.7 ± 32.3 mg/dl; C4, 18.3 ± 9.0 mg/dl to 22.2 ± 14.4 mg/dl; prednisolone (PSL), 14.3 ± 13.4 mg to 9.2 ± 4.7 mg; hydroxychloroquine (HCQ), 229 ± 179 mg to 267 ± 206 mg; MMF, 571±731 mg to 667±752 mg. [Conclusions] SLE with moderate activity or less has an additional effect of BEL combined with immunosuppressants. No severe infections were observed after the start of BEL, but IgG after the start was slightly decreasing, which we need to pay attention to.

P38-9

Clinical features in patients with systemic lupus erythematosus treated with belimumab and its efficacy

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Conflict of interest: None

[Objective] To clarify the clinical features in patients with systemic lupus erythematosus (SLE) treated with belimumab (BLM) and its efficacy. [Methods] This study included 23 cases treated with BLM in University of Tsukuba hospital. We retrospectively evaluated 1) baseline characteristics, 2) purpose of BLM therapy, 3) clinical course in 13 cases for 52 weeks, and 5 cases for 104 weeks, and 4) adverse events (AE). [Results] 1) Mean age was 35.2±10.2 years old. Mean SLEDAI-2K and anti-DNA antibody (ADNA) titer were 7.0±3.6 and 42.3±52.5 IU/mL. Mean prednisolone (PSL) dose was 15.3±8.8 mg/day. BLM was administrated by subcutaneously in 17 cases and by intravenously in 6 cases. 2) BLM was used for remission induction in 3 cases, to control disease activity in 9 cases refractory to previous therapy, for maintenance therapy in 1 case, and to reduce PSL dose in 10 cases. 3) Dose of PSL was significantly reduced at 52 and 104 weeks. The SLEDAI-2K and ADNA titer were improved significantly at 52 weeks. They were also improved at 104 weeks, but not statistically significant. 4) Six cases experienced AE. Although severe AE were not reported, BLM was discontinued in 3 cases. [Conclusions] BLM might be effective for the improvement of disease activity and the reduction of PSL dose in patients with SLE.

P38-10

Short-term effects of belimumab on patients with SLE who have difficulty reduce glucocorticoids

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Conflict of interest: None

[Objective] We investigated the short-term effects of BEL on patients with SLE who have difficulty reduce glucocorticoids. [Methods] Nine SLE patients were introduced BEL at our hospital from December 2017 to the end of October 2020. We investigated changes in SLEDAI, serum ds-DNA antibody titer, and prednisolone (PSL) dose at 12 weeks. [Results] Patients were 7 females and 2 males. The average age at the time of BEL introduction was 45.2 ± 11.7 years, disease duration was 8.0 ± 3.9 years, SLEDAI was 7.3 ± 7.6, serum ds-DNA antibody titer was 29.8 ± 16.8 IU / ml, PSL. The oral dose was 11.1 ± 7.7 mg / day. Twelve weeks after the introduction of BEL, SLEDAI was 3.6 ± 1.9 and the oral dose of PSL was 8.8 ± 5.0 mg / day. The serum ds-DNA antibody titer was significantly reduced to 18.7 ± 13.1 IU / ml ($p<0.05$). No adverse events were observed due to the introduction of BEL. [Conclusions] In SLE cases in which glucocorticoid dose reduction was difficult, BEL showed no SLE active relapse, at least in the early stages of introduction, and a significant decrease in anti-ds-DNA antibody was observed.

P38-11

Experience with belimumab in our department

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Conflict of interest: Yes

[Objective] We evaluated the effect in patients treated with belimumab in SLE. [Methods] We observed the disease activity and clinical course of 15 SLE patients received belimumab in our department between April 2018 and March 2020 for 6 months. We analyzed PBMCs by flow cytometry at baseline, Month 3. [Results] Of the 15 patients, 10 patients who remained on belimumab for 6 months were studied. In all cases, there was an increase in complement levels. In the 6 patients with positive anti-dsDNA at baseline, anti-dsDNA levels were reduced. 3 patients achieved an SRI-4 response, but only 1 of them could reduce PSL dosage. 2 patients could reduce PSL but they were not SRI4 responders. 2 patients had worsening of BILAG scores, and Naïve B cells increased after 3 months in both cases. [Conclusions] The serological makers improved after the start of belimumab. It is necessary to continue to investigate in the long term whether the improvement of serological abnormal findings contributes to the maintenance of low disease activity and the reduction of PSL dose. We observed changes in B cell subsets early after belimumab treatment. At that point, we may be able to predict responsiveness to treatment. Further studies are needed.

P38-12

The efficacy of glucocorticoid dose reduction by the combination use of hydroxychloroquine in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] To clarify the efficacy and predictors of prednisolone (PSL) sparing effect by the combination use of hydroxychloroquine (HCQ) in systemic lupus erythematosus (SLE) during maintenance therapy. [Methods] SLE patients who were treated with PSL less than 15 mg as maintenance dose and were initiated HCQ and continued over 24 weeks were enrolled. We excluded the patients who added another immunosuppressant after HCQ initiation. We retrospectively examined the changes in disease activity, PSL dose and C3, C4 concentration as well as clinical backgrounds before HCQ initiation. [Results] Seventy-nine patients were enrolled. Age and disease duration were 40.6±12.3 and 11.5±8.7 years, respectively. PSL dose was significantly reduced from the baseline at 24 and 48 weeks SLEDAI score, hypocomplementemia and anti-dsDNA antibody titer also significantly improved after the initiation of HCQ. We also identified that low titers of anti-dsDNA antibody (≦32 U/ml) is a predictive factor of possible PSL reduction within 24 week after HCQ initiation ($p=0.027$). [Conclusions] Combination use of HCQ could reduce PSL dose during maintenance therapy in SLE patients and this seemed to be more susceptible with low titers of anti-dsDNA antibody at the initiation of HCQ.

P38-13

Questionnaire survey related to non-prescription of hydroxychloroquine in SLE patients and the subsequent change in prescription rates

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Department of General Medicine, Tenri Hospital

Conflict of interest: None

[Objective] HCQ is the standard treatment for SLE, but the prescription rate at our hospital is low compared to other countries' cohort. We

previously conducted a questionnaire survey on the reasons for non-prescription. The purpose of this study was to investigate the subsequent change in prescription rates. [Methods] At of the end of October 2019, 138 of the 280 SLE patients visiting our hospital had not been prescribed HCQ. We conducted a questionnaire survey regarding the reasons for non-prescription. We investigated changes in the prescription rate up to the end of September 2020, and compared the background and the questionnaire responses. [Results] There were 21 cases with new prescription and 117 cases without, and the prescription rate increased from 50.8% to 58.2%. Patient factors related to prescription include short duration of illness, high SLEDAI, high dsDNA, short years after graduation of the physician. Among the questionnaire responses, "I forgot to prescribe" correlated with new prescription, and "I could not prescribe because of patients' concern about side effects" tended to have no new prescription. [Conclusions] After the questionnaire survey, the HCQ prescription rate increased by 7.4%, and "forgot to prescribe" correlated with the new prescription.

P38-14

The investigation of hydroxychloroquine (HCQ) dosage and intervention to the high-dose and renal dysfunction cases by the pharmacist for SLE patients

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Conflict of interest: None

Objective: HCQ is used as the standard treatment for SLE, but due to concerns about retinal toxicity. EULAR 2019 recommend not exceed 5 mg / kg of actual body weight and dose down in patients with renal dysfunction by JCR guidelines. In this study, we investigated the patients in our rheumatic division receiving HCQ, and intervened in cases for which the above recommendations. **Methods:** For SLE patients (103 cases) who have continued HCQ for more than 1 year from January 2019 to July 2020, we investigated age, gender, height, weight, HCQ dose, renal function, retrospectively from the medical records, and proposed dosing down in cases of prescribed HCQ 5 mg/kg or more or eGFR (mL/min/1.73 m2) 50 or less. **Results:** The median age was 46 years, 90 females (87.4%), height 157.1 cm, weight 54 kg, Cr 0.72 kg / dL, eGFR 71, HCQ dose per actual body weight 4.4 mg/kg/day. more than 5 mg/kg/day case were 28 (27.2%), eGFR 50 or less were 16 cases (15.5%) and less than the package insert 39 cases (37.9%). I proposed the dose reduction for 8 cases. **Conclusions:** It is considered that the HCQ therapy was carried out more safely when the pharmacist decided the dose in cooperation with the doctor. We would like to continue to follow up and intervene to reduce the future risk of developing retinopathy.

P38-15

Validation of an algorithm for identifying Systemic Lupus Erythematosus (SLE) cases in administrative health claims datasets: pilot study

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Conflict of interest: None

[Objective] Administrative health claims (AHC) datasets can be valuable for disease surveillance. Several studies have validated the accuracy of an algorithm for identifying SLE patients worldwide. However, no evidence is available in Japan. This study aims to validate an algorithm for identifying SLE cases in AHC datasets in Japan. [Methods] We performed a medical chart review of outpatients who have at least one SLE-related ICD 10 code from Division of Rheumatology, Showa University Hospital from 1 January to 31 December 2019. We used 1997 ACR criteria as a reference standard. We validated different combinations of SLE-related ICD10, test, drug, and supervision charges for intractable diseases. We used PPV as a primary outcome. [Results] 523 patients had at least one SLE-related ICD 10 code. patients were classified as having SLE and 259 patients were classified as not having SLE based on our reference standard definition (study SLE prevalence 49.5%). The accuracy of the algorithm of "test+drug, +and supervision charges for intractable diseases" within 1 year performed well with 91.1% PPV (95%CI 86.1-94.7). [Conclusions] We recommend this algorithm as the standard AHC case definition for SLE in Japan. We will conduct further research in an expanded departments and hospitals.

P38-16

Risk factors for mycophenolate mofetil-related adverse events

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Conflict of interest: None

[Objective] Mycophenolate mofetil (MMF) is a key drug used to treat systemic erythematosus (SLE). Blood concentrations vary considerably; it is difficult to assay the drug in routine clinical settings. We sought clinical variables identifying an ideal MMF dose. We focused on drug-drug interactions between glucocorticoids and MMF; the former drugs reduce MMF blood concentrations in a manner that is not well understood. [Methods] We retrospectively analyzed 88 SLE patients treated with MMF in our hospital. We subjected clinical parameters, concomitant medications, and adverse events to multivariate analysis. [Results] We recorded 47 adverse events (11 cytopenias, 11 abdominal symptoms, 11 zoster infections, 14 other severe infections). The odds ratio for cytopenia (which correlates with the MMF blood concentration) was 4.12 in patients on prednisolone 10 mg/day or less ($p = 0.04$). [Conclusion] Glucocorticoid tapering increases the risk of MMF-associated adverse events; overdoses must be prevented.

P38-17

Characteristics of patients showing normal serum complement levels at the diagnosis of SLE

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Conflict of interest: None

[Objective] To clarify the clinical characteristics of patients with systemic lupus erythematosus (SLE) showing normal serum complement levels. [Method] We included 114 patients with SLE. Patients who showed normal serum levels of C3, C4, and CH50 at the initial diagnosis of SLE were classified into normal level group (N-group), whereas those showing hypocomplementemia were classified into low level group (L-group). Clinical findings were compared between two groups. [Results] Eleven patients were classified into N-group (9.6%). There were no significant differences in the distribution of age or sex between two groups. SLEDAI-2K scores and frequency of renal involvement were significantly lower in N-group than in L-group. The positivity of anti-ds-DNA antibody was significantly less frequent in N-group than in L-group despite no significant differences in other autoantibodies. [Conclusion] This study suggested that lower disease activity and severity may be clinical characteristic of SLE patients showing normal serum complement levels at the onset of disease compared with those having hypocomplementemia.

P38-18

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

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Conflict of interest: None

[Objective] To analyze the association between hypocomplementemia and infectious disease complications in SLE. [Methods] The patients registered in the multicenter SLE registry "LUNA" were divided into two groups by the lower limit of standard CH50 value at one year from registration. We compared the incidence of infection requiring hospitalization during the one year. [Results] Of the 522 registered patients, 58 (11.1%) belonged to the low CH50 group. The low CH50 group showed significantly lower age (43.0 ± 12.4 vs 47.5 ± 14.7, p = 0.012), higher disease activity (SLEDAI score; 6 (IQR 4-10) vs 4 (2-6), p < 0.01), lower usage rate of azathioprine (13.8% vs 3.45%, p = 0.021) and higher usage rate of tacrolimus (53.1% vs 50.0%, p = 0.029) as compared to the non-low CH50 group. There were no significant differences in the usage of other immunosuppressants and the dosage of glucocorticoid between the groups. There was no significant difference in the incidence of infection requiring hospitalization in the past year between the low CH50 group and the non-low CH50 group (1.72% vs 1.94%, p = 1.00). [Conclusions] We could not find an association between complement and infectious disease complications in SLE.

P38-19

Examination of polypharmacy in systemic lupus erythematosus patients; data from the LUNA registry

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Conflict of interest: None

Examination of polypharmacy in systemic lupus erythematosus patients; data from the LUNA registry [Objective] Polypharmacy (PP) associates with an increased risk of adverse drug reactions and reduction of adherence. Patients with systemic lupus erythematosus (SLE) are considered to have many organ disorders and require multiple drugs for complications due to side effects of steroids. In this study, We investigated the problems and characteristics of PP in SLE patients. [Methods] We investigated the patients registered in the multicenter SLE registry "LUNA". PP was examined in relation to patient background, disease activity, concomitant medications, risk of hospitalization, and risk of adverse events. [Results] 306 patients with SLE were included. 88% were female and median age were 45 years (IQR 35-56). The median number of all medications was 9 (IQR 7-12). PP was associated with older age, higher oral steroid doses, higher SDI and lower health-related quality of life (Lupus Pro), and associated with an increased risk of hospitalization. There were no significant association between PP and adverse events. [Conclusion] PP is common in patients in SLE. PP in SLE may be associated with an increased risk of hospitalization.

P39-1

Lupus nephritis with microangiopathy successfully treated with rituximab and belimumab combination therapy

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Conflict of interest: None

A 28-year-old woman was diagnosed with systemic lupus erythematosus (SLE) due to erythema, cytopenia, and positive for anti-double-stranded DNA antibody four years earlier, but she stopped follow-up because of her own convenience. She developed proteinuria and renal dysfunction: UPCR 1.8 g/gCr and sCr 3.2 mg/dL two months earlier. Kidney biopsy revealed lupus nephritis (LN) class IV, and she received oral prednisolone (PSL) 50 mg per day and mycophenolate mofetil. Induction therapy for LN failed to achieve remission, and she developed thrombotic microangiopathy (TMA). Although cyclophosphamide, tacrolimus, or plasma exchange were not effective, intravenous rituximab (RTX) and belimumab (BLM) combination therapy immediately improved her condition, and PSL was gradually tapered. RTX and BLM combination may be a therapeutic option for the treatment of refractory LN and TMA.

P39-2

Clinical characteristics of 4 male cases of elderly onset systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Elderly-onset systemic lupus erythematosus (SLE) patients who develop over the age of 50 tend to have a higher proportion of men, and their clinical features have been reported to differ from younger SLE patients. We analyzed to clarify the clinical characteristics of elderly-onset SLE patients. [Methods] We investigated the clinical characteristics of 4 elderly male patients diagnosed with SLE in our department during the three years from 2017 to 2020. Both antinuclear and anti-dsDNA antibodies were positive in all cases. [Results] In all cases, the age of onset was 75 years or older and showed leukopenia, pleurisy, and / or pericarditis. Only one patient had kidney injury and proteinuria. SLEDAI in these patients ranged from 7 to 30, and hypocomplementemia was observed with high SLEDAI patients. All of their treatment was initiated with PSL or mPSL pulses therapy. Hydroxychloroquine was continued in only one case. [Conclusion] Serositis was observed in all cases, and steroids were effective for it. In patients with nephritis, urinary protein was prolonged even after the pulse therapy, and various complications occurred. The period from onset to diagnosis is 1 to 3 months except for one case, it is necessary to keep in mind that even elderly men develop SLE.

P39-3

Two case of severe lupus nephritis successfully treated with Belimumab

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Conflict of interest: None

[Background] BLISS trial confirmed the effectiveness of Belimumab (BEL) for SLE, but severe lupus nephritis has been excluded. The efficacy of BEL for lupus nephritis has not been sufficiently examined. [Case 1] A 52-year-old woman was diagnosed with SLE by photosensitivity, pericardial effusion, lymphocyte/thrombocytopenia, anti-double strand DNA antibody, anti-Sm antibody, antinuclear antibody. Renal biopsy was performed, and showed lupus nephritis (ISN/RPS Class 4+5). We administered steroid half pulse, IVCY and 40 mg of PSL, but urinary protein was sustained. Urinary protein decreased after the introduction of BEL treatment. [Case 2] A 81-year-old woman was diagnosed with SLE by arthritis, lymphopenia, anti-Sm antibody and antinuclear antibody and treated with PSL 15 mg. After 3 years, urinary occult blood, urinary protein, and hypoalbuminemia appeared. Renal biopsy was performed and showed lupus nephritis type 5. We increased the dosages of PSL and administered MMF/Tac, but urinary protein was sustained. Urinary protein decreased after the introduction of BEL treatment. [Clinical Significance] In these cases, BEL was effective in reducing urinary protein. It was suggested that BEL may be useful in patients with severe refractory lupus nephritis.

P39-4

A case of COVID-19 infection mimicking a flare of systemic lupus erythematosus

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Conflict of interest: None

[Case] A 61-year-old female was diagnosed with SLE due to polyarthritis, rash, lymph node adenopathy, low complement, a positive ANA test and a positive anticardiolipin IgG antibody. Methotrexate, prednisolone (PSL) and hydroxychloroquine were started for peripheral arthritis. Eight days before admission, she visited our hospital because of worsening polyarthralgia and appetite loss. We suspected that she developed lupus flare because she presented worsening arthralgia and no fever and airway symptoms. We increased the dose of PSL from 5 to 7.5 mg and planned to see her again a week later. However, five days before admission, she presented with water diarrhea and visited our hospital again. We suspected the lupus enteritis and performed abdominal CT with enhanced contrast. CT showed enteritis and incidental ground glass shadows on the lower lobes of both lungs. She admitted to our hospital and COVID-19 PCR test was positive the next day. She was discharged on the 12th day of illness without exacerbation of pneumonia. [Clinical significance] Patients with COVID-19 may present with musculoskeletal symptoms. When seeing the patients with rheumatic diseases, it is necessary to distinguish COVID-19 without easily judging the symptoms as those derived from rheumatic diseases.

P39-5

A case of catastrophic antiphospholipid antibody syndrome with ultra-high titers of antiphospholipid antibodies that has been event-free for 23 years

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Conflict of interest: None

The case is a 72-year-old female, who was noted to be positive for antinuclear and anti-SSA antibodies 23 years ago. Blood samples were positive for high tigters of antiphospholipid antibodies, and aspirin was started. The patient had passed for 23 years without the development of thrombosis. The patient came to our department because of the general malaise which had been persistent for one month before. Blood sampling showed a marked increase in D-dimer and marked animia and thrombocytopenia. Contrast-enhanced computed tomography showed new thrombosis in the spleen, kidneys, and portal vein. The diagnosis of catastrophic antiphospholipid antibody syndrome (CAPS) was made, and continuous intravenous heparin, intravenous steroids, plasma exchange and high-dose immunoglobulin therapy were promptly initiated. She was also diagnosed with active systemic lupus erythematosus after a blood draw revealed hypocomplementemia. High-dose intravenous cyclophosphamide therapy was introduced and the patient gradually improved. Patients with ultra-high titers of antiphospholipid antibodies may develop CAPS even if they have no history of thrombosis. Early diagnosis of CAPS may be life-saving, and we will review the management of CAPS with a review of the literature.

P39-6

A case of lupus enteritis and cytomegalovirus colitis treated with surgical resection and immunosuppressive therapy

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Conflict of interest: None

A 57-year-old woman with systemic lupus erythematosus (SLE) with low dose prednisone and hydroxychloroquine presented with fever, watery diarrhea, and abdominal pain. Abdominal CT scan found the wall thickening and edema of the colon, and colonoscopy revealed mucosal shedding, deep ulcer extended to muscle layer, and colonic stenosis. Pathological examination of biopsy specimens did not find lupus enteritis and mycobacterium and cytomegalovirus (CMV) infections. Because of perforations of sigmoid colon and ileum, the diseased sections of bowel were removed by laparotomy and stoma was created. Pathological examinations showed typical inclusion bodies associated with CMV in the colon, and vasculitis associated with lupus enteritis in the ileum. After surgery, proceeding anti-CMV therapy and intensive immunosuppressive therapy (high dose prednisone and mycophenolate mofetil) successfully controlled CMV infection and lupus enteritis. Here we reported a case of intestinal perforations caused by lupus enteritis and CMV colitis treated with surgical resection, anti-CMV therapy and intensive immunosuppressive therapy. Preceding surgical treatment might be beneficial to following safety intensive immunosuppressive therapy.

P39-7

The quartet of anticoagulants, plasma exchange, intravenous immunoglobulin, and Rituximab was beneficial in critical alveolar hemorrhage and cytopenia in antiphospholipid antibody syndrome (APS)

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Conflict of interest: None

64-year-old female with systemic lupus erythematosus (SLE) associated to antiphospholipid antibody syndrome (APS) referred to our hospital due to impaired consciousness and hemoptysis. She was treated with warfarin and aspirin for APS. Two months ago, the dose of her warfarin was reduced because of subcutaneous bleeding. When hospitalized, chest CT scan revealed alveolar hemorrhage as panlobular infiltration shadows in both lungs. Initially, antithrombotic drugs were discontinued, then she was treated with steroid pulse therapy in combination with wide-spectrum antibacterial drugs. Alveolar hemorrhage was not improved, furthermore, RBC and platelet decreased. Heparin treatment under intubation improved alveolar hemorrhage, however, cytopenia was not improved. After plasma exchange (PE) followed by Intravenous immunoglobulin (IVIG), pulmonary infiltrates disappeared and cytopenia was recovered. But the state of reduced activity was broken by stopping anticoagulants due to sudden upper arm hemorrhage. Pancytopenia recurred. Restarted heparin and another IVIG were not effective. At last, rituximab improved cytopenia completely. Our case demonstrated the therapeutic potential of the combination of those options in APS.

P39-8

Transition from intravenous epoprostenol to oral selexipag and inhaled iroprost in a patient with severe pulmonary arterial hypertension associated with systemic lupus erythematosus

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Conflict of interest: None

We report a case of a 25-year-old woman with severe pulmonary arterial hypertension associated with systemic lupus erythematosus (SLE-PAH). She underwent strong immunosuppressive therapy (steroid pulse therapy and intravenous cyclophosphamide) and pulmonary vasodilation therapy (intravenous prostacyclin, oral phosphodiesterase type 5 inhibitor and endothelin receptor antagonist). Eventually, she was successfully transitioned from intravenous epoprostenol to oral selexipag and inhaled iroprost without re-exacerbation. Her mean pulmonary arterial pressure has improved from 56 mmHg to 20 mmHg after 3 months of treatment. Although intravenous prostacyclin therapy has made it possible to improve functional status, quality of life and mortality of patients with PAH, it carries an increased risk of line-associated complications. A combination of oral and inhaled prostacyclin can be an attractive alternative.

P39-9

A case of systemic lupus erythematosus (SLE) with giant cell arteritis (GCA)

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Conflict of interest: None

A 74-year-old man developed pleurisy at the age of 42 and polyarthralgia at the age of 55. He was diagnosed with SLE because he was positive for anti-dsDNA antibody. Although he had been treated with steroids, high CRP levels persisted for a long time. Inflammation Aortitis was suspected by PET-CT examination for the purpose of screening the source. Therefore, temporal artery biopsy showed infiltration of giant cells. Therefore, it was considered that SLE was complicated by GCA. There are some reports that elderly-onset SLE patients have atypical findings, but no reports of GCA complications are found.

P39-10

A case of golimumab-induced lupus erythematosus in rheumatoid arthritis

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Conflict of interest: None

A 42-year-old man with ACPA-positive rheumatoid arthritis was hospitalized for the evaluation of leukopenia, anemia, proteinuria with hematuria and high fever. He had been treated with methotrexate (MTX), which had not improved his arthritis. Two years before the admission, golimumab (GLM) 50 mg every 4 weeks had been added. Five months before, MTX had been stopped due to liver cirrhosis, ascites and esophageal varices bleeding. One month before, the discontinuation of MTX had worsened his arthritis and GLM dose had been increased to 100 mg every 4 weeks. On admission, the titer of anti-dsDNA antibody was elevated, though the titer had been within normal limit eight years before. The biopsied renal tissue revealed ISN/RPS class IV lupus nephritis. Because the discontinuation of golimumab did not improve his systemic lupus erythematosus (SLE), high-dose prednisolone and mycophenolate mofetil were administered and his lupus gradually improved. In this case, SLE developed after the administration of GLM. This clinical course suggests that the development of SLE was induced by GLM. There are several reports of drug-induced lupus caused by TNF-α inhibitors, but GLM-induced lupus is rare. We report this case with literature review.

P39-11

Successful treatment of fever and arthritis by ustekinumab in a patient with psoriasis vulgaris having received several biological agents against interleukin (IL)-17

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Conflict of interest: None

A 56-year-old man with psoriasis vulgaris had been treated sequentially with secukinumab, brodalumab and ixekizumab since year X-5 at the Division of Dermatology in our medical center without clinical improvement. In late January of year X, fever, fatigue, and joint pain in the left elbow appeared. Antinuclear antibody, which had been consistently negative (only with 80-fold cytoplasmic staining) until December in year X-2 became 1280-fold positive with speckled pattern (positive for anti-RNP and negative for anti-Sm and anti-dsDNA; cytoplasmic staining disappeared). Symptoms persisted even after discontinuation of anti-IL-17 biologics, and he was referred to the Division of Rheumatology. A diagnosis as systemic lupus erythematosus (SLE) was made because of the presence of fever, oligoarthritis, interstitial pneumonia and lymphocytopenia with fulfilling the 2019 ACR/EULAR classification criteria for SLE. An IL-12/23 inhibitor ustekinumab was started based on the evidence from a global phase 2 clinical trial. Fever disappeared within 2 days and oligoarthritis improved subsequently. In addition, the PASI score improved from 5.1 to 2.0 at one month of ustekinumab therapy.

P39-12

A case of chronic TAFRO syndrome mimicking systemic lupus erythematosus

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Conflict of interest: None

A 71-year-old-man was admitted to our hospital with fever and abdominal pain 4 years ago. Systemic CT revealed mesenteric, right hilar and bilateral mediastinal lymphadenopathy and nodular shadows just above the right diaphragm. Laparoscopic mesenteric lymph node resection showed no malignancy without increase in serum IL-2R level. No suggestive findings of granulomatosis or vasculitis were detected by bronchoscopy. Therefore, he was discharged with careful follow-up because the cause of these symptoms was unknown. Next year, exudative pleural effusion was appeared. As thrombocytopenia was progressed in June, bone marrow puncture was performed and fibrosis was suspected. In September, he began to suffer arthralgia. Because antinuclear antibody (ANA) was positive, he was suspected autoimmune disease and referred to our Hospital. Although he was suspected of systemic lupus erythematosus (SLE) because of Hemolytic anemia, arthralgia and ANA positivity, finally he was diagnosed as TAFRO syndrome based on pleural effusion, thrombocytopenia, elevated CRP and Castleman's-like lesion in lymph node specimen. 60 mg/day of prednisolone was started and symptoms were improved promptly. and This case was difficult to diagnosis as TAFRO syndrome because of the symptoms were mimicking SLE.

P39-13

A case of systemic lupus erythematosus that developed during the course of multiple cardiac lipoma

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Conflict of interest: Yes

43-year-old woman with multiple cardiac lipoma. From November X-1 year, heart failure symptoms due to worsening of cardiac lipoma appeared, and in December she was admitted to the cardiology department. Cardiac diastolic dysfunction due to cardiac lipoma was existed and judged to require surgery. On the other hand, fever, edematous erythema, pleural effusion, pericardial fluid, leukocytopenia and hypocomplementemia were existed and antinuclear antibody, antiphospholipid antibody and anti-ds-DNA antibody showed positive. Therefore, she was diagnosed with systemic lupus erythematosus (SLE). Pericardial window and lipomactomy were performed in January X year and administration of prednisolone 30 mg was started. After the treatment, fever, serological activity, erythema and pleural effusion were improved. Cardiac lipoma is a rare disease that is often asymptomatic but can cause problems such as blood flow obstruction and arrhythmias. It occurs in a wide range of age groups, and its relationship with gender has not been clarified. There were no reports of cardiac lipoma with SLE and the mechanism was unknown, but it was considered to be a rare case.

P39-14

A case of HIV infection with SLE-like symptoms, abnormal tests and improvement by administration of antiviral drugs

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Conflict of interest: None

The case is a young adult male. He had a slight fever from February X and visited our hospital in March. WBC3500 / μl (lym840 / μl), Plt 54,000 / μl, ANA640 × (homo + speckled), dsDNA antibody 20 IU / ml, cardiolipin IgG positive, β2GPI positive, complement reduction (C3:59 mg/dl C4:13 mg/dl) etc. were recognized and introduced to our department on May X. Although there was a chief complaint of strong fatigue, no significant abnormal findings were found on the physical findings. Diagnosed as SLE based on classification criteria. No organ damage was observed, so follow-up was performed under HCQ administration. WBC gradually declined during the course, and remained around 2000 / μl. Low complement and Plt decline were flat, and fatigue and low-grade fever symptoms did not improve. In August X + 1, he presented with PCP infection (positive for Grocott's staining of the washing solution and positive for PCR), and HIV infection was discovered. After that, HCQ was discontinued and HIV infection could be controlled by starting an anti-HIV drug. It was thought that the HIV infection was expressing SLE-like symptoms. Since SLE is common among young people, that is, at the risk of HIV infection, it was suggested that HIV screening may be necessary at the time of initial onset.

P39-15

A case of early introduction of belimumab in a patient with systemic lupus erythematosus with immune thrombocytopenic purpura

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Conflict of interest: None

[Case] A 76-year-old man had a rash on the auricle 4 months before the onset, and polyarthralgia and a rash on the limbs 1 month later. Then, interstitial pneumonia appeared, and systemic lupus erythematosus was suspected from antinuclear antibody positivity, and he was referred to our hospital. At the time of referral, thrombocytopenia was observed, and the diagnosis of systemic lupus erythematosus (SLE) and immune thrombocytopenic purpura (ITP) was made based on the positive antiplatelet antibody and high PA-IgG level. Treatment was started with steroid pulse therapy, and thrombocytopenia progressed even after treatment with PSL 40 mg (0.8 mg / kg) in combination with tacrolimus (TAC), and when belimumab (BLM) was administered, the platelet count gradually increased. And clinical improvement of SLE was obtained. [Clinical significance] In this case, BLM was introduced to ITP associated with SLE, and a response was obtained, leading to rapid tapering of steroids. BLM is known to suppress the production of autoantibodies such as dsDNA IgG by suppressing self-reactive B cells. Antibodies to platelets are also involved in the pathogenicity of ITP, suggesting that BLM may be effective for ITP as well.

P39-16

A case of SLE in which a repeat kidney biopsy was effective

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Conflict of interest: None

[BACKGROUND] Various viral infections can induce SLE-like pathologies and influence treatment strategies. [Case] 60-year-old female, chief complaint was fever, skin rash and hematuria. Laboratory results showed an elevated inflammatory response, anemia, decreased complement, decreased renal function, and atypical lymphocytes. Initially, the patient was suspected to have a viral infection and was followed up carefully. However, due to prolonged symptoms, leukopenia, thrombocytopenia, increased urine protein and appearance of cast in urine, SLE was suspected and further investigation was carried out. In addition to low complement, positive RNP and Sm antibodies, a renal biopsy diagnosed lupus nephritis type IVa and treatment was started with 50 mg of prednisolone. A renal biopsy was performed again because of persistent hematuria and poor renal function after the start of treatment and the presence of interstitial nephritis due to cytomegalovirus infection rather than SLE. Renal function improved markedly after earlier steroid tapering. [Conclusion] The patient's renal function deteriorated with steroid therapy and improved with steroid reduction. If the patient's urine or other findings worsen during the course of treatment, another renal biopsy should be considered.

P39-17

Intraperitoneal injection of triamcinolone acetonide improved refractory massive ascites in a patient with systemic lupus erythematosus

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Conflict of interest: None

A 28-year-old woman was admitted to our hospital due to generalized edema. Two months before admission, she was suspected to have connective tissue disease because of leukopenia and the positivity of the anti-nuclear antibody, anti-SS-A antibody and anti-DNA antibody. The level of serum albumin was 0.7 g/dL, C-reactive protein was 0.12 mg/dL, and complement components C3 and C4 were 47 and 10 mg/dL, respectively. She also had nephrotic syndrome (urinary protein, 7.7 g/day). CT revealed pleural effusion, peritoneal effusion, and generalized lymphadenopathy. Protein losing enteropathy was denied. Systemic lupus erythematosus (SLE) was diagnosed; prednisolone 45 mg daily was started. Tacrolimus (TAC) and mycophenolate mofetil were added, however, the ascites was refractory, requiring frequent abdominal parecentesis. Despite switching from TAC to cyclosporine, three doses of cyclophosphamide pulse therapy, and the addition of hydroxychloroquine and belimumab, the massive ascites still persisted. Finally, intraperitoneal administration of triamcinolone acetonide (100 mg) improved the ascites. Intraperitoneal triamcinolone acetonide might be a feasible and viable option to manage refractory ascites associated with SLE.

P39-18

A case with systemic lupus erythematosus positive for anti-Sm and anti-RNP antibodies in spite of homogeneous pattern by fluorescent anti-nuclear antibody methods

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Conflict of interest: None

[Case presentation] A 17-years-old women complained malar rash and photosensitivity in 20XX-1. In June 20XX, she developed auricular erythema, proteinuria, pancytopenia, and liver disfunction and was hospitalized. The laboratory data showed pancytopenia, fluorescent antinuclear antibody (FANA) at 1:1280 with homogeneous pattern, anti-dsDNA antibody at 46.9 IU/mL, hypocomplementemia (C3 20 mg/dL, CH50<10 U/mL), and hyperferritinemia at 2541.5 ng/mL. The anti-Sm and anti-RNP antibodies were positive at ≧480 U/ml and ≧200 U/ml by CLEIA method, respectively. Despite hemophagocytosis was not detected in bone marrow biopsy, she was diagnosed as having systemic lupus erythematosus with hemophagocytic syndrome. Renal biopsy showed lupus nephritis type II with full house pattern by immunofluorescent staining. Steroid pulse therapy followed by prednisolone (50 mg/day) and mycophenolate mofetil (1000 mg/day) improved her condition. [Clinical significance] In this case, pattern of FANA was only homogenous, no speckled, however, both anti-Sm and anti-RNP antibodies were strongly positive by CLEIA methods. We considered this case was significant in reexamining the characteristics of the antigen used in the CLEIA method and in propose of measuring several antibodies regardless pattern of FANA.

P39-19

A case of severe neuropsychiatric systemic lupus erythematosus (NPSLE) successfully treated with plasma exchange (PE) therapy

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Conflict of interest: None

A 69-year-old woman who presented with respiratory distress because of massive pleural fluid and pericardial fluid. She was diagnosed with SLE on the basis of malar rash, antinuclear antibodies and anticardiolipin antibodies positive, low complement fractions. Pleural fluid was thought to be due to serositis with SLE. Although she had not neuropsychiatric syndromes, brain MRI showed a wide range of high intensity lesions with hyperintensity on FLAIR. She was treated with PSL and HCQ. At first we could control the activity of SLE but after that neuropsychiatric syndromes appeared with serositis relapse during PSL dose reduction. MRI showed a marked increase in the number and size of CNS lesions. Although she was treated with m-PSL pulses, followed by IVCY, her symptoms were not ameliorated. However, PE therapy was apparently effective, and MRI findings, hypocomplementemia and neuropsychiatric syndromes all improved dramatically. PE therapy may be a potent therapy in combination with immunosuppressive treatment for SLE. Although the direct therapeutic mechanism has not be elucidated, the efficacy of PE in this case may be due to the removal of autoantibodies, immune complex and inflammatory mediators. Future studies will be necessary to determine and confirm suitable case for PE therapy in NPSLE.

P39-20

A case of systemic lupus erythematosus (SLE) with simultaneous tumors

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Conflict of interest: None

Simultaneous tumors were found in SLE patients undergoing immunosuppressive therapy. [Case] A 42-year-old woman with a history of passive smoking. [Present history] SLE was diagnosed in X-17, and prednisolone (PSL) and cyclosporine were introduced in remission. She developed lupus nephritis (LN) in X-11 and was treated with PSL and tacrolimus (Tac), but relapsed repeatedly. In X-2, LN relapsed and was diagnosed as Class IV (A / C) by renal biopsy. LN remained in remission with multi-target therapy of PSL, Tac, and mycophenolate mofetil, but She fell in X and was admitted to our hospital due to a fracture of both femurs. [Course after hospitalization] Right hemiplegia appeared after admission, and we revealed squamous cell carcinoma of lung and intracranial diffuse large B-cell lymphoma. Local lung radiotherapy and rituximab and whole-brain radiation therapy were performed for them. Both tumors shrank and MMT improved from 0 to 1. SLE remained in remission and continued treatment with PSL alone. [Invention] SLE patients have a high risk of developing malignant tumor. No report was confirmed that examined the risk of developing malignant tumor in multi-target therapy. It is necessary to pay attention to the development of malignant tumor when performing immunosuppressive therapy.

P39-21

A case of systemic lupus erythematosus (SLE) with treatment-resistant myositis successfully treated with belimumab

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Conflict of interest: None

Case presentation: A 30-year-old woman presented with multiple joint pains in year X-9. Although ACPA and RF were negative, RA was diagnosed based on clinical symptoms. MTX, TAC, ADA, and ETN were administered, but the effect was insufficient. Interstitial pneumonia was observed in year X-8; it was considered to be drug-induced and was improved by discontinuation of ETN and PSL 50 mg. Afterward, treatment with ABT and MTX left moderate disease activity, and CPK increased from year X-7. In year X-2, she was referred and admitted to our department due to weakness of the proximal muscle. CPK 2659 IU/l, anti-ds-DNA Ab 97 IU/ml, anti-SS-A Ab >1200 U/ml, and other disease-specific autoantibodies were negative. Muscle biopsy showed T cell infiltration and C1q deposition on the blood vessel wall. mPSL pulse, post-treatment with PSL 55 mg and IVIg were performed. Some improvement was observed, but the CPK level remained at about 400 IU/l. HCQ introduced in year X-1 did not result in significant change. When belimumab was introduced in year X, general malaise improved and CPK was normalized. Discussion: Myositis due to SLE is relatively rare and, in this case, myositis made it difficult to diagnose SLE. Belimumab may thus be the most effective treatment for SLE myositis.

P39-22

A case with positive anti-nuclear antibodies (ANA), a prolonged APTT and elevated serum levels of lupus anticoagulant (LAC) by Propylthiouracil (PTU) treatment for Basedow disease

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Conflict of interest: None

The patient, a 25-year-old woman who was diagnosed as Basedow disease and had been treated with propylthiouracil (PTU) for 2 years, presented with arthralgia and positive MPO-ANCA. Additional tests revealed a positive anti-nuclear antibodies (ANA), a prolonged APTT, elevated lupus anticoagulant (LAC), and a positive anti-dsDNA antibody. A systemic screening test didn't reveal any blood clots. After switching PTU treatment to potassium iodide treatment, the arthralgia disappeared, each antibody was normalized, and APTT was shortened to almost normal level. Thyroidectomy was performed without anticoagulant therapy. This case suggests that PTU may induce temporal abnormalities in blood coagulation tests. Here, we report the clinical course of this patient.

P39-23

A case of aplastic anemia diagnosed during the initial treatment of systemic lupus erythematosus

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Conflict of interest: None

A 56-year-old female was admitted to the hospital with complaints of fatigue and fever. Anasarca, renal dysfunction, pancytopenia, bilateral pleural, and pericardial effusion were observed. A bone marrow examination showed no obvious abnormality. SLE was diagnosed based on sun sensitivity, polyarthritis, serositis, renal dysfunction, pancytopenia, high ANA titer, anti-dsDNA antibody positive, hypocomplementemia, and direct Coombs positive. Starting with PSL and MMF, serositis, renal dysfunction, hypocomplementemia, anti-dsDNA antibody titers were improved. However, the pancytopenia was prolonged, and drug-induced myelosuppression was suspected. MMF was discontinued, but no recovery of pancytopenia was observed. After a month of MMF withdrawal period, CyA administration was started in consideration of aplastic anemia. The patient was diagnosed with AA associated with SLE due to bone marrow hypoplasia from 2nd examination, high levels of marrow fat on spinal MRI, and high levels of blood thrombopoietin. Pancytopenia is a common finding in SLE. In most cases, treatment of SLE is also effective for pancytopenia. However, there are few cases of aplastic anemia with SLE in treatment-resistant pancytopenia. We report a case of AA associated with SLE with a review of the literature.

P39-24

Examination of lupus nephritis with persistent hypocomplementemia after multi-target therapy

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Conflict of interest: None

[Case] A 41 years old, male. He was referred to our department due to abnormal urinalysis, 6 years ago. SLE was diagnosed from discoid eruption, lymphocyte 853, ANA positive, anti dsDNA antibody 19, anti-Sm antibody 242, CH50 16.5, C3 46, C4 8. Renal biopsy revealed lupus nephritis IV G (A). PSL 40 mg / day was started, and MZB 150 mg was added. On day 28, urinary protein disappeared, complement tended to rise, and PSL decreased. However, when chills occurred, complement decreased and the eruption worsened, so steroid pulse therapy and PSL 40 mg and TAC was added. He was transferred to another hospital, 5 years ago, and was referred again, 1 year ago. PSL 10 mg + MZB 150 mg + TAC 3 mg was continued, and urinary findings and anti-dsDNA antibody remained negative, but hypocomplementemia persisted. HCQ were added, but hypocomplementemia persisted. [Conclusions] It has not been concluded whether the treatment should be strengthened only by lowering complement and increasing immune complex even after clinical remission. It can be confusing as to whether immunosuppressive drugs should be maintained in small doses or whether other immunosuppressive drugs or biologics should be added for serological remission. We report this case as a suggestive case for considering the treatment of lupus nephritis.

P39-25

A case of SLE with secondary thrombotic thrombocytopenic purpura

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Conflict of interest: None

A 51-year-old woman with a history of TMA to thrombocytopenia caused by SLE and Tac in X-4 and X-3. She was attending our department for SLE, SjS, APS, etc. She was diagnosed with nausea, general malaise and diarrhea in March, X. She was admitted to our hospital because of poor food intake and elevated CRP with Cre 7.2 mg/dL, thrombocytopenia with crushed erythrocytes, and high ferritin levels, suspected to be due to acute renal failure, TMA and macrophage activation syndrome. She was treated with steroid pulse therapy for 3 days from the 1st day. HD and PEx were started on the 2nd day. He was diagnosed with acquired secondary TTP secondary to SLE with low ADAMTS13 activity and high ADAMTS13 inhibitor levels on the 4th day. He was started on the same day with PSL 1 mg/kg/day. RTX 375 mg/m2 was started on the 8th day. By the 24th day, she had improved to 100,000 platelets/μL by the time of 8 HD and 10 PEx and 3 RTX courses, and she was terminated from HD and PEx. She was discharged on the 83rd day of the illness without any recurrence of symptoms. This is a case of TTP secondary to SLE in a patient with a history of thrombocytopenia due to SLE and drug-induced TMA. We discuss and report on various pathologies of thrombocytopenia associated with SLE through this case.

P39-26

A case of elderly-onset SLE with necrotizing vasculitis in the gallbladder wall

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Conflict of interest: None

[Case] A 76-year-old woman. From March 20XX, she developed ankle dorsiflexion difficulty and right peroneal nerve palsy. Since the blood test performed at that time was positive for ANA, she was referred for the purpose of detailed examination and treatment, and anti-dsDNA, aPL antibody positive, hypocomplementemia, immune complex positive, and thrombocytopenia were observed., She was admitted in June for the purpose of detailed examination and treatment for SLE. Examination during hospitalization revealed a mass lesion with a diameter of 14.6 × 8.7 mm. A gallbladder tumor was suspected, and she underwent laparotomy for cholecystectomy in July. The gallbladder mass was a cholesterol polyp, but necrotizing vasculitis was found in the wall of the gallbladder, which was considered to be secondary vasculitis secondary to SLE. She was admitted to our hospital again in September for the purpose of treatment, and was relieved by PSL, HCQ and IVCY. [Discussion] We experienced an elderly-onset SLE patient who developed right peroneal nerve palsy and presented with necrotizing vasculitis in the gallbladder wall and lupus nephritis. Elderly-onset SLE patients with necrotizing vasculitis in the gallbladder wall are considered rare and will be reported with a review of the literature.

P39-27

A case of elderly-onset systemic lupus erythematosus (SLE) that has been treated for several years as RS3PE syndrome

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Conflict of interest: None

[Case] A 68-year-old man [Current medical history] At the age of 63, he had systemic joints pain, was diagnosed as RS3PE, and was treated with 5 mg/day of prednisolone (PSL). At the time of exacerbation of joint symptoms, the dose of PSL was increased up to 20 mg/day, however, disease activity was not successfully controlled. Two months before admission, a systemic eruption appeared, and one month later, exacerbation of arthralgia, malaise, and loss of appetite were observed. Joint echo at our hospital revealed enthesitis of both knees and tendonitis of both ankles. Laboratory tests showed WBC 6900/μL (lymphocytes 730/μL), CRP 4.36 mg/mL, C3 74.8 mg/dL, C4 18.6 mg/dL, CH-50 40.8 U/ml, ANA (1:2560) (1:2560 in homogenous pattern), and dsDNA 760 IU/mL. Skin biopsy showed IgG deposits between epidermal cells and IgA and C3 deposits on the blood vessel wall, and the lupus band test was positive. The patient was diagnosed with SLE, and the dose of PSL was increased to 40 mg/day. [Discussion] When we see a patient who has arthritis or tendinitis, it is necessary to consider not only rheumatoid arthritis but also SLE as different diagnosis.

P39-28

Rituximab improved refractory thrombotic microangiopathy associated with systemic lupus erythematosus in two patients

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Conflict of interest: None

We describe two refractory cases of SLE-associated thrombotic microangiopathy (TMA). Case 1: A 30-year-old woman was admitted to our hospital due to fever, chest pain and renal failure. She had an 18-year history of SLE and had been treated with prednisolone (PSL) 17 mg daily, azathioprine and tacrolimus. SLE recurred along with pancytopenia, pericarditis, lupus nephritis and TMA. Despite treatment with increased PSL to 35 mg daily, cyclophosphamide 25 mg daily and 12 cycles of plasma exchange (PE), thrombocytopenia persisted. Case 2: A 39-year-old woman was admitted to our hospital due to dyspnea, pancytopenia and renal failure. She was diagnosed as having SLE, TMA and heart failure. Despite treatment with glucocorticoids, intravenous cyclophosphamide and 15 cycles of PE, she became dependent on hemodialysis and thrombocytopenia persisted. In both cases, rituximab was initiated to manage refractory TMA and thrombocytopenia was gradually improved. Although PE is basically performed to treat SLE-associated TMA, it is a highly invasive and expensive procedure. The early introduction of rituximab might be an important strategy to manage SLE-associated refractory TMA from both medical and economical aspects.

P39-29

A case of rituximab in response to refractory antiphospholipid antibody syndrome with repeated cerebral infarction

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Conflict of interest: None

[Cases] 45-year-old man [Chief complaint] Fever, Both lower leg edema [Present illness] Antiphospholipid antibody positive in X-10 years. Edema and pain in both lower leg were observed in early October X-1. There was no thrombosis in contrast CT, and aspirin was added. In January of X, both lower leg edema persisted, and he was referred to the hospital. We diagnosed systemic erythematosus (SLE) based on antinuclear antibody 320 times (Speckled type), low complement, thrombocytopenia, anti-DNA antibody positive, direct Coombs test positive, and antiphospholipid antibody positive. Both lower leg edema showed inflammatory findings on MRI, and muscle biopsy showed myositis. Myositis-specific antibodies and ANCA antibody were negative, and SLE caused myositis, and we treated with steroids. The symptoms were improved, but cerebral infarction (CI) was observed. Antiphospholipid antibody syndrome (APS) was diagnosed and warfarin was added. Aspirin and warfarin improved, but a new CI was observed. The activity of APS was not controlled, and rituximab was introduced. There was no recurrence and he was transferred to rehabilitation. [Discussion] We treated APS with aspirin and warfarin, but CI repeated. It was a rare case that we were able to control the activity of APS by rituximab administration.

P39-30

A case in which rituximab (RTX) and plasmapheresis showed therapeutic effects on systemic lupus erythematosus (SLE) with refractory cerebrovascular accident

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Conflict of interest: None

In May X, 42-year-old woman had diagnosed with systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome (APS) due to pancytopenia, proteinuria, etc. While starting aspirin, treatment was started with methylprednisolone (mPSL) 500 mg / day and cyclophosphamide intravenous therapy (IVCY) 800 mg / 2 weeks. Tacrolimus 3 mg / day and mycophenolate mofetil 1500 mg / day were added for induction treatment. High anti-ds-DNA antibody and low complement levels were prolonged, so hydroxychloroquine 200 mg / day and belimumab were added. In June X+1, she was transported due to impaired consciousness and fever. A close examination revealed subcortical hemorrhage. Since bleeding associated with SLE was considered, mPSL 500 mg / day and IVCY 800 mg / 2 weeks were started. Since there was little improvement in serology, rituximab (RTX) 540 mg / week was added to induce remission. However, a new lacunar infarction appeared on head MRI. Therefore, when plasma exchange was performed, the anti-dsDNA antibody turned negative and subsequently reached a state of remission. We report a case in which RTX and plasma exchange showed a therapeutic effect on SLE with intractable cerebrovascular accident, with a review of the literature.

P39-31

The characteristics of Elderly-onset systemic lupus erythematosus (EOSLE) (The report of three cases)

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Conflict of interest: None

[Objective] EOSLE is difficult to diagnose due to the lack of typical findings and many diseases to be differentiated. We report three cases and their characteristics. [Case 1] 74 year old female presented with fever. She had no symptoms and abnormal physical findings of SLE except fever. Serological tests and urinalysis presented antinuclear antibody and kidney injury and proteinuria. Class IIIA/C lupus nephritis was observed. She also had antiphospholipid antibody and was diagnosed with SLE only with a fever. [Case 2] 83 year old female was diagnosed with RA by former doctor and recieved MTX and adalimumab. A rash appeared on the face. She was diagnosed with SLE with lupus pernio and polyarthritis. [Case 3] 79 year old male presented with edema of the face and lower legs. He had no symptoms and abnormal physical findings. He was diagnosed with nephrotic syndrome. The renal pathological results showed class II lupus nephritis. He was diagnosed with SLE with elderly-onset nephrotic syndrome. [Conclusion] EOSLE can be behind with a diagnosis due to their atypical symptoms. It may be difficult to understand because it is treated as other diseases and its condition is modified. We should treat carefully and take appropriate interventions so as not to overlook their condition and its changes.

P39-32

A case of lupus nephritis relapse with remission by administration of mycophenolate mofetil, tacrolimus and itraconazole, maintained effective tacrolimus blood concentration

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Conflict of interest: None

[Case] 44-year-old female [Clinical Course] Oct 1999, She presented facial erythema, arthritis, nephritis, anti-Sm antibody positive and leucopenia/lymphopenia, diagnosed SLE. PSL30 mg was effective. May 2001, she presented severe nephrosis. Renal biopsy revealed WHO classification Va. After mPSL1 g pulse, PSL 60 mg and AZP100 mg were effective. Nov 2003, relapsed. After mPSL1 g pulse, PSL 40 mg was effective. Jan 2005, relapsed. PSL60 mg and CyA225 mg were ineffective. Switching from CyA to MZB200 mg was effective. mPSL4 mg and MZB200 mg were maintained for remission. Sep 2014, relapsed. Switching from MZB to TAC 5 mg was ineffective. Renal biopsy revealed 2013 classification V. mPSL16 mg and TAC6 mg were ineffective. Adding MZB200 mg was effective, followed by TAC5 mg. Feb 2019, relapsed. mPSL24 mg, MZB 200 mg and MMF1500 mg were ineffective. mPSL40 mg, TAC3 mg and MMF1750 mg were effective. ITCZ capsule 50 mg was used, resulting in

effective TAC trough blood concentration. Serum albumin increased from 2.2 to 2.7 mg/dl, urine total protein decreased from 2.83 to 1.13 g/day. mPSL was tapered to 4 mg and serum albumin increased to 3.5 mg/dl. Azosemide was used with systemic edema improvement. [Clinical Significance] Lupus nephritis relapse remains in remission by steroid, TAC and MMF, deriving benefit from interaction between ITCZ and TAC.

P39-33

Two cases of SLE with hemolytic anemia that SLEDAS was more useful in disease evaluation and assessing therapeutic effects than SLEDAI-2K

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Conflict of interest: None

[Background] SLEDAS is a new disease activity measure of SLE, which has much better to detect disease activity and clinically meaningful changes, as compared with SLEDAI-2K. Here we report two cases of SLE with hemolytic anemia in which SLEDAS was useful in assessing disease status. [Case 1] A 50-year-old woman has fever, arthralgia, and rash of both lower limbs. She was diagnosed with SLE, for pancytopenia, hemolytic anemia, antinuclear antibody positivity, and anti-dsDNA antibody positivity. Disease activity was SLEDAI-2K 13 points, SLEDAS 28.83 points. SLEDAI-2K didn't changed at 4 points at 1 and 2 months after treatment, while SLEDAS showed improvement from 11.08 points to 2.08 points. [Case 2] A 61-year-old man was diagnosed with SLE at the age of 30 and treated with PSL 2 mg. He has fever and was diagnosed with SLE relapse from hemolytic anemia, hypocomplementemia, and elevated anti-dsDNA antibody. Disease activity was SLEDAI-2K 8 points, SLEDAS 21.83 points. One month after treatment, SLEDAI-2K achieved 0 points, but hemolytic anemia didn't improve and SLEDAS scored 9.37 points. [Clinical significance] SLEDAS was suggested to evaluate the disease status and therapeutic effects of SLE with higher accuracy than conventional scores, especially in the case with hemolytic anemia.

P39-34

Case in which RTX (rituximab) was significantly effective for refractory SLE (systemic lupus erythematosus) alveolar hemorrhage

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Conflict of interest: None

[History] A 46-year-old man was admitted to our hospital with complaints of facial erythema and multiple arthralgia. At admission, he was diagnosed as SLE based on antinuclear antibody positive, anti-double-stranded DNA antibodies 138.2 U / ml, and C3 48 mg / dL. [Treatment] He started prednisolone (PSL) at 1 mg/kg from the second day of hospitalization, but his complement remained low. Since a cough appeared on the 12th day, chest CT was performed and a ground-glass opacity (GGO) was seen. The shadow didn't improve with antibiotics. He also received steroid pulse and intravenous cyclophosphamide (IVCY) 0.5 g / m2, but a new GGO appeared. We performed a bronchoscopy to investigate the GGO. Because hemosiderin phagocytes were found in the bronchoalveolar lavage fluid, we diagnosed alveolar hemorrhage due to SLE. PSL and IVCY didn't improve alveolar bleeding, thus RTX 375 mg / m2 was administered four times every other week. RTX improved alveolar bleeding and did not recur, so we reduced the dose of PSL. [Discussion] This case, RTX was effective refractory SLE. There are few reports investigating the effects of RTX on alveolar hemorrhage due to SLE. The mechanism is unknown. To investigate the mechanism, we measured the lymphocyte subset before and after RTX administration.

P39-35

A case of systemic lupus erythematosus associated with IgG4-related nephropathy

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Conflict of interest: None

30 years ago, A 58-year-old woman developed a subarachnoid hemorrhage and underwent surgery. Thereafter, she had blood tests performed at her physician's office about once a year. The blood tests performed a year ago showed a Cr of less than 1.0 mg/dL. She had been aware of hand joints, anorexia, and general malaise since February, and her symptoms gradually worsened. The patient was referred to our department because of renal dysfunction (Cr 2.7 mg/dL) in blood tests. Systemic lupus erythematosus was suspected due to the presence of antinuclear antibodies (>2560x), anti-ds-DNA antibodies (30 U/mL), and anti-cardiolipin antibodies (23 U/mL). He was also admitted to our department because of IgG 2137 mg/dL and IgG4 173 mg/dL, and IgG4-related diseases were also suspected. A kidney biopsy was performed on the second day of hospitalization. Glomeruli were nearly normal. The interstitium was infiltrated by numerous plasma cells, which were contained IgG4-positive plasma cells. Fluorescence antibody analysis showed no staning, but electron microscopy showed high electron density deposits in the subendothelium, which led to the diagnosis of lupus nephritis ISN/RPS classification class I. Prednisolone was administered at 30 mg/day, and Cr was reduced to 1.6 mg/dL.

P39-36

A case of systemic lupus erythematosus (SLE) who developed generalized pustular psoriasis (GPP) after administration of hydroxychloroquine (HCQ)

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Conflict of interest: None

[Case] 49-year-old, female [Chief complaint] Generalized erythema, fever [Clinical course] In X-8, she had dry eye, and a blood test showed several autoantibodies such as anti-nuclear antibody were positive. In X-6, she visited our hospital with systemic edema and was diagnosed as SLE and protein-losing gastroenteropathy by arthritis, blood test, protein leakage scintigraphy. Full-dose PSL started. PSL was discontinued in X-3. In January X, general malaise, elevation of anti-dsDNA antibody, and hypocomplementemia were observed, and PSL 20 mg/day and HCQ 300 mg/day started for relapse of SLE. In March, generalized painful erythema appeared with fever. HCQ withdrawal and corticosteroid pulse therapy improved symptoms but generalized erythema got worse while reducing PSL. Although acute generalized exanthematous pustulosis (AGEP) was a differential disease, we diagnosed her with GPP by clinical findings and skin biopsy that demonstrated parakeratosis and spongiform in epidermis with infiltration of neutrophils. Etretinate 50 mg/day was added to PSL 50 mg/day and eruption improved. No relapse was seen after reducing etretinate and PSL. [Discussion] HCQ-induced GPP is rare. We report about the similarities and differences between GPP and AGEP on SLE with some literature review.

P39-37

A case of lupus nephritis with withdrawal of steroids and successful pregnancy and childbirth without recurrence

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Conflict of interest: None

The case is a 41-year-old woman. At the age of 25, fever and rash. Blood tests showed leukocytopenia, antinuclear antibody, anti-ds DNA antibody and anti-Sm antibody and also low complement were recognized. The patient was diagnosed with systemic lupus erythematosus (SLE). However, symptom were improved, so the patient was followed up with no medication. At the age of 31, fever, butterfly erythema, and arthritis was recognized, so the patient was admitted. Since urinary protein were positive, renal biopsy was performed. As a result, LN was WHO Class IV-S (A/C) and prednisolone (PSL) 50 mg / day and tacrolimus (TAC) were administered. The clinical course was good, but due to TAC induced liver

dysfunction, so the patient was treated with prednisolone alone. At the age of 34, PSL was stopped because of good clinical coarse, and she was stable without using any drug. Pregnancy was turned out at the age of 38. The activity of SLE was stable without using steroids or immunosuppressive drugs and she gave birth to a healthy baby at the age of 39. Two years have passed since the birth, her condition is stable with no recurrence.

P39-38

A case of lupus nephritis patient co-existing with renal thrombotic microangiopathy

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Conflict of interest: None

A 24-year old woman with a history of proteinuria was admitted to our hospital, presenting with arthritis of right ankle and facial and leg edema. She also had hypertension, proteinuria, hematuria, and pancytopenia. She was diagnosed with SLE based on SLICC criteria (Acute/subacute cutaneous rashes, Alopecia, Synovitis, Serositis, Renal, Leucopenia, Anemia, Thrombocytopenia, Anti-dsDNA, ANA, Low complement). SLE activity was high with SLEDAI scored 30. She was treated with methyl prednisolone (PSL) pulse therapy, followed by high-dose PSL for pancytopenia and mycophenolate mofetil (MMF) for Lupus nephritis. Renal biopsy showed INS/RPS class IV complicated with thrombotic microangiopathy (TMA), which was considered to cause her severe hemolytic anemia and thrombocytopenia. TMA is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and organ damage. TMA is associated with some disorders, including SLE and systemic sclerosis. Among various lupus renal vascular changes, TMA presents with the severe clinical manifestation. Patients with TMA are reported to presented with poorer outcome compared with the non-TMA group. The presence of a thrombotic event, unexplained hypertension, thrombocytopenia, or hemolytic anemia should prompt consideration for TMA syndromes.

P39-39

A case of bullous systemic lupus erythematosus presenting both IgG and IgA antibodies for collagen VII with differential diagnosis to linear IgA/IgG bullous dermatosis

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Conflict of interest: None

Background; Vesiculobullous lesions develop in less than 5% of systemic lupus erythematosus (SLE) patients. Gammon et al. reported three categories for blistering cutaneous conditions in SLE. The first category presents with characteristic histopathological features of SLE, including liquefaction degeneration and vacuolization at the basement membrane zone (BMZ). The second category is a group of SLE complicated with various autoimmune blister diseases. The third category is bullous SLE in a narrow sense with specific IgG autoantibodies for type VII collagen. Case; We present a case of a 34-year-old Japanese woman with SLE who developed skin lesions with vesicles scattered on the face, chest and abdomen. Direct and indirect immunofluorescence of the skin biopsies showed linear depositions of IgA and IgG along the BMZ. Enzyme-linked immunosorbent assays showed IgG and IgA antibodies against type VII collagen. Discussion; Among autoimmune blister diseases, deposits of other immune complexes, in addition to the main pathogenic antibodies, are occasionally detected. Therefore, the same patterns of immune complex deposition with IgG and IgA may appear in different autoimmune blister diseases, which makes it difficult to make a diagnosis.

P39-40

A case of systemic lupus erythematosus with psychosis and myelitis

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Conflict of interest: None

[Case] 37 years old, male. In year X-4, he was diagnosed with systemic lupus erythematosus (SLE). Cerebrospinal fluid (CSF) protein levels were high, however he had no neuropsychiatric symptoms. Hemophagocytic syndrome was observed, so he was relieved by high-dose steroid therapy. From January X, he showed paranoid and incoherent behavior and was diagnosed with schizophrenia. From May, he showed tremor, freezing of gait and mental lethargy, and lost the sensation of urination and stool, and had difficulty in walking due to leg paralysis. We diagnosed with neuropsychiatric SLE (NPSLE) based on psychiatric symptoms, cognitive dysfunction, myelitis and increase of protein and interleukin-6 (IL-6) in CSF. He was treated with methylprednisolone pulse therapy, followed by 60 mg/day (1 mg/kg/day) of PSL, and intravenous cyclophosphamide. He showed little improvement in the sensation of urination and stool, however improvement in cognitive function, lower limb muscle strength and levels of protein and IL-6 in CSF. [Clinical significance] When psychiatric symptoms are observed in treating with SLE, it is difficult to distinguish between NPSLE, endogenous psychosis such as schizophrenia, and steroid psychosis, so this point will be discussed and reported with past literature findings.

P39-41

A case of antinuclear antibody-negative SLE complicated by class IV lupus nephritis with full-house pattern on renal biopsy

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Conflict of interest: None

A 30-year-old male had a checkup and urine examination detected 2+ proteinuria in December 2019. He visited our hospital with a complaint of foamy urine and leg edema in early February 2020. Laboratory test demonstrated massive proteinuria (urine protein/Cr ratio of 3.98 g/gCr), hypoalbuminemia (2.5 g/dl) and 3+ hematuria, then a renal biopsy was performed on suspicion of glomerulonephritis. Although ANA was negative (less than 1: 40), anti-ds-DNA antibody (215 IU/ml) and lupus anticoagulant were positive, SLE was suspected. He had gradually complicated hypocomplementemia (C3:66 mg/dl) and pericarditis, then renal pathology revealed class IV-G (A) lupus nephritis with full-house pattern on IF, he was diagnosed with SLE. We started corticosteroid pulse therapy followed by prednisolone (PSL) 60 mg/day and intravenous cyclophosphamide pulse therapy, the response was favorable. Then we initiated hydroxychloroquine and mycophenolate mofetil, PSL was gradually tapered, he was discharged from the hospital on 29th day. We report the case with review of the literatures.

P39-42

A case of antinuclear antibody (ANA)-negative systemic lupus erythematosus (SLE) with highly elevated CK levels

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Conflict of interest: None

49-year-old woman, erythema appeared on the face and upper limbs. She had a fever, general malaise and difficulty in standing up. Blood tests showed ANA-negative, and elevated levels of CK and aldolase. We observed that proximal muscle symptoms, proteinuria, arthritis, and anemia. Erythema was found on the cheeks and limbs, but no dermatomyositis (DM)-specific eruptions such as heliotrope rash appeared and no myositis-specific autoantibodies were found. MRI showed high signal in both sides of the buttocks and thighs on STIR. According to the SLICC SLE classification standard 2012, she had malar rash, oral ulcer, leukopenia and lymphopenia, hypocomplementemia, and the direct Coombs test was positive, so she was diagnosed with SLE. It was possible that the muscle symptoms might be due to an overlap between SLE and DM. Prednisolone was started at 1 mg/kg, and rash were getting thinner, muscle strength was

gradually restored, and urinary protein decreased. Hydroxychloroquine was added, then the erythema almost disappeared. It was atypical for SLE that various antibodies were negative and the patient mainly complained of muscular symptoms. As it was difficult to diagnose whether the SLE and DM overlap or the SLE, we report this case.

P39-43

A case of anti-centromere antibody-positive glomerulonephritis with pathological diagnosis of lupus nephritis on renal biopsy

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Conflict of interest: None

A 72-year-old woman with chronic kidney disease presented to the hospital with leg edema, proteinuria of 15.7 g/gCr and serum creatinine elevation of 2.29 mg/dL. She was admitted to the hospital to examine and treat nephrotic syndrome and rapid progressive glomerulonephritis. Her laboratory tests showed an elevated anti-nuclear antibody level (1:640 in a discrete speckled pattern) and anti-centromere antibody (ACA), but other autoantibodies were negative. Renal biopsy was performed revealing diffuse proliferative glomerulonephritis with active crescents. Immunofluorescence study revealed "full-house" immunofluorescence staining. We diagnosed her as lupus nephritis (LN), but no other clinical or serological evidence of SLE were found. We also diagnosed her as limited cutaneous systemic sclerosis. We suspected Sjögren's syndrome from the results of chewing gum test and lip biopsy. She was treated with glucocorticoids, mycophenolate mofetil and cyclosporin as induction therapy, but was forced to reduce them because she got cytomegalovirus enteritis. Improvement of her proteinuria and hematuria was partial. There is only one case report of LN with ACA. The etiology may be different from that of typical LN, so further studies in more patients are needed.

P39-44

Three cases of lupus-like symptoms / systemic lupus erythematosus (SLE) with Epstein-Barr virus (EBV) infection

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Conflict of interest: None

[Case 1] A 46-year-old man was diagnosed with infectious mononucleosis (IM). Two months later, he was hospitalized with fever, polyarthralgia, pancytopenia, and painless stomatitis. EBV-VCA IgM negative, EBNA IgG positive conversion, antinuclear antibody (ANA) positive, anti-Sm antibody positive, hypocomplementemia were appeared. He was diagnosed with SLE after IM and steroid and Tacrolimus were started. [Case 2] A 35-year-old woman was hospitalized with fever, sore throat, and systemic lymphadenopathy. EBV-VCA IgM, and IgG were positive, and she was diagnosed with IM. However, ANA, anti-ds-DNA antibody and biological false positive were seen and immune complex elevation, prolonged hypocomplementemia and pancytopenia were observed. We finally diagnosed her with SLE caused by EBV infection, and steroid and hydroxychlorokin were started. [Case 3] A 33-year-old man had edematous erythema on his face and treated as cutaneous lupus erythematosus. ANA was negative and he did not match the diagnostic criteria for SLE. He had high peripheral blood EBV-DNA and EBV-encoded small RNAs (EBER) positive lymphocytes were seen on liver biopsy, which confirm diagnosis of chronic active EBV infection. [Discussion] We report on the relationship between EBV and SLE with a review of the literature.

P39-45

A case of late onset systemic lupus erythematosus complicated with hemophagocytic lymphohistiocytosis

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Conflict of interest: None

[Case] 74-year-old man was admitted to our hospital with anorexia. Because he had sustained slight fever, pancytopenia, and high titer of anti-nuclear antibody, he was referred to our department. He was diagnosed systemic lupus erythematosus (SLE) based on low compliment, high titer of anti-dsDNA antibody and PA-IgG, and positive direct coombs test. Although we administered steroid pulse therapy, thrombocytopenia was not improved, and he required frequent platelet transfusion. We performed bone-marrow biopsy and diagnosed hemophagocytic lymphohistiocytosis (HLH), though his ferritin level was 549 ng/mL. He was treated with high dose intravenous immunoglobulin, cyclophosphamide pulse therapy, and cyclosporine A, then his thrombocytopenia was improved. He was gradually decreased prednisolone and maintained remission. [Clinical implication] The course of SLE in elderly people is considered to be milder. But these patients have occasionally non-specific symptoms and severe clinical course. We need to consider HLH, when cytopenia was resistance to therapy, even in low ferritin level. In addition, we need to treat these patients more intensive even they are elder.

P39-46

A case of SLE-induced macrophage activating syndrome (MAS) improved with IVIg and etoposide

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Conflict of interest: None

[Case] 36 years old male. [Chief complaint] Fever [Present illness] From November 15, 20XX, anorexia and difficulty in movement appeared. A former doctor diagnosed MSSA sepsis and treated with CEZ. Although improvement in CRP level was once observed, it worsened again. He was diagnosed as SLE because he showed positive for antinuclear antibody and anti-dsDNA antibody, hypocomplementemia, and pancytopenia. PSL was started but was not effective, so he was transferred to our hospital. Urinary deformed erythrocytes and high level ferritin of 16716 ng/ml were found, so we diagnosed him as lupus nephritis and SLE-induced MAS, while bone marrow puncture revealed adipose marrow but no hemophagocytosis. Steroid pulse therapy, cyclosporine, and plasmapheresis worked insufficiently for MAS, while IVCY was effective, which is forced to stop due to adenovirus cystitis and pseudomonas aeruginosa bacteremia. After that we treated him with IVIg and etoposide, and MAS became in remission. [Discussion] Adult onset Still's disease and SLE are known as the collagen diseases that cause MAS. The treatment regimen for MAS associated SLE has not been established. We report this case which has good clinical course with IVIg and etoposide.

P39-47

A Case of Femur Born Thrombosis After Myocardial Infarction In The Patient Of SLE Complicated APS

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Conflict of interest: None

[Case] A male patient with lupus nephritis class IV and APS occurred 18 years ago, and started high dose PSL and TAC. His bilateral femoral head necrosis was occurred 8-year ago, he underwent left hip arthroplasty; however, his right hip is conservatively with NSAIDs; then, the pain has been sometime happened. His #7 myocardial infarction was occurred 5-week ago, and he hospitalized 2 weeks and followed with warfarin keeping the range of PT-INR. When the day, his right gonalgia was occurred. On the 4th day, he was stopped taking warfarin because of his INR 8.0. On the 7th day, as the day is his visit date, we recognized no visual nor palpa-

tion abnormality. CT and MRI of his knee was performed because bleeding knee joint cavity or his veinal thrombosis was suspected. The born thrombosis of his distal end of right femur was suspected by the image of CT and MRI. He was started taking warfarin 2 mg/day with INR 2.2. On the 11th day, he was elevated taking warfarin 6 mg/day with INR 1.15. [Significance] When APS is complicated with SLE, thrombosis and embolus of organs become a problem, but the frequency of bone infarction is very rare. We experienced a case of SLE with APS that caused bone infarction at a time when thrombus control was unstable after myocardial infarction.

P40-1

Evaluation of the time-dependent change of pathogenic CD4+ T cells in lupus model mice induced by topical treatment with Toll-like receptor antagonist imiquimod

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Conflict of interest: None

[Objective] To evaluate time-dependent change of CD4+T cell in lupus model mice induced by TLR antagonist imiquimod (IMQ). [Methods] 1) After C57BL/6 mice were treated with topical IMQ for 8 weeks, lupus phenotype was confirmed with anti-DNA IgG in sera and deposition of C3 and IgG in kidneys. 2) After the treatment with IMQ for 2, 4, or 8 weeks, superficial antigens expressing in CD4+ T cells were analyzed by flowcytometry (FCM). 3) CD4+ T cells were stimulated in vitro, and cytokine expression was evaluated with FCM. 4) Cytokine concentration in the culture supernatant collected in 3) was measured by ELISA. [Results] 1) Anti-DNA IgG was significantly increased, and immunofluorescent staining revealed marked deposition of C3 and IgG in kidneys in IMQ-treated mice. 2) ICOS, PD-1 and CXCR3 were significantly up-regulated in IMQ-treated mice at 2 weeks compared with control mice, and tend to be increased with time-dependent manner. 3) IFNg or IL-10-producing cells and IFNg and IL-10 co-producing cells tend to be increased in IMQ-treated mice at 4 and 8 weeks. 4) IFNg tend to be increased in IMQ-treated mice. [Conclusions] Time-dependent up-regulation of ICOS, PD-1 and CXCR3 and facilitation of IFNg and IL-10 production in CD4+ T cells might be involved in IMQ-induced lupus like pathology.

P40-2

Involvement of SOCS1 (suppressor of cytokine signaling 1) in the process of SLE pathogenesis

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Conflict of interest: None

[Objective] We reported that T-cell-specific SOCS1 (suppressor of cytokine signaling 1)-deficient mice caused SLE. However, we found that the pathogenesis of SLE is also exacerbated in SOCS1 transgenic mice (SOCS1 Tg), in which the pathogenesis of SLE is induced. In this study, we will investigate the mechanism by which SLE pathology is exacerbated in SOCS1 Tg. [Methods] 1) We prepared four types of mice, pristine induced SLE in SOCS1 Tg and control wild-type mice (WT), and PBS injection control mice. From each, $CD4^+CD25^+$ regulatory T cells (Treg) were harvested and co-cultured with naïve T cells to analyze the inhibitory potential of Treg. 2) The B16 melanoma cell line was transplanted into SOCS1 Tg and WT. [Results] 1) Treg derived from SLE induced WT were less inhibitory than those derived from mice without SLE. Treg derived from SLE induced SOCS1 Tg were even less inhibitory. 2) The B16 melanoma cell line transplanted into SOCS1 Tg was more increased compared to WT. [Conclusions] The melanoma cell line experiments suggest that cytokine is suppressed in SOCS1 Tg. Although the inhibitory capacity of Treg is reduced by Treg plasticity in SOCS1-deficient mice, even in this cytokine suppressed state of SOCS1 Tg, the inhibitory capacity of Treg is reduced during the pathogenesis of SLE.

P40-4

PD-1 expression levels on follicular T cell subsets affect disease severity in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] Recently, several reports indicated the altered proportion of TFH subsets and TFR/TFH balance in patients with SLE. But precise mechanisms of PD-1 expression on TFH cells in their regulations are partly understood. In the present study, we investigated the association between TFH subsets including TFR cells, disease activity, and plasma cytokines in patients with SLE. [Methods] Circulating TFH subsets and TFR cells from patients with SLE (n= 19) and healthy controls (HCs) (n= 10) were analyzed with flow cytometry. Plasma cytokine levels of the patients were measured with ELISA. [Results] PD-1 expressions on circulating TFR cells were higher in SLE patients than in HCs. PD-1 expression intensities of TFH1, TFH2 and, TFR cells were positively correlated with anti-DNA antibody titers, SLEDAI scores, whereas plasma IL-21 concentrations were associated only with that of TFR cells. [Conclusions] PD-1 expression levels, not frequencies, of TFH subsets and TFR cells could affect the severity of SLE. Besides, $PD\text{-}1^{high}$ TFR cells might cause exacerbation of the disease. We are now investigating the functions of each $PD\text{-}1^{high}$ TFH subsets and TFR cell.

P40-5

Interferon alpha producing and phagocytic capacity of monocytes in Systemic Lupus Erythematosus is associated with disease activity

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Conflict of interest: None

[Objective] We previously reported that interferonα (IFNα) production by monocytes activated with stimulator of IFN genes (STING) pathway is enhanced in patients with systemic lupus erythematosus (SLE). In this study, we evaluated monocytes for their capacity to produce IFNα and phagocytose in SLE patients. [Methods] Peripheral blood mononuclear cells (PBMC) isolated from SLE or healthy control (HC) were stimulated with 2'3'-cGAMP, a ligand for STING, and incubated with fluorescence (FITC)-labeled Latex Beads. Intracellular staining for IFNα was performed, and IFNα-positive and FITC- Beads-positive monocytes were analyzed by flow cytometry. [Results] IFNα-positive or FITC- Beads-positive cells were observed in STING-stimulated monocytes, and the frequency of these populations was higher in SLE. IFNα- and FITC-Beads-double positive cells were present in SLE patients with high disease activity, but not in HC and patients with stable disease. [Conclusions] There were two different subsets of monocytes with IFNαproducing or phagocytic capacity upon STING pathway activation. We found another subset that possess capacity to produce IFNα and phagocytose in SLE patients with high disease activity. These IFNαproducing-monocytes with phagocytic capacity may be related to the pathogenesis of SLE.

P41-1

Successful therapy with riociguat in patients with early interstitial lung disease due to systemic sclerosis: a report of two cases

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Conflict of interest: None

(Background) Riociguat has demonstrated antifibrotic effects in animal models. However, a recently published, RISE-SSc trial failed to demonstrate a significant difference between riociguat and placebo in terms of the inhibition of progression of skin sclerosis and ILD in patients with early diffuse cutaneous SSc. Herein, we reported two cases with dif-

fuse SSc, early ILDs of whom were improved after an introduction of riociguat. (Clinical courses) (A) a 47-year-old female (anti-Scl-70 antibody (+), disease duration 12 months) and (B) a 72-year-old male (anti-centromere antibody (+), disease duration 75 months) were included. They complained of recently developed dry cough and gradual worsening of other clinical manifestations. A CT scan of the chest showed early ILD in both cases. After initiating riociguat, a follow-up CT scan demonstrated an improvement of ILD in both cases. Pulmonary function test before and after the initiation of riociguat revealed FVC% of 139.9 and 139.6 and %DLCO of 83.7 and 96.1, respectively in case (A) and FVC% of 100.9 and 97.5 and %DLCO of 125.9 and 111.5, respectively in case (B). Riociguat has been well tolerated without a significant adverse event in both cases. (Conclusion) Riociguat may benefit early phase of SSc-related ILD.

P41-2

A case of symptoms similar to systemic scleroderma (SSc) after nivolumab / ipilimumab combination therapy

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Conflict of interest: None

[Case] The case was a man in his 60s. Nivolumab / ipilimumab combination therapy was investigated for renal cell carcinoma (RCC). Antinuclear antibody was 320 times (Speckled pattern) and anti-SS-A antibody 1200 U/ml. There were no findings dry eye, dry mouth, skin sclerosis, and arthralgia. this therapy was started. After this therapy, nivolumab alone therapy was started. Then, there were complaints of joint pain of the fingers. We suspected arthritis due to immuno-related adverse event: irAE and started oral administration of corticosteroid (PSL) 10 mg/day. But Symptoms did not improve. A skin biopsy was performed. In the pathology, SSc such as lymphocyte infiltration mainly composed of lymphocytes was suspected. anti-Scl-70 antibody, anti-centromere antibody, and anti-RNA polymerase III antibody were negative, and no symptoms associated with SSc such as interstitial pneumonia were observed. RCC has shrunk. [Clinical significance] We experienced a case of symptoms similar to SSc after nivolumab / ipilimumab combination therapy. There are few reports of irAE after nivolumab / ipilimumab combination therapy with SSc-like symptoms. Although irAE often presents with symptoms similar to autoimmune diseases, there are many cases of autoantibody negative. Difficult to diagnose.

P41-3

Clinical characteristics of patients with systemic sclerosis having myositis and severe lower gastrointestinal involvement

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Conflict of interest: None

[Objective] To elucidate clinical characteristics of patients with systemic sclerosis (SSc) who have myositis and severe GI involvement. [Methods] Among patients with SSc who were admitted to our hospital between April 2013 and June 2020, we identified cases having myositis and severe lower GI involvement on their admission. Severe GI involvement was defined as intestinal pseudo-obstruction and/or pneumatosis cystoides intestinalis. The diagnosis of myositis was made by the attending physician. [Results] A total of seven patients (all were female and 4 were diffuse cutaneous type) were evaluated. Six patients were positive for anti-nuclear antibodies, one for anti-Scl-70 and two for anti-U1-RNP. All patients were treated with PSL, four with IVCY and two with IVIG for myositis and SSc. Myositis was improved in all patients, however, severe lower GI involvement occurred after the myositis had been improved in cases where severe lower GI involvement was preceded by myositis. In a case where myositis and severe lower GI involvement occurred simultaneously, treatment with PSL was effective for myositis, but not for severe lower GI involvement. [Conclusions] We herein reported clinical characteristics of patients with SSc having myositis and severe lower gastrointestinal involvement.

P41-4

The titer of Anti-topoisomerase I antibody and clinical features in systemic scleroderma

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Conflict of interest: None

[Objective] Systemic sclerosis (SSc) is an intractable autoimmune disease and is known that the organ damage and prognosis are affected by autoantibodies. Some reports show that the titers of anti-topoisomerase I antibodies (anti-Topo1) are associated with disease activity. The relationship of titers of anti-Topo1 with their clinical characteristics is studied. [Methods] Sixteen cases of anti-Topo1-positive SSc were subjected. Age, gender, comorbidity, antinuclear antibodies, organ damage, and laboratory data were collected retrospectively. These parameters were compared between two groups: Topo1 antibodies 16-fold or more (Topo-H group, n=8) and less than 16-fold (Topo-L group, n=8). [Results] The mean age of the patients was 56.2 years, with 3 males and 13 females. The Topo-H group had a longer duration from disease onset to diagnosis compared to the Topo-L group (8.9 vs 0.9 years). There was no significant difference in organ damage between the two groups, however, serious complications such as renal crisis or death tended to be more frequent in the Topo-H group (42.8% vs 14.3%) though it did not reach statistical significance (p=0.569). [Conclusions] SSc patients with high titers of anti-topo1 should be followed-up with caution because they can progress to fatal complications.

P41-5

Analysis of nail fold capillary changes by therapy in patients with systemic sclerosis

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Conflict of interest: None

We analyzed nail fold capillary changes by therapy in patients with systemic sclerosis (SSc). We assessed the capillary of nail fold in 30 patients with SSc by capillaroscopy and dermascopy. We assessed between relationship capillary changes and respiratory changes, skin sclerosis in paitiens with SSc. Patients with early and active SSc showed active nail fold capillary changes, giant capillary or capillary enlargement. These changes decreased by administration of cyclophosphamide or corticosteroids. But prostanoids or bosentan did not change the active changes of nail fold capillary. Decrease of active changes of nail fold capillary changes did not relation between respiratory changes, respiratory function and skin sclerosis changes in patients with SSc. Capillary density also did not increase by corticosteroids or cyclophosphamide, prostanoids and bosentan. We could not predict the effect of therapeutic drugs by nail fold capillary changes in patients with SSc.

P41-6

A case of systemic sclerosis (diffuse cutaneous)-polymyositis overlap syndrome with lethal arrhythmia

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Conflict of interest: None

[Case] 37 years old, man. The patient was diagnosed with diffuse cutaneous systemic sclerosis (SSc) in September X. There was abdominal pain and elevated creatinine kinase (CK), but there was no evidence of

myositis on needle electromyography, MRI, and autoantibodies. In February X+1, the patient had lethal arrhythmia that led to shock and implantation of ICD. The patient was referred to our department in May. The modified Rodnan total skin thickness score (mRSS) was 33 points. The abdominal pain and CK elevation were determined to be myopathies associated with SSc and were treated with prednisolone (PSL) 20 mg and intravenous cyclophosphamide. The skin gradually softened and the abdominal pain disappeared. In January X+4, abdominal, upper arm, and forearm pain occurred, and CK increased. The mRSS was 12 points. In anti-ARS, the antibody was positive, the diagnosis of polymyositis of overlap was made. The dose of PSL was increased to 30 mg and the myalgia gradually improved. [Discussion] Left ventricular dysfunction and conduction problems are more common in SSc patients with myopathy and myositis. The treatment of myocardial complications in SSc requires appropriate evaluation because of the potential impact on future cardiac complications that may have a prognostic value.

P41-7

Risk factors and prognostic factors in scleroderma renal crisis

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Conflict of interest: None

[Objective] To clarify risk and prognostic factors of scleroderma renal crisis (SRC). [Methods] Nine cases diagnosed with SRC in University of Tsukuba hospital between 2010 and 2020 were included in this study. We retrospectively evaluated 1) background, 2) clinical findings, 3) treatment, and 4) compared the clinical features between the improved group (n=4), and the unimproved group (end-stage renal failure; n=1, death; n=4). [Results] 1) Cases were classified into seven of diffuse and two of limited cutaneous systemic sclerosis. Five cases were overlap syndrome (systemic lupus erythematosus: 1, rheumatoid arthritis: 2, polymyositis: 2). Corticosteroid (average dose of PSL; 17.4 mg/day) or calcineurin inhibitors were prescribed in seven and five cases, respectively. 2) Serum creatinine (s-cre) was elevated to abnormal range at diagnosis of SRC in all cases. Thrombotic microangiopathy was observed in six cases. 3) All cases were treated with ACE inhibitors. Plasma exchange was performed in three cases. 4) S-cre values and schistocyte before treatments were significantly higher in the unimproved group (p=0.032, p=0.0495). [Conclusions] Use of corticosteroids and calcineurin inhibitors might be the risk factors for SRC. S-cre and schistocyte before treatments might affect disease prognosis.

P41-8

A case of intestinal cyst-like emphysema in a scleroderma and rheumatoid arthritis patient diagnosed with intestinal perforation due to free gas in the abdominal cavity

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Conflict of interest: None

[Case] A 76-year-old woman with Raynaud's symptoms and arthritis in X-8 years. She was diagnosed with diffuse cutaneous systemic sclerosis due to skin sclerosis and concave scars, and rheumatoid arthritis. She was treated with beraprost sodium, tocopherol acetate, and tocilizumab and was stable for a long time. X-1 years, early satiety and frequent diarrhea appeared. Lower gastrointestinal endoscopy showed no findings, and treated with esomeprazole magnesium hydrate and mosapride citrate. In X years, edema of both lower legs appeared. She had an appetite and no changes in bowel movements. There were no changes in vital signs, and general condition was good. The abdomen was swollen but no guarding. Blood tests showed no inflammatory changes. X-ray showed free air, and CT imaging showed intestinal cyst-like emphysema. Intestinal perforation was suspected, and emergency laparotomy was performed, but no perforation site was found. After 3 days, the feeling of fullness and edema disappeared. [Clinical significance] Although there have been few reports related to the Rheumatology, intestinal emphysema may be accompanied by free air, and the judgment of laparotomy may be asked. In many cases, conservative therapy is possible. we report on the pathophysiology based on the literature.

P41-9

4 cases of administering the antifibrotic medicine Nintetanib for interstitial lung disease associated with systemic scleroderma

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Conflict of interest: None

Pulmonary disease is a symptomatology of systemic scleroderma, and exacerbation of interstitial pneumonia often defines the prognosis of patients. Therefore, treatment of interstitial pneumonia is important. According to the 2016 guidelines, there were few medication options and the immunosuppressant cyclophosphamide was used. However, the immunosuppressant cyclophosphamide is known not to improve the prognosis of patients due to its side effects. The recent tentative proposal mentions the administration of the immunosuppressant mycophenolate mofetil and the administration of the antifibrotic medicine nintetanib, which has been covered by insurance since December 2019. Among the collagen disease lungs, interstitial pneumonia due to scleroderma is mainly fibrosis like idiopathic pulmonary fibrosis, and its effect was confirmed by a clinical trial of the antifibrotic medicine nintetanib. We experienced 4 cases in which the antifibrotic medicine nintetanib was used in cases where interstitial pneumonia was difficult to control and cases in which fibrosis progressed. There were some cases of acute exacerbation and death, and unexpected side effects. We report the results of 4 cases with some review of the literature.

P41-10

Experience of using nintedanib for interstitial pneumonia with systemic scleroderma in our department

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Conflict of interest: None

[Objective] Report the experience of using nintedanib (Nin) for interstitial pneumonia with progressive systemic scleroderma (SSc-ILD) in our department. [Methods] 22 patients who used Nin for SSc-ILD. [Results] The following is the median (quartile). Age 69.5 (50.3-74.3) years, 19 females. Diffuse type 12 cases, anti-Scl-70 antibody positive 9 cases. The duration of ILD was 51 (30.3-85.5) months, and KL-6 803 (499.3-1210) U / ml, % FVC 74.2 (64.7-83.7) %, and% DLco 43.7 (32.2-58.2) %. Extensive disease occurred in 13 cases. Nin was used in 6 patients at the same time as induction therapy for SSc-ILD and in 16 patients with maintenance therapy. At the start of Nin, PSL was used in 17 patients at 5.5 (1.5-13.5) mg/day. AZA was used in 3 cases, TAC in 8, MMF in 5, and CSA in 2. Six months after the start of Nin, KL-6 was measured in 19 cases and % FVC was measured in 11 cases, and no significant deterioration was observed in either case. The duration of Nin was 180 (60-262.5) days, and 9 patients discontinued oral administration due to diarrhea, gastrointestinal symptoms, and liver damage. [Conclusion] In many cases, immunosuppressive therapy and Nin were used in combination for progressive SSc-ILD. No significant deterioration of ILD was observed during the 6-month observation period.

P41-11

Treatment of Myocardial Fibrosis in Systemic Sclerosis with Tocilizumab

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Conflict of interest: None

[Background] Systemic sclerosis (SSc) is a chronic and systemic disease characterized by extensive vascular dysfunction and progressive fibrosis of the skin and organs. In recent years, tocilizumab (TCZ) has been attraction attention as a treatment for SSc as well. Therefore, we report on our observation of improvements in myocardial fibrosis in SSc using TCZ. [CASE] 44 year-old female. In 2015, the patient was diagnosed with lc SSc. PVC accounted for as much as 16.86% of the patient's total heart rate. The patient received 2000 mg MMF for cardiac lesions, but cardiac scintigraphy performed 3 months later indicated a deterioration of BMIPP uptake with an EF of only 45.4%. In light of these developments, the patient was started on TCZ (8 mg/kg every 4 weeks), which led to improvements in symptoms, myocardial scintigraphy, and cardiac MRI. Six months later, PVC comprised only 0.017% of the total heart rate, and the patient's EF improved to 58.9%. BMIPP uptake by myocardial scintigraphy and cardiac MRI findings both showed complete normalization around 3 years after the start of the treatment. [Conclusion] Our finding suggest that TCZ may be effective for treating cardiac lesions in patients with SSc.

P41-12

A case of combined deficiency of copper, zinc, and vitamin B1 due to gastrointestinal disorders caused by systemic sclerosis

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Conflict of interest: None

[Cases] 37-year-old female. The Raynaud phenomenon appeared in the year X-15, and she was diagnosed with dermatomyositis, systemic sclerosis (SSc), and systemic erythematosus over the next few years with heliotrope rash, muscle pain and weakness, polyarthritis, lymphocytopenia, difficulty of opening her mouth, and skin sclerema of the fingers. In the year X-1, she was hospitalized for intestinal pseudo obstruction caused by SSc. In the year X, meal intake became poor due to mouth ulcers from one week before hospitalization. She was admitted to the hospital due to anemia, impaired renal function with dehydration. Not only anemia but also leukocytopenia was clarified, and sensory impairment of legs and ulceration of the fingers and elbows were also observed. As the cause of these various symptoms, deficiency of copper, zinc, vitamin B1 was observed. Dietary guidance and oral supplements and drugs were given to her, and various deficiencies were improved. [Consideration] Gastrointestinal disorders of SSc are well known, severe cases are about 5% in Japan. Deficiency of various nutrients can occur, but at the same time it is revealed that a variety of nutrients are deficient in cases that can be improved by oral supplementation therapy is considered rare.

P41-13

A case of systemic scleroderma complicated with renal crisis andpulmonary arterial hypertension

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Conflict of interest: None

[Case] A 72-year-old woman developed a cold symptom two weeks ago, and was subsequently admitted to our department because of worsening headache, nausea, and general malaise. After hospitalization, localized systemic scleroderma (lcSSc) was diagnosed based on findings such as skin sclerosis of the face and limbs, capillary dilation, and bleeding points of the nail epithelium. The patient was diagnosed with scleroderma renal crisis based on lcSSc because of hypertension emergency, ruptured erythrocytic anemia, thrombocytopenia, broken red blood cells in peripheral blood and decreased haptoglobin. In addition, the right pulmonary artery pressure was 29 mmHg, pulmonary artery wedge pressure was 5 mmHg by right heart catheterization, and there was no shadow defect in pulmonary scintigraphy. The result was a definitive diagnosis of pulmonary arterial hypertension. For renal crisis, administration of captolyl and calcium inhibitor resulted in normal blood pressure. A pulmonary vasodilator was started for pulmonary arterial hypertension. [Clinical significance] There have been very few reports of combined renal crisis and pulmonary arterial hypertension in systemic scleroderma. This is reported with some literature considerations.

P41-14

Three cases of acute / subacute interstitial lung disease associated with anti RNA polymerase 3 antibody positive systemic sclerosis

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Conflict of interest: None

Interstitial lung disease (ILD) has been reported to be less frequent and milder in anti RNA polymerase 3 (RNAP3) antibody positive Systemic sclerosis (SSc). However, we experienced 3 cases of anti RNAP3 antibody positive SSc with acute/subacute ILD. Case 1: A 72-year-old woman developed dyspnea in a month. Chest HRCT showed subacute exacerbation of ILD. MRC grade 3, % FVC 46.8%, KL-6 1679 U / mL, AaDO2 37.8 mmHg. Treatment with prednisolone, intravenous cyclophosphamide (IVCY), and mycophenolate mofetil improved ILD. Case 2: A 55-year-old woman diagnosed with SSc-ILD four years ago progressed subacutely and HRCT showed that the extent of fibrotic lesions exceeded 20%. MRC grade 2, % FVC 78.0%, KL-6 1290 U / mL, AaDO2 32.7 mmHg, pneumothorax, intestinal emphysema, and malabsorption syndrome were complicated. Nintedanib was started. Case 3: A 78-year-old woman diagnosed with SSc-ILD 5 years ago developed dyspnea within a week and had a rapid exacerbation of ILD on chest HRCT. MRC grade 4, KL-6 5212 U / mL, AaDO2 146.6 mmHg. Multidisciplinary treatment with steroid pulse therapy, IVCY, cyclosporine, endodoxin adsorption was performed, but she died. Since ILD could be exacerbated acutely / subacutely even in anti-RNAP3 antibody positive SSc, careful follow-up was considered necessary.

P41-15

A case of diffuse cutaneous systemic sclerosis with serositis successfully treated by glucocorticoid

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Conflict of interest: None

83-year-old woman noticed systemic edema and Raynaud's phenomenon (RP) in October 2019. She was suspected of having heart failure because of high BNP. Although coronary angiography revealed no abnormality, she was treated by diuretics from February 2020 with improvement of systemic edema. However, as thickening of the skin on her fingers became clear and anti-nuclear antibody (ANA) was positive, she was introduced to our Hospital for further examination. She was diagnosed as diffuse cutaneous systemic sclerosis (dcSSc) with skin thickening over MCP joint of hands, nail fold bleeding, RP, interstitial pneumonia and ANA positivity. She experienced acute dyspnea in August and was re-admitted in our Hospital in September. Chest CT showed pleural and pericardial effusion and echocardiography revealed diastolic dysfunction. She was treated with oxygen therapy and diuretics. Despite of these treatments, her symptoms did not improve. Because the nature of pleural effusion was exudative and there was no possibility of infections and malignancy, she was diagnosed

as serositis associated with dcSSc. 30 mg of prednisolone (PSL) was initiated and her symptoms improved gradually. In this case, PSL wad effective both pleural and pericardial effusion associated with dcSSc.

P42-1

ADAM-17 is expressed human lung fibroblasts

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Conflict of interest: None

[Objective] A disintegrin and metalloprotesase (ADAM)-17 is protease that is thought to have an important role in tissue destruction and inflammatory reaction. We examine the expressions of ADAM-17 using human lung fibroblasts (HLF) to investigate the role of ADAM-17 in interstitial lung disease (ILD) involved with collagen diseases. [Methods] ADAM-17 in serum in rheumatoid arthritis (RA) (n=22), systemic scleroderma (SSc) (n=38), mixed connective tissue disease (MCTD) (n=12), and overlap syndrome (n=8) was measured using ELISA. The association with clinical manifestations and clinical data were examined. ADAM-17 expression in TNF-α stimulated lung fibroblasts was also determined using immunohistological staining, ELISA, and Western blotting. [Results] ADAM-17 in serum in RA, SSc, MCTD, and overlap syndrome was significantly higher compared to healthy control. In addition, ADAM-17 in ILD was significantly higher compared to non-ILD. ADAM-17 was expressed on TNF-α stimulated HLF. ADAM-17 in TNF-α stimulated HLF conditioned medium was also elevated compared with in non-stimulated HLF conditioned medium. [Conclusions] We showed ADAM-17 was expressed on HLF. These results suggest that ADAM-17 may play a role in lung fibrosis through shedding of inflammatory cytokines.

P42-2

Warming arms using a disposable warmer pad alleviates Raynaud's phenomenon in systemic sclerosis: The single-arm multicenter clinical trial

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Conflict of interest: Yes

[Objective] Raynaud's phenomenon (RP) suffers systemic sclerosis (SSc) patients, for which effective treatment has not been established. We previously reported warming arms or neck relieved RP in SSc. We conducted the multicenter clinical trial to confirm the therapeutic effect of the warming arms for RP in SSc. [Methods] SSc patients were recruited in the 7 hospitals. Following 2 weeks of observation, they applied disposable warmers on both upper arms for 2 weeks and repeated this procedure twice. Throughout the study, patients recorded self-assessment of RP as Raynaud´s Condition Score (RCS) daily. Primary endpoint was the difference in RCS between warming and non-warming period. The study was approved by the Osaka University Clinical Research Review Committee and registered for jRCT (jRCTs052190086). [Results] 30 patients were enrolled in the study and 28 cases were included in the analysis. The mean RCS of warming period was significantly lower than that of non-warming period (1.98 and 2.66, respectively, $P<0.001$, paired t test). 4 cases of burn were reported as treatment related adverse events, all of them were mild in severity. [Conclusions] Warming upper arms by disposable warmer pads alleviates RP in SSc.

P42-3

A case of elderly onset, refractory systemic sclerosis with myositis

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Conflict of interest: None

A 74-year-old man visited our hospital for detailed examination because of swelling of limbs from around September 2019, dyspnea on exertion from April 2020, and developing a fever. At the first medical examination, diffuse skin scleroderma and increase of CK 1563 U/L were observed. Immuno-serologically, anti-nuclear antibody, anti-Scl70 antibody, anti-RNP antibody, and anti-RNA polymerase 3 antibody were all negative. Chest CT showed bilateral mid-lower lung fields with reticular shadows. Based on ACR /EULAR classification criteria, he was diagnosed with systemic sclerosis. Prednisolone 30 mg/day and intravenous cyclophosphamide pulse therapy were started on day 7 of admission. After that, improvement of CK value and inflammatory response was observed, but progressive exacerbation of interstitial pneumonia was observed. Therefore, high-dose intravenous immunoglobulin therapy was performed on day 17 and tacrolimus was also added from day 23. As a result, the condition of interstitial pneumonia was stable, but on day 28, schistocyto, thrombocytopenia, and renal dysfunction were observed. Suspected thrombotic microangiopathy, tacrolimus was discontinued on day 38. We report the overlapping syndrome of systemic sclerosis and myositis with a review of the literature.

P42-4

A case of systemic sclerosis with highly suspected immune-mediated necrotizing myopathy

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Conflict of interest: None

[Case Report] A 73-year-old woman. She was aware of Raynaud's phenomenon, skin thickness to the forearm and had interstitial lung disease (ILD, KL-6 = 4556 U / mL) with anti-topoisomerase I antibody. She was diagnosed as having systemic sclerosis (SSc) and nintedanib was administrated for ILD. Then, she revealed muscle weakness and myalgia predominantly in the proximal muscle with an increased CK value (=248 U/mL). Electromyography showed mild myogenic changes. Muscle biopsy demonstrated both necrosis and regeneration change of muscle fibers without lymphocyte infiltration, perifascicular atrophy and rimmed vacuole, suggesting immune-mediated necrotizing myopathy (IMNM). After 20 mg of daily prednisolone was initiated, myalgia disappeared along with a normalization of CK value. [Discussion] Although SSc may also present with necrotizing myopathy, lymphocyte infiltration is common (Ann Rheum Dis, 2009; 68: 1474). There was no experience of using statins in this case. In case of IMNM, CK value is usually extremely high from the first visit, so high-dose steroid therapy is indicated. In this case, the CK value was less than twice of the normal value and a low-dose steroid was effective. To date, there have been no reports of cases of scleroderma complicated with IMNM.

P42-5

A case of TMA due to normotensive scleroderma renal crisis during treatment for localized dermatomyositis systemic scleroderma / polymyositis

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Conflict of interest: None

[Case] A 71-year-old woman [Current medical history] Since about X-3, she has been visiting a local dermatologist for chilblains on both hands. General malaise appeared from June X, and he was referred to our dermatology department for a detailed examination. A diagnosis of local-

ized skin sclerotic systemic scleroderma was made at the dermatologist, but muscle weakness and high CK were observed, and overlap syndrome was suspected. In August, the patient was admitted to our department for further examination. [Progress after hospitalization] Polymyositis was diagnosed by MRI and muscle biopsy, and treatment was started with PSL 30 mg (0.8 mg/kg) and TAC 1 mg in September. Besides, marked thrombocytopenia and crushed erythrocytes appeared. Since hypertension was not observed during the course of hospitalization, he was diagnosed with thrombotic microangiopathy (TMA) due to normotensive scleroderma renal crisis, and was admitted to the ICU and underwent plasma exchange twice. On the 52nd day of illness, he failed to receive treatment and died of heart failure due to worsening oxygenation. It was a secondary TMA because the activity of ADAMTS13 was normal and the ADAMTS13 inhibitor was also negative.

P42-6

A case in which cyclosporine and methotrexate was effective for macrophage activation syndrome associated with MCTD

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Conflict of interest: None

[Case] 48-year-old woman [Chief complaint] Fever, rash, arthralgia [Present illness] From the age of 40, she was aware of finger sclerosis and Raynaud's phenomenon, and was diagnosed scleroderma by near doctor. From June X, fever, rash, and arthralgia appeared, and she was referred to our hospital. [Progress] Her blood test showed increased inflammatory response, high ferritin level, cytopenia of 2 lineages, and liver damage, but these findings improved spontaneously, and she discharged. However, the symptoms recurred, she was readmitted. At that time, activated macrophages were confirmed by bone marrow examination, so she was diagnosed with macrophage activation syndrome (MAS). In addition, she was diagnosed as MCTD based on her symptoms and serological findings. Although the steroid pulse therapy and the high-dose steroid therapy was performed, an inflammatory response and ferritin level prolonged. Therefore, the cyclosporine and methotrexate were added, and various findings were improved. After the steroid tapering, she was discharged. [Clinical significance] The treatment has not been established for MAS secondary to collagen disease. This case is a rare case in which the combined use of cyclosporine and methotrexate was useful for MAS followed by MCTD, so we report this case.

P42-7

A case of Systemic Sclerosis Complicated with Rheumatoid Arthritis Accompanied by Refractory Ascites Resistance to Glucocorticoid and Successful Response to Tocilizumab

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Conflict of interest: None

[Case] A 57-year old woman was admitted to our hospital with abdominal bloating. X-15 years, she was diagnosed with systemic sclerosis (SSc) at the previous hospital. On admission, abdominal computed tomography scan revealed considerable ascites accumulation. The ascites was exudative, included mononuclear cells. In addition, ascitic fluid cultures were negative, and cell block specimens showed no evidence of malignancy. Her serum and ascitic interleukin-6 levels were increased to 41.6 pg/mL and 14,900 pg/mL, respectively. Ascites accumulation was resistance to diuretics, steroid pulse therapy, and cell-free and concentrated ascites reinfusion therapy. During the course, she was diagnosis with rheumatoid arthritis (RA), which showed DAS28-ESR of 4.62. On the 119th day of hospitalization, the patient was treated with tocilizumab (TCZ) for RA. After TCZ induction, her polyarthralgia gradually subsided and the ascites decreased. On the 140th day of hospitalization, she was transferred to another hospital. Unfortunately, however, she died from hemorrhagic shock due to GI bleeding in the following year. [Clinical Significance] We report a patient with SSc and RA accompanied by refractory ascites successfully treated with TCZ and discuss her condition based on the pathological findings.

P42-8

A case of secondary alveolar proteinosis with systemic scleroderma and rheumatoid arthritis

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Conflict of interest: None

55 years old, female. She was diagnosed with SSc due to skin sclerosis, Raynaud's symptom and sclerosis, and positive centromere antibody 16 years ago. 6 years later she complained fingers and wrists arthritis. X-rays revealed bone erosion which led to RA diagnosis. Despite the treatment with MTX, PSLTAC, low disease activity remained. 6 years later after RA diagnosis, soon after the ABT induction, the treatment was withdrawn because of the fever, cough and hypoxia (SpO2: 92%). Lung CT showed GGO in the bilateral upper lobes. Infection was excluded by bronchoscopy, high-dose PSL was initiated for IP with SSc. Oxygen level recovered and TCZ was used to modify both RA and SSc. A year later, IP relapsed and was resistant to high dose PSL. Cryobiopsy was performed and alveolar proteinosis: PAP was suspected histologically. Anti-GM-CSF antibody was negative which suggest secondary PAP, and treated with RTX, in addition to high-dose PSL. PAP is a rare respiratory disease that causes accumulation of lung surfactant proteins in the alveoli. Autoimmunity is the 90% cause of the disease and the remaining 10% are considered to be secondary. Malignant hematological tumors, Behcet's disease and other collagen diseases, inhalation of dust and toxic gases have been reported as underlying disease.

P42-9

A case of anti-topoisomerase1antibody positive systemic sclerosis that developed rapidly progressive skin sclerosis and pulmonary arterial hypertension during treatment for primary Sjögren syndrome

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Conflict of interest: None

The case is a woman in her 70s with undergoing immunosuppressive therapy for lymphocytic interstitial pneumonia with Sjögren syndrome (SS). The patient suddenly developed skin sclerosis and digital ulcers from a year ago and complained of marked shortness of breath during exertion four months later. Computed tomography showed only a gradual exacerbation of interstitial pneumonia, and no findings suggestive of pulmonary veno-occlusive disease. Cardiac catheterization showed an increase in mean pulmonary artery pressure of 32 mmHg, and we diagnosed pulmonary arterial hypertension (PAH). We also diagnosed systemic sclerosis with new positive anti-topoisomerase I antibody and marked skin sclerosis with TSS score of over 30. We increased the dose of corticosteroid and started cyclophosphamide every 2 weeks and endothelin receptor antagonist. Immunosuppressive treatment was successful. Although cases of collagen disease complicated with pulmonary hypertension (PH) are often experienced, cases of rapid systemic skin sclerosis and PH at the same time with the appearance of autoantibodies are rare. We report a case of systemic sclerosis in which autoantibodies became positive and acute onset and rapidly progressive skin sclerosis and PAH developed during SS treatment.

P43-1

A case of anti-OJ antibody-positive anti-ARS antibody syndrome diagnosed by muscle biopsy

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Conflict of interest: None

[Case] A 65-year-old woman. She consulted a former doctor in April X, and was referred to our department in May after admitting an increase in muscle deviation enzymes, and was admitted to our department for detailed examination and treatment. At admission, the value was as high as CK 2622 U / L, arthralgia on both fingers and mechanical's hands, and chest CT images showed interstitial shadows in both lung fields. Therefore, anti-ARS antibody syndrome was suspected and the test was performed, but the anti-ARS antibody was negative. Electromyography showed myogenic changes in the deltoid and iliopsoas muscles. A muscle biopsy was performed from the left deltoid muscle, and as a result of the muscle biopsy, perifascicular necrosis was found, and the possibility of antisynthetase syndrome was most considered. From the results of RNA immunoprecipitation, anti-OJ antibody and anti-U1RNP antibody were detected, and anti-ARS antibody syndrome was diagnosed. [Discussion] In this case, anti-ARS antibody syndrome was suspected from the clinical course, and the MESACUP™ Anti-ARS test was performed, but the test was negative. From the results of muscle biopsy, antisynthetase syndrome was suspected, and RNA immunoprecipitation was performed, and anti-OJ antibody positivity was found.

P43-2

A case of anti-MDA5 antibody positive rapidly progressive interstitial pneumoniae refractory to aggressive treatment including tofacitinib and simple plasma exchange

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Conflict of interest: None

A 56 year-old man presented with 2 weeks history of cough and fever. 3 days prior to admission, CT scan showed grand glass opacity (GGO) in his bilateral lungs. So he was referred to our hospital. Vital sign were BP108/64 mmHg, HR78/min, RR18/min, BT37.1°C and SpO2: 94% (room air). Physical examination was not significant for skin lesion. Laboratory test showed elevated KL6 and ferritin (2657.9 ng/ml). Despite absence of typical cutaneous manifestations, pulsed steroid therapy and high dose tacrolimus were administered as initial therapy for suspected rapidly progressive interstitial lung disease (ILD). On day 4, he became hypoxia. So we administered intravenous cyclophosphamide 800 mg. After that, anti-MDA5 antibody came back with strongly positive result (2110 index). From day 8, tofacitinib 10 mg/day, simple plasma exchange (PE) 6 times, high dose intravenous immunoglobulin 0.4 g/kg and endotoxin absorption were subsequently started due to worsening of hypoxia and GGO. However he had died on day 24. This case illustrates anti-MDA5 positive ILD refractory to aggressive multitarget treatment. Further treatment option may be needed for cases refractory to conventional triple therapy. Literature review of possible new therapy option will be presented with clinical course of this case.

P43-3

A case of anti-MDA5 antibody-positive dermatomyositis treated with immunosuppressive therapy including tofacitinib and found to be associated with pulmonary embolism at autopsy

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Conflict of interest: None

[Case] The case is a 42-year-old woman. The patient was admitted to the hospital because of fever and dyspnea. Her SpO_2 was 91% and Gottron signs and inverse Gottron signs were seen, and anti-MDA5 antibodies were present. Methylprednisolone pulse therapy, cyclophosphamide and tacrolimus were administered. The ferritin level was 159.5 ng/ml. Her respiratory condtion worsened and she was placed on a ventilator. The patient was judged to be refractory to treatment and was started on tofacitinib. She died on the 48th day of illness. Pathological autopsy revealed fibrosis of the stroma throughout both lungs, hyaline membrane formation of the alveolar walls. An organic thrombus was found in the inferior vena cava and complications of pulmonary artery thrombosis and pulmonary infarction were observed. [Discussion] The autopsy revealed severe fibrotic lesions as well as thrombosis. Although the relationship between thrombosis and TOF is unclear, caution should be exercised when using TOF on dermatomyositis because of other thrombogenic factors, such as concomitant use of high-dose steroids.

P43-4

Successful IVIg treatment in patients with anti-MDA5 antibody positive dermatomyositis presenting severe thrombocytopenia

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Conflict of interest: None

A 69-year-old woman visited our hospital with a complaint of rash and general malaise. Dermatomyositis was diagnosed based on heliotrope rash, Gottron sign, weakness of upper and lower limbs, increased creatinine kinase, and high inflammatory markers. Interstitial pneumonia was observed in chest CT and the anti-MDA5 antibody titer and serum ferritin was high. Treatment with prednisolone (PSL) and tacrolimus (Tac), and cyclophosphamide was started. Platelets gradually decreased from the 4th day after hospitalizaiton and on the 15th day, platelet decreased by 1000 / μl with bleeding tendency. No decrease in leukocyte or hemoglobin levels was observed, and bone marrow biopsy showed only mild blood cell phagocytosis. Considering the possibility of drug-induced thrombocytopenia, Tac was changed to cyclosporine and PSL was changed to dexamethasone, but platelets did not increase. Since PA-IgG was high and the decrease of platelet was refractory to platelet transfusion, immune thrombocytopenia was considered as a pathological condition of thrombocytopenia. After IVIg treatment, a rapid increase in platelet count was observed and platelet count increased by 153000 / μl on the 76th day. IVIg is effective when anti-MDA5 antibody-positive dermatomyositis is associated with thrombocytopenia.

P43-5

A case of antisynthetase syndrome stable for more than 20 years relapsed with pulmonary hypertension and interstitial pneumonia following bladder carcinoma

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Conflict of interest: None

[Case] A 68-year-old man came to the hospital with a chief complaint of dyspnea on exertion for the past month. He had a history of an anti-Jo-1 antibody positive polymyositis stable for more than 20 years. A chest CT showed bilateral interstitial pneumonia (IP). A diagnosis of pulmonary hypertension (PAH) was made based on mean PAP 46 mmHg on right heart catheterization. For the relapse of anti-synthetase syndrome (ASS), he was treated with PSL 1 mg/kg and IVCY, and IP and PAH improved. He also had back pain and multiple vertebral metastatic tumors were found on MRI. Bone marrow biopsy suggested urothelial cancer, and bladder cancer was diagnosed from bladder polyp biopsy. [Discussion] PAH with ASS is infrequent and usually with a poor prognosis. Our case improved without the use of vasodilators, and immunosuppressive therapy may be effective in the early stages without intimal fibrosis of the pulmonary arteries. Although there is a report about the association between polymyositis and bladder cancer, the risk of malignancy is usually low in ASS, and a case of bladder cancer with anti-Jo-1 antibody has not been reported. In our case,

bladder cancer is considered to be a trigger of a relapse, and our case might give some suggestions about a pathology of ASS.

P43-6

A fatal case of immune-mediated necrotizing myopathy developing respiratory muscle dysfunction without markedly elevated serum creatine kinase concentrations

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Conflict of interest: None

A 69-year-old woman with systemic sclerosis was referred to our hospital because of muscle weakness, elevated creatine kinase (CK) levels and pulmonary arterial hypertension (PAH). Although she was clinically diagnosed with polymyositis and treated with glucocorticoid (GC), tacrolimus and pulmonary vasodilators, she discontinued immunosuppressants by her own choice. Four years later, her muscle symptoms worsened and she was newly diagnosed with immune-mediated necrotizing myopathy (IMNM) based on muscle biopsy. Shortly thereafter, she was admitted due to stress cardiomyopathy. Heart failure resulted in rapid resolution by supportive therapy, whereas progression of type 2 respiratory failure occurred. Worsening PAH was not confirmed by right heart catheterization. Generalized muscle atrophy and mild CK elevation (200 to 350 U/L) were observed. We considered the possibility that respiratory muscle dysfunction was caused by IMNM, and she was treated with GC. Although her respiratory function improved temporarily, she died of worsening respiratory failure while tapering GC. Pathological autopsy revealed necrotic and regenerating fibers in intercostal muscle. Progressive respiratory dysfunction due to IMNM could occur in patients with low CK levels and muscle atrophy.

P43-7

A case of anti-Mi2 Ab positive myositis with erosive bone lesion

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Conflict of interest: None

[Preface] AntiMi-2 Ab is one of myositis related autoantibody. Clinical characteristics of Mi2-positive case are scanty of myositis and pulmonary involvement, and often associate with skin lesion. [Cace] We experienced A case of AntiMi-2 Ab positive female case. She came to our clinic with introductory letter from orthopedic. Skin lesion was observed on head and finger. Laboratory showed RF negative, ANA positive, AntiMi-2 Ab positive, normal CK. Xp showed bone erosion on DIP, PIP. Skin biopsy was suggestive of irregular psoriasiform hyperplasia, without parakeratosis, atypical for psoriasis. [Conclusions] Definite differential diagnosis was difficult between antiMi-2 Ab positive case with bone erosions with or without psoriasis.

P43-8

Treatment for disease flare in a patient with dermatomyositis who had developed steroid psychosis during the initial treatment

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Conflict of interest: None

A 51-year-old woman developed fever and erythema in August, year X. Prednisolone (PSL) 15 mg/day started at the previous hospital was unsuccessful and she was transferred to our hospital. Gottron's sign, mechanic's hand, muscle weakness, polyarthritis, high creatinine kinase level (CK), high C-reactive protein (CRP) level, positive anti-PL-7 antibody and rheumatoid factor were observed, and the chest images showed interstitial pneumonia (IP). Methyl-PSL pulse therapy followed by PSL 60 mg/day was introduced as well as intravenous pulse cyclophosphamide (IVCY) and subsequent intravenous immunoglobulin therapy. PSL dose was rapidly tapered to 20 mg/day because of steroid psychosis, and she was followed at an outpatient clinic. She developed fever, polyarthritis, muscle weakness with elevated CK and CRP levels and the exacerbation of IP. She was readmitted to the hospital, and tacrolimus and tocilizumab were added with a stable dose of PSL at 10 mg/day. Myositis, polyarthritis, and IP remarkably improved with the above treatment. The present case is considered informative for the management of patients with autoimmune rheumatic diseases showing steroid psychosis.

P43-9

Rapidly progressive interstitial pneumonia associated with anti-MDA-5-positive clinically amyopathic dermatomyositis mimicking rheumatoid arthritis: A case report

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Conflict of interest: None

A 56-year-old woman presented with joint pain and swelling 4 months ago. She was diagnosed as having rheumatoid arthritis (RA) based on high levels of rheumatic factor and anti-CCP antibodies. Considering the ground-glass appearance of both sides of the lower lung fields, she was treated with salazosulfapyridine (SASP) and a low dose of prednisolone (PSL). However, two weeks later, fever, hepatic dysfunction, and erythema (at the flexion of both upper limbs) appeared. Since adverse drug reactions were suspected, SASP and PSL were discontinued. However, she had sustained fever, worsening arthritis, and mild progression of interstitial pneumonia (IP). Although medications for RA treatment were started at that time, she showed rapid progression of IP, and was, therefore, referred to our hospital. She was diagnosed as having clinically amyopathic dermatomyositis (CADM) based on polyarthritis, papules with signs of necrosis, Gottron's sign, IP, and positive anti-MDA-5 antibody result. CADM with IP improved following high-dose steroid therapy in combination with IVCY and cyclosporine. Regarding the differential diagnosis of RA, we should remember that inflammatory myositis, especially in patients with anti-MDA-5 antibodies, may be preceded by arthritis and positive anti-CCP antibodies.

P43-10

A rare case of anti-OJ antibody-positive polymyositis overlapped with systemic lupus erythematosus and Sjogren's syndrome

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Conflict of interest: None

[Case] A 33-year-old female was suffered from pain and deformity of bilateral MCP joints for 8 years. She was initially treated as rheumatoid arthritis. Fever, muscle weakness, and shortness of breath developed a month ago. She was admitted into our hospital and diagnosed with polymyositis according to the presence of high serum myogenic enzyme, anti-OJ antibody (Ab)-positive, electromyographic abnormality, and histological myositis findings. Also, complications of systematic lupus erythematosus (SLE) and Sjogren's syndrome (SS) were diagnosed according to the presence of Jaccoud arthritis, lymphocytopenia, anti-Sm Ab positive, anti-SS-A Ab positive, hypocomplementemia, urinary protein, and focal lymphocytic sialadenitis in a minor salivary gland. After diagnosis, she was successfully treated with oral prednisolone 50 mg/day, 1 mg/kg, and steroid was tapered without relapse. [Clinical significance] Myositis-specific anti-OJ Ab is detected in less than 5% of cases of idiopathic inflammatory myositis. It was known that patients with anti-OJ Ab-positive polymyositis are a good prognosis, regardless of complications with interstitial pneumonia. We examined a rare case of anti-OJ Ab-positive polymyositis overlapped with SLE and SS, which was not reported previously.

P43-11

Characteristics of 2 cases in anti-HMGCR antibody-positive necrotic myopathy (IMNM)

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Conflict of interest: None

[Case 1] A 64-year-old man presented with muscle weakness in both thighs and creatine phosphokinase (CK) value were increased. Thigh MRI and muscle biopsy indicated hype-intensity region with fat suppression and poor inflammatory cell infiltration, active muscle fiber necrosis and regeneration changes, respectively. A positive anti-HMCGR antibody confirmed the diagnosis of IMNM. The patient was started on steroid pulse therapy followed by oral prednisone (PSL) 35 mg/day with Tac 3 mg/day. But was little improvement, treatment with intravenous immune globulin (IVIG) resulted in rapidly decreased CK value. [Case 1] A 63-year-old woman presented with thigh myalgia. She had no limbs muscle weakness, but CK and Aldolase value were increased. Thigh MRI and muscle biopsy showed a high signal range in STIR, and muscle fiber necrosis changes, respectively. A positive anti-MNGCR antibody confirmed diagnosis of IMNM. The patient was started on PSL 40 mg/day, but relapsed when reduced to PSL 20 mg/day. Treatment with IVIG and Tac 2 mg/day disappeared myalgia [Discussion] We experienced two cases of HMGCR antibody-positive necrotic myopathy with no history of taking statins and complications of malignant tumors.

P43-13

A case of anti-transcriptional intermediary factor 1-gamma (TIF1-gamma) antibody-positive dermatomyositis (DM) accompanied with primary peritoneal cancer

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Conflict of interest: None

A 70-year-old woman was presented with proximal muscle weakness and erythema in the face and dorsum of both hands. She had surgical histories of breast cancer and stomach cancer 10 years and 5 years ago, respectively. Blood tests revealed elevated CPK levels and a positivity for anti-TIF1γ antibody (Ab). Myogenic changes in proximal muscles were confirmed by electromyography. Based on these findings, the patient was diagnosed with anti-TIF1γ Ab-positive DM. Combination therapy of prednisolone, tacrolimus, and IVIG was initiated since her dysphagia was rapidly worsening. Malignancy screening tests, including mammography, gastrointestinal endoscopies, and contrast material-enhanced CT were done, but no evidence of malignancy was found. One month later, because of the elevation of serum CA15-3 and CA125 levels, we underwent a second CT and found a mass in the peritoneum. FDG-PET/CT showed high uptake in the peritoneal nodules. The pathological examination of the peritoneum specimen revealed PAX8-positive serous adenocarcinoma, which was different from her previous cancers. She was then diagnosed with primary peritoneal cancer. Here we report the first case of anti-TIF1γ Ab-positive DM accompanied with primary peritoneal cancer diagnosed by thorough malignancy screening tests.

P43-14

A case of nonmyopathic anti-signal recognition particle antibody-positive interstitial pneumonia

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Conflict of interest: None

The patient was diagnosed with chronic cough in X-10 years and asthma in X-1 year. Chest CT scan revealed bilateral shadows. SBT/ABPC and AZM were started, but there was no improvement. BAL specimen with negative culture and an elevated lymphocyte ratio. Since there was a characteristic dermatomyositis skin rash, combination of PSL, TAC, and IVCY treatment. After the start of treatment, cough symptoms and a 6-minute walk test, the lung interstitial marker (KL-6) and imaging tests showed improvement. At a later date, diagnosed as having anti-SRP antibody-positive interstitial pneumonia with poor muscle symptoms. Discussion: Anti-SRP antibodies have been reported to be involved in the development of autoimmune necrotizing myopathies. The myopathy causes severe symmetrical muscle weakness, such as weakness of the respiratory muscles, but rarely with extramuscular symptoms such as interstitial pneumonia, Raynaud's symptoms and arthralgia. Intensive and prolonged administration of steroids and immunosuppressive drugs is often required. It has been reported that the serum CK level correlates with the anti-SRP antibody titer. We report here a case of a patient with anti-SRP antibodies who had no muscular symptoms, conspicuous interstitial pneumonia, and responded to initial treatment.

P43-15

A case of rapidly progressive anti-SRP-positive immune-mediated necrotizing myopathy

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Conflict of interest: None

A 37-year-old previously healthy woman presented with proximal muscle weakness. One month prior to this presentation, the patient developed difficulty in climbing stairs and washing her hair. One week prior, she could hardly roll over nor hold herself upright on the bed, and was referred to our hospital. Examination showed significant proximal muscle weakness in upper and lower extremities. Serum creatinine kinase (CK) and troponin T levels were elevated at 5861 U/L and 2.7 ng/mL, respectively. Chest X-ray, electrocardiogram, and echocardiography were not significant. Serology was positive for anti-SRP antibody. Muscle biopsy of the left thigh showed necrotic muscle fiber with perifascicular mononuclear cellular infiltrates, consistent with anti-SRP-positive immune-mediated necrotizing myopathy (IMNM). Immunoglobulin, prednisolone and rituximab improved her symptoms. She was transferred to a rehabilitation center. Anti-SRP-positive IMNM is a rare form of autoimmune myopathy and characterized by severe proximal muscle weakness. This unusual case illustrated rapidly progressive necrotizing myopathy leading to immobility within one month. Other potential complications may include life-threatening cardiac and pulmonary involvement. Early diagnosis and prompt treatment is required.

P43-16

A case of rapidly progressive interstitial lung disease associated with lung adenocarcinoma in the absence of erythema with sausage-like finger swelling and anti-centromere and anti-Jo-1 antibodies

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Conflict of interest: None

A 76-year-old woman became aware of dyspnea and admitted to the hospital. Fine inspiratory crackles were heard, sausage-like hand swelling was noted without erythema. CEA 70.5 ng/ml, CYFRA 32.8 ng/ml, and no elevation of myogenic enzymes were noted. Antinuclear antibodies 640 times (discrete speckled pattern), anti-Jo-1 antibody, anti-centromere antibody were positive positive, and anti-MDA-5 antibody and anti-TIF-1 antibody were negative. CT scan showed diffuse frosted pattern of mottled, and lymph node enlargement. Histological studies were performed and CK 7 (+), CK 20 (-), and TTF1 (+) cells were detected in lymph nodes, and primary lung adenocarcinoma was diagnosed. The patient was diagnosed with rapidly progressive interstitial pneumonia and was immediately treated with 1000 mg of methylprednisolone, followed by tofatinib and tacrolimus. The patient had a rapidly progressive interstitial lung disease associated with primary lung cancer. The patient can not to be categorised into any of classifications of inflammatory myopathy. With the widespread use of myositis-specific antibodies, the number of cases similar to this case is likely to increase.

P43-17

Association of Soluble Programmed Death-1 with Polymyositis and Dermatomyositis

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Conflict of interest: None

[Objective] Programmed cell death protein 1 (PD-1) are expressed on T follicular helper cells, and play a pivotal role in the pathomechanisms of autoimmune diseases. However, little has been reported on myositis and PD-1. We aimed to investigate the association of soluble PD-1 (sPD-1) with polymyositis (PM) and dermatomyositis (DM). [Methods] We retrospectively measured the serum levels of sPD-1, and interleukin-21 (IL-21) by enzyme-linked immunosorbent assay in patients with PM/DM, systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and healthy controls (HCs). [Results] The serum levels of sPD-1 in PM/DM patients (n = 69) were significantly higher than those in SSc patients and HCs ($p < 0.01$ in both comparisons), but not those in SLE patients ($p = 0.24$). No significant difference was observed between the groups of PM, classic DM, and amyopathic DM, or between PM/DM patients with and without interstitial lung disease. The serum levels of IL-21 in PM/DM patients were significantly higher than those in SLE patients ($p < 0.01$), but not those in SSc patients or HCs. [Conclusions] The present study demonstrated the elevated serum levels of sPD-1 in PM/DM patients and might suggest their pathophysiologic association with PM/DM.

P43-18

Efficacy of hydroxychloroquine for refractory multiple skin ulcers in a case of anti-MDA-5 antibody-positive dermatomyositis

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Conflict of interest: None

Anti-MDA-5 antibody-positive dermatomyositis presents with a variety of skin lesions on the fingers and other multiple organs. Despite the improvement of myopathy and pulmonary disorders of dermatomyositis with administered steroids and immunosuppressive drugs, the skin lesions may be refractory. A 52-year-old Japanese woman was referred to our hospital in November because of malaise, Raynaud's phenomenon, hand swelling, and hand ulceration before two months. There was no muscle weakness, but she had Gottron's papules on her fingers, elbows, and knees. HRCT showed patchy ground-glass opacities in the bilateral lung fields. She was positive for anti-MDA-5 antibody. We diagnosed with dermatomyositis and interstitial lung disease (ILD). Malignancy screening revealed left breast cancer, then fulvestrant was started. Prednisolone (PSL) 40 mg/day and tacrolimus were started. The ILD improved, but the skin lesions worsened and huge ulcers appeared on multiple fingers and footpads and both heels. Three months later, we added hydroxychloroquine (HCQ) 200 mg/day to the prescription. The skin ulcers gradually crusted over and improved, allowing for a further reduction in PSL. HCQ may be considered in case of poor improvement of skin lesions.

P43-19

Clinically amyopathic dermatomyositis that was resistant to triple therapy and tofacitinib, but successfully treated with plasm exchange therapy

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Conflict of interest: None

A 71-year-old male presented with erythema and joint pain one month before admission. He also developed dyspnea. Physical examination showed Heliotrope rash, Gottron's papules, V-neck rash, multiple swollen and tender joints, and fine crackles. Neither muscle pain nor weakness were observed. Although CK didn't increase, ferritin and KL-6 were elevated, and anti-MDA5 antibody was 3490 index. RF, ACPA, and anti-SSA antibody were also positive. CT revealed ground-glass opacity (GGO) in the lower lung lobes. He was diagnosed with CADM and RA. Triple therapy with high-dose glucocorticoid, intravenous cyclophosphamide, and tacrolimus was started. Rashes and arthritis disappeared, but interstitial pneumonia progressed. Tofacitinib (TOF) was added 37 days after admission, but it was ineffective. Thus, plasma exchange (PE) was started, and ferritin and KL-6 decreased quickly and GGO disappeared. After 10 times of PE, remission was maintained. Recently, there are several reports that TOF or PE is effective to resistant CADM. In this case, PE was effective, while TOF was ineffective. Compared to the previous reports, the addition of TOF was later and the titer of anti-MDA5 antibody was higher. This might have affected the responsiveness.

P43-20

Efficacy of rituximab in anti-MDA5 antibody positive dermatomyositis

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Conflict of interest: None

We report three refractory cases of anti-MDA5 antibody positive dermatomyositis (MDA5-DM), in which rituximab (RTX) was useful for remission. [Case 1] A 49-year-old man with MDA5-DM indicated interstitial lung disorder (ILD) and ulcerative eruptions. The exacerbation of ILD and ulcer was demonstrated even in concomitant administration of prednisolone (PSL), calcineurin inhibitor (CNI), and intravenous infusion of cyclophosphamide (IVCY). RTX was additionally administered, resulting in achieving improvement. [Case 2] A 47-year-old man with MDA5-DM was treated with PSL and CNI. IVCY was concomitantly administered because of a progressive ILD; however, it was ceased because of inducing drug eruption as well as its ineffectiveness. RTX was alternatively administered, leading to remission. [Case 3] A 29-year-old woman with MDA5-DM, who simultaneously showed ILD, developed pancytopenia due to macrophage activation syndrome after initiating PSL and CNI. She was additionally treated with IVCY and plasmapheresis, which were ultimately ineffective. RTX was administered, resulting in immediately achieving improvement. [Conclusions] RTX may be a useful remedy in the refractory patients with MDA5-DM.

P43-21

A case of anti-MDA-5 antibody-positive dermatomyositis that developed only with rash and arthritis

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Conflict of interest: None

A 65 year-old woman was referred to our department with a chief complaint of rash and arthritis. There were no myopathies or elevated myogenic enzymes, and no lung lesions were present on chest CT. Since both RF and ACPA were strongly positive, treatment was provisionally started as rheumatoid arthritis. Since there was a possibility of dermatomyositis (DM), tacrolimus was selected as DMARDs, and PSL 10 mg/day was also used in combination. A biopsy was performed on the rash, and the findings were consistent with dermatomyositis. Therefore, anti-MDA-5 antibody was measured. Although the patient was positive for anti-MDA-5 antibody, the rash and arthritis improved rapidly with tacrolimus 2 mg/day and PSL 10 mg/day, so the treatment was continued while confirming that there was no lung lesion by chest CT examination. After that, chest CT showed no lung lesions, the anti-MDA-5 antibody finally became negative. Patients with anti-MDA-5 antibody-positive DM are fatal to rapidly

progressive interstitial pneumonia, so high-dose steroid, cyclophosphamide, and tacrolimus triple therapy is the standard choice. We experienced a case in which tacrolimus and low-dose steroid combination therapy was successful for anti-MDA-5 antibody-positive dermatomyositis in the absence of lung lesions.

P43-22

Two cases of rapidly progressive interstitial lung disease associated with anti-aminoacyl tRNA synthetase antibody

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Conflict of interest: None

Anti-melanoma differentiation-associated gene 5 (MDA5) antibody is related to rapidly progressive ILD (RP-ILD) with poor prognosis, while the presence of anti-aminoacyl tRNA synthetase (ARS) antibody indicates relatively chronic time course. Here, we report two cases of RP-ILD with anti-ARS antibody. A 77-year-old male, without any history of autoimmune disease, and a 71-year-old female, with a history of polymyositis treated with corticosteroid (CS) and methotrexate, presented with dyspnea. They developed severe hypoxemia and chest high-resolution computed tomography showed ground-glass opacity throughout the entire lung field. They had anti-ARS antibody and were diagnosed with RP-ILD associated with myositis. We treated both of them with high dose CS, followed by intravenous cyclophosphamide (IVCY) and oral tacrolimus under ventilator support. They weaned from ventilator on day 36 and day 5 respectively. We successfully treated 2 cases of anti-ARS antibody-related RP-ILD with CS, IVCY and tacrolimus based on the recommended treatment strategy for ILD related to anti-MDA5 antibody. Immunosuppressive therapy combining IVCY and calcineurin inhibitors should be considered for RP-ILD with respiratory failure regardless of the autoantibody status.

P43-23

A case of anti Ku antibody positive polymyositis with concomitant myocarditis induced by pregnancy

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Conflict of interest: None

36-year-old female. elevating muscle enzymes persisted for several days before delivery. There was no muscle weakness, but objective findings showed myopathic changes and findings suspected of myocarditis. The muscle biopsy showed inflammatory cell infiltrates, which were predominantly CD8 T cells in the endomysial area of the skeletal muscles. Myocardial biopsy showed CD8 T cells infiltrates into the myocardium. It was positive for anti Ku antibody. No scleroderma was observed. Therefore, we diagnosed polymyositis (PM) with myocarditis. She was started on steroids. Multiple intravenous immunoglobulin therapy were performed and immunosuppressive agents were added or changed due to treatment resistance. Finally, steroids were discontinued due to uneventful course. The anti Ku antibody was reported as an autoantibody found in cases with scleroderma and PM. Raynaud's phenomenon and interstitial pneumonia have been reported frequently, but none of them were found in this case. Moreover, complications with myocarditis are rare. In addition, most PM during pregnancy have a poor prognosis. However, in this case, she finally achieved discontinuation of steroids. Since the clinical features are not uniform, we report on these findings based on a review of the literature.

P43-24

A case of anti-MDA5 Ab positive DM with rapidly progressive interstitial lung disease just after the delivery and required plasma exchange therapy

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Conflict of interest: None

The patient was 36 years old and May 20XX, she had systemic skin rush complicated with joint pain, swelling and a high fever a week after the delivery. The patient was diagnosed as psoriasis arthritis and treated with 8 mg/w of methotrexate. However, symptoms were getting worse and respiratory symptom appeared. Thus, she was admitted to our hospital at September 20XX. On the admission, the patient had a fever, hypoxia, and skin rash which was compatible with DM, though creatine kinase level was within normal range. Chest CT indicated grand grass opacity expanded to bilateral lung field. the patient was diagnosed as rapidly progressive interstitial lung disease (RP-ILD) complicated with clinically amyopathic DM (CADM) and treated with high dose glucocorticoid. However, disease activity was getting worse and anti-MDA5 antibody (Ab) turned out to be positive. Thus, she was immediately received plasma exchange therapy, together with CI and IVCY therapy followed to methylprednisolone pulse therapy (1,000 mg daily for 3 days). With the intensive treatment, disease activity was getting stabilized. We describe a case of anti-MDA5 antibody positive DM developing RP-ILD just after the delivery and required plasma exchange therapy in addition to intensive treatment.

P43-25

A case in which tofacitinib (TOF) was useful for rapidly progressive interstitial pneumonia (IP) of anti-MDA5 antibody-positive dermatomyositis (DM)

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Conflict of interest: None

[Case] 63 year-old gentleman [Medical history] He had facial erythema, fever and fatigue from several weeks ago. He could not stand up and was referred to our hospital. He had Gottron sign, muscle weakness and elevated creatine phosphokinase. [Clinical course] We diagnosed DM and administered prednisolone 60 mg (1 mg/kg). After that anti-MDA5 antibody test was positive. Chest CT showed no IP. We started a triple therapy of steroid pulse, cyclophosphamide high-dose intravenous injection (IVCY), and tacrolimus. Interstitial shadows of the lungs gradually appeared, we continued IVCY every 2 weeks and performed 3 courses steroid pulse, high-dose intravenous immunoglobulin therapy, and simple plasma exchange. However, because IP progressed gradually, we administered TOF. Since then, his condition improved. [Discussion] It is known that anti-MDA5 antibody-positive DM is frequently associated with IP, and overproduction of multiple cytokines plays an important role of in its development. The prognosis is improving due to multi-target therapy, but the prognosis is still poor. The effectiveness of JAK inhibitors which inhibited multiple cytokines, for anti-MDA5 antibody-positive DM has been reported, and TOF was able to suppress the disease in this case as well.

P43-26

A case report of clinically amyopathic dermatomyositis with progressive interstitial pneumonia treated with nintedanib

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Conflict of interest: None

[Case report] A 31-year-old man. Approximately four years before this presentation, he presented with polyarthralgia and shortness of breath and received a diagnosis of clinically amyopathic dermatomyositis (cADM) based on the presence of interstitial pneumonia, skin eruption and anti-MDA-5 antibody. Although the combination therapy of several immunosuppressants was initiated and continued, his symptoms and results of pulmonary function have been getting worse for the next few years. He had received repeated temporary increase of PSL for worsening dyspnea. Three months before this admission, dyspnea developed again and new ground glass shadow in his chest CT appeared while taking 15 mg per day of PSL. So PSL was increased to 40 mg and nintedanib was administered, together with mycophenolate mofetil. [Clinical significance] cADM is characterized by progressive interstitial pneumonia despite the intensive

treatment of steroids and immunosuppressants. As it has been shown that nintedanib suppresses the progression of interstitial lung disease, it may have an effect on the treatment of cADM. However, it remains unknown which cADM patients should be treated with nintedanib and when it should be started. We discussed the role of nintedanib for the treatment of cADM through our case.

P43-27

A Case of Anti-TIF1-gamma antibody Positive Dermatomyositis Refractory to Intensive Therapies Concurrent with Malignant Lymphoma

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Conflict of interest: None

[Introduction] It is reported that characteristics of inflammatory myopathies differ by types of antibodies. Anti-TIF1γ antibody positive dermatomyositis (DM) is related to dysphagia, severe skin lesion and malignancies. We report a case of anti-TIF1γ antibody-positive DM diagnosed with malignant lymphoma 4 months after from myositis symptom onset. [Case] 52-year-old woman presented with pain and weakness of both thighs and pruritic rash which had persisted for 2 weeks. Laboratory test showed CPK 6000 IU/L and positive anti-TIF1γ antibody. Treatments with glucocorticoid, methotrexate, intravenous immunoglobulin and rituximab were started but not effective and the titer of antibody didn't decrease. After admission, we searched for malignancies and found no evidence of malignancies. Few weeks after, ocular motility disorder and elevation of LDH developed. PET-CT and bone marrow biopsy revealed malignant lymphoma with central nervous system infiltration and the patient was transferred to an another hospital. [Conclusion] It is reported that patients with anti-TIF1γ antibody positive DM have high risk of malignancies including malignant lymphoma. Physicians should search for malignancies aggressively especially in refractory cases.

P43-28

Clinical study of high dose intravenous immunoglobulin (IVIg) therapy for polymyositis in our department

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Conflict of interest: None

[Objective] We examine the clinical efficacy of IVIg therapy in patients with polymyositis (PM) who are refractory to steroid and immunosuppressant treatment. [Material and Methods] We retrospectively analyzed 4 patients from 2017 to 2020 regarding the changes in myogenic enzymes and MMT scores before and after IVIg therapy. [Results] All cases were female and ranged in age from 25 to 74 years (mean 55 years). One of 4 cases was positive for anti-SRP antibody. In the initial treatment, steroids were and immuunosuppressants administered to all patients. At the time of introduction of IVIg therapy (0.4 g / kg / day × 5 days), the average CK valure was 1119 U / l. A decrease in MMT (mean MMT score 81.75) was observed compared to the first diagnosis. The frequency of IVIg administration was 2 to 8 times, and the interval was 4 to 19 months. The decrease in CK value was observed from 1 week after the administration, and remained up to 14 weeks. After the final IVIg, the average min CK value was 600 U / l and the average MMT score was 87.75. Although the CK value did not normalize, maintenance of muscle strength until the next administration were achieved. [Conclusions] Our data indicated repeated administration of IVIg therapy for resistant PM patients ensures muscle strength maintenance.

P43-29

Initial treatment of myositis and dermatomyositis: A single-center study

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Conflict of interest: None

[Objective] The purpose of this study is to clarify the contents and effectiveness of initial treatment of myositis and dermatomyositis (PM/DM). [Methods] Among patients newly diagnosed with PM/DM in our hospital from February 2011 to October 2019, we excluded those with clinically amyopathic dermatomyositis and overlap syndrome. We retrospectively analyzed the electronic health records of 25 patients. [Results] Patients included 6 men and 19 women, with an average age of 57.6 years. Eight patients had PM and 17 had DM. The average CK level before glucocorticoid therapy initiation was 3041.4 U/L, and the average initial dose of prednisolone was 53.2 mg/day. After starting glucocorticoid therapy, many cases demonstrated a maximum reduction in CK levels after a few days by steroid treatment and resting effect, but in more than 70% of cases, a transient increase in CK levels was observed within 1-3 weeks thereafter. Initial doses of glucocorticoid were continued for an average of 23.8 days. [Conclusions] In patients with PM/DM, a significant decrease in CK levels are observed after the start of glucocorticoid therapy, but it does not always continue to decrease thereafter. Thus, it is important not to hesitate to use immunosuppressive drugs in combination with glucocorticoids.

P43-30

Pathogenicity of IgG from patients with anti-MDA5 antibody positive dermatomyositis in rapidly progressive ILD and model mice production

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Conflict of interest: None

[Objective] Anti-MDA5 antibody positive dermatomyositis is poor prognosis disease that frequently presents rapidly progressive interstitial lung disease (ILD). Although anti-MDA5 antibody has been reported that it is related to disease activity, pathogenicity of anti-MDA5 antibody has not been revealed. In this study, we evaluated pathogenicity using plasma of patients and aimed to establish model mice. [Methods] We intravenously injected IgG purified from plasma of patients with anti-MDA5 antibody positive dermatomyositis in rapidly progressive ILD into C57BL/6J and DBA/1J mice. Then we analyzed lung pathology, serological cytokines, and flow cytometry of spleen cells. [Results] Inflammatory cell infiltration and alveolar hemorrhage were confirmed with a certain probability from lung pathology of mice injected IgG from patient serum as compared with IgG from healthy donor. However, there were no significant differences in serum cytokines and flow cytometry of spleen cells. [Conclusions] This result suggested pathogenicity of IgG containing anti-MDA5 antibody, and we report results of comparative studies to improve reproducibility of model mice production.

P43-31

Examination of clininal features of 4 cases of anti-TIF1-gamma antibody positive dermyositis in our hospital

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Conflict of interest: None

[Objective] In Japan, anti-TIF1-γ antibody is positive in about 17% of adult dermatomyositis (DM), of which the malignant tumor complication rate is very high at about 65%. In this study, we examined the clinical features of anti-TIF1-γ antibody positive DM patients in our hospital.

[Methods] We examined four patients with anti-TIF1-γ antibody positive DM who were hospitalized from May 2018 to December 2019. [Results] (1) A 51-year-old woman. She noticed erythema on her body, and an angiomyolipoma was observed in the kidney. (2) A 72-year-old woman. She had been aware of erythema on her body, and weakness in extremities, nodular goiter had been pointed out. It was large enough to cause tracheal deviation, and a thyroidectomy was performed. (3) A 58-year-old woman. She noticed erythema and limb myalgia. A right parotid gland mass was found, suspected to be pleomorphic adenoma. (4) A 77-year-old woman. She noticed erythema all over her body. Advanced gastric cancer was observed, and chemotherapy for the cancer was started. [Conclusions] 3 of the 4 cases were benign tumors and 1 case was malignant. All cases were examined for skin symptoms, and tumors were found by general screening tests. Careful tumor search is essential when diagnosing of this disease.

P43-32

A case of successful multidisciplinary treatment including plasma exchange therapy for rapidly progressive dermatomyositis-related interstitial pneumonia (anti-PL-7 antibody positive)

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Conflict of interest: None

The case was a 71-year-old man. Since May 2020, he became aware of low-grade fever and dyspnea during exertion, and was treated with antibiotics at the diagnosis of bacterial pneumonia at a previous hospital, but he was referred to our hospital without improvement. Based on the rapidly progressing interstitial pneumonia, erythema, and anti-ARS antibody positivity (later found to be anti-PL-7 antibody), the patient was diagnosed with dermatomyositis associated with interstitial pneumonia and treatment was started. From the 1st day of illness, steroid pulse, cyclophosphamide, cyclosporine and blood purification therapy were used in combination to induce remission. The patient gradually improved and was discharged on the 78th day of illness. In recent years, dermatomyositis has been known to exhibit a characteristic clinical picture for each antibody, and attention has been focused on the high rate of rapidly progressive interstitial pneumonia, especially in anti-MDA5 antibody-positive cases. On the other hand, there are some reports suggesting that the prognosis may be poor even in anti-PL-7 antibody-positive cases. Bibliographic reports suggesting the usefulness of plasma exchange for this disease are being accumulated, and we will report them after summarizing them.

P43-33

A case of drug refractory dermatomyositis with dysphagia improved by rehabilitation

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Conflict of interest: None

Case: A 22-year-old female came to previous hospital, complaining of proximal muscle weakness and skin rash on her face and knuckles. The patient was diagnosed as dermatomyositis due to an increase of creatine kinase and erythrocyte sedimentation. Treatment with oral prednisolone improved her symptoms, she was discharged on Day 14. But during tapering prednisolone, she complained a sudden inability to swallow solid foods and liquids. The patient showed saliva retention on pharynx, in spite of her proximal muscle power was improving. Treatment with intravenous immunoglobulins, intravenous methylprednisolone and intravenous cyclophosphamide was applied but her symptoms did not improve. She transferred to our hospital on Day 68 to strengthen dysphasia rehabilitation. A video fluoroscopic swallowing study revealed inadequate pharyngeal contraction, but no silent aspiration. She started eating liquid food on Day 76, and on Day 105, she was discharged as she could eat bite sized solid food. Clinical significance: This case showed the importance of rehabilitation for drug refractory dermatomyositis with dysphasia.

P43-34

A case in which tofacitinib was introduced for anti-MDA5 antibody-positive dermatomyositis-related interstitial pneumonia and was discontinued after remission

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Conflict of interest: None

[Chief complaint] Dyspnea, rash, arthralgia. [Clinical history] The case was a 45-year-old woman. She was aware of a rash on her trunk, limbs, and fingers and difficulty breathing, and was introduced our department. [Course] Muscle weakness, elevated CK, elevated CRP, arthralgia, and Gottron's sign were observed, and CT showed interstitial shadow. We diagnosed her as Dermatomyositis-related interstitial pneumonia. She had also hemophagocytic syndrome, and anti-MDA5 antibody was positive, we started steroid pulse therapy, calcineurin inhibitors, and intravenous cyclophosphamide therapy. Although we started plasma exchange on the 3rd day, new interstitial shadows were observed on day 7th day, so we started Tofacitinib (TOF). CT on the 21st day confirmed improvement of lung shadow, so we started steroid tapering. Interstitial pneumonia (IP) gradually improved, and she was discharged on the 83rd day. Two months later, she developed a subcutaneous abscess. Although we stopped TOF, IP has not recurred. [Discussion] We performed multidisciplinary treatment for the anti-MDA5-positive patient, but the progression of IP could not be suppressed. The use of JAK inhibitors was able to suppress the progression, and we were able to stop the JAK inhibitors. This is reported with literature review.

P43-35

A case of anti-MDA-5 dermatomyositis associated with hoarseness and inflammatory edema of the vocal cords that improves with immunosuppressive therapy

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Conflict of interest: None

[Background] While anti-MDA-5 dermatomyositis causes more oral ulcers than anti-MDA-5 dermatomyositis, reports mucosal lesions other than the oral mucosa are few. We present a case of anti-MDA-5 dermatomyositis associated with inflammatory edema of the vocal cords that improved with immunosuppressive therapy. [Case] The patient was a 41-year-old woman with a non-specific medical history who presented with a dry cough for 3 months; erythema of the face, shoulders, and back for 2 months; and sore throat and hoarseness for 1 month. Physical examination revealed an oral mucosal rash, an inverse Gottron papule, purpura with ulcers on the shoulders, and nailfold bleeding, with no evidence of muscle weakness. Laryngoscopy revealed hoarseness associated with inflammatory edema of the vocal cords. A diagnosis of anti-MDA-5 dermatomyositis was made, and a combination of steroids, tacrolimus, and cyclophosphamide was given. She responded well to immunosuppressive therapy, and the MDA-5 antibody titer decreased from 2300 to 50 within 4 months of treatment. Her laryngeal findings, sore throat, and hoarseness improved 5 months after treatment. [Conclusion] Inflammatory edema of the vocal cords was thought to be caused by anti-MDA-5 dermatomyositis, as it improved with the course of treatment.

P43-36

A case of anti-MDA5 antibody-positive dermatomyositis with consciousness disorder

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Naha City Hospital

Conflict of interest: None

[Case] 63 year-old gentleman [Chief complaint] facial erythema and

fever [Medical history] He had facial erythema, fever and fatigue from several weeks ago. He could not stand up and was referred to our hospital. He had Gottron sing, muscle weakness and elevated creatine phosphokinase. He was hospitalized on suspicion of dermatomyositis. After admission, he had consciousness disorder such as couldn't do easy calculations and tell the time. No abnormalities were found on head MRI or cerebrospinal fluid examination. We diagnosed dermatomyositis and administered prednisolone 60 mg (1 mg/kg). After that anti-MDA5 antibody test was positive. Chest CT showed no interstitial pneumonia. We started a triple therapy of steroid pulse, cyclophosphamide high-dose intravenous injection, and tacrolimus. One week after the start of treatment, his consciousness disorder gradually improved. [Discussion] SLE and Sjogren's syndrome are well-known rheumatic diseases accompanied with consciousness disorder, but rarely in dermatomyositis. In this case, consciousness disorder was observed before the start of steroids and improve after treatment. His manifestations were not steroid psychosis. We report our experience of dermatomyositis with consciousness disorder, along with some literature review.

P43-37

A case of Dermatomyositis After 30 Years in Remission Following Polymyositis

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Conflict of interest: None

[Case] 79 years, Female [Chief complaint] Erythema, malaise [Current medical history] At the age 42, she was diagnosed with polymyositis and got remission by steroid treatment. Then the age of 61, she was diagnosed with granulosa cell carcinoma of the ovary and had a resection. Then she had histories of re-surgery and chemotherapy for recurrence. 3 months prior to her admission, CT scan showed a suspicion of recurrence. 1 month prior to her admission, she had skin rashes. After 2 weeks, she was diagnosed impairment of liver disfunction, so she was referred to our hospital. She was admitted to the hospital because of the heliotrope rash, and CK 9840 mg/dL, which indicated dermatomyositis. Positive for anti-Tif1-γ antibody; no ILD was found on CT. Steroid treatment was started after the muscle biopsy. Biopsy pathology showed the expression of MxA specific for dermatomyositis on immunostaining. [Discussion] Comparison of the pathological findings showed that there were more CD8+ T lymphocytes in polymyositis and more CD4+ T lymphocytes in dermatomyositis. On the other hand, due to the similarity of therapeutic response, it has been suggested that those represent a spectrum of inflammatory myositis. We report here a case of dermatomyositis after 30 years of remission of polymyositis.

P43-38

A case of anti-SRP antibody positive inflammatory muscle disease with pericardial effusion

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Conflict of interest: None

A 71-year-old female was referred and admitted to our department due to myalgia and muscle fatigue in the proximal muscles, dysphagia, a high serum CK level (1,885 mg/dL), and high-intensity areas in the proximal muscles including the right deltoid muscle of MRI STIR images. On admission, the manual muscle test showed muscle weakness (4/4) in the proximal muscles, and electromyography revealed myogenic changes. She also had pleural and pericardial effusions, hypoxemia, and bilateral leg edema, which we considered to be due to the right cardiac failure by pericardial effusion. We diagnosed her with polymyositis and started oral prednisolone at a dose of 1 mg/kg/day. Her muscle symptoms and serum CK level improved rapidly by glucocorticoid therapy and discharged on day 57. Although the glucocorticoid therapy combined with tacrolimus improved the symptoms of right cardiac failure, the pericardial effusion remained until discharge. Only the anti-SRP antibody was seropositive by a screening of myositis-associated autoantibodies. This is a rare case of anti-SRP antibody-positive inflammatory muscle disease with pericardial effusion.

P43-39

Plasma exchange as a treatment for anti-MDA-5 antibody positive dermatomyositis

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Himeji Red Cross Hospital

Conflict of interest: None

Case: A 40-year-old woman complained hand, elbow and knee arthralgias for four months. She also presented heliotrope rash and Gottron's sign. She became bedridden one month before and she referred to our hospital. We diagnosed her with dermatomyositis because of muscle weakness, myalgia, elevated CRP and CK. Chest CT showed an NSIP pattern of interstitial pneumonia. We administered prednisolone 60 mg/day and tacrolimus 4 mg/day. We performed cyclophosphamide pulse therapy because of anti-MDA-5 antibody positivity. After that, myogenic enzymes decreased relatively early. However, serum ferritin and anti-MDA-5 antibody titer were still high. We performed plasma exchanges for 7 times from day 38. Her serum ferritin and anti-MDA-5 antibody titer decreased sharply and she didn't experience any flares. She was discharged to a rehabilitation facility on day 110. Discussion: Many patients with anti-MDA-5 antibody-positive dermatomyositis have a poor prognosis due to rapidly progressive interstitial pneumonia, and intensive immunosuppressive therapies such as triple therapy have been proposed. However, it is difficult to say that standard treatment has been established. There are several reports on the effectiveness of plasmapheresis, and we report this with a review of the literature.

P43-40

Refractory case of interstitial pneumonia with dermatomyositis associated with double cancer

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Conflict of interest: None

[Case] A 77-year-old man visited to hospital with facial erythema and lower muscle weakness. He was diagnosed with dermatomyositis by interstitial pneumonia, elevation of creatine kinase level, and MRI findings. Myositis specific antibodies were not detected. He was suspected with cholangiocarcinoma, but treatment with high dose glucocorticoid had to be done because of progressive hypoxemia. Methylprednisolone pulse, high-dose prednisolone (60 mg/day), intravenous gamma globulin and intermittent high-dose intravenous cyclophosphamide therapy (IVCY) was not effective, Calcineurin inhibitor could not be taken orally due to cough. Two times methylprednisolone pulse and IVCY were not effect, too. After 50 days hospitalization, he died due to respiratory failure. Pathological autopsy revealed diffuse alveolar damage and Intrabile duct Cholangiocarcinoma with infiltration into extrabile duct adipose tissue and metastasis to nearby lymph nodes, and prostate cancer. [Clinical significance] Dermatomyositis is often associated with malignancy, but cholangiocarcinoma is rarely reported. This case was negative for myositis-related antibody and refractory to treatment. We must be considered to early surgical treatment when paraneoplastic syndrome is suspected.

P43-41

Case of oral ulcer as an initial symptom of anti-MDA5 dermatomyositis with rapidly progressive interstitial pneumonia

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Conflict of interest: None

Skin ulcer is associated to high Anti-MDA5 antibody titer and poor prognostic factor of interstitial pneumonia (IP) among Anti-MDA5 dermatomyositis patients. However, few cases of oral ulcer as the initial symptom were reported and we present such case with rapidly progressive IP. 63-year-old women with no significant medical history presented to our hospital with 5 days of gingivalgia around the left lower jaw, chilalgia and sore throat. Gottron's sign, Koebner's phenomenon, mechanic's hand, inverse Gottron's sign as well as aphthous stomatitis on apex and lateral edge of the tongue were see at initial examination. No weakness of the extremities was seen. Chest CT showed non-segmental ground glass opacities localized on subpleural of bilateral basal lung. Blood test revealed of CK 18 U/L, ferritin 526 n/mL, and Anti-MDA5 antibody above 500 U/ml. Pulse steroid therapy, intravenous cyclophosphamide and tacrolimus were started initially with no response and repetition of pulse steroid therapy, Tofacitinib, Rituximab therapy were effective to IP. Now this patient is frequently suffering from opportunistic infection. We discuss with literature that oral ulcer might be equivalent clinical importance to skin ulcer as a poor prognostic factor of IP.

P43-43

A case of anti-PL-7 antibody positive dermatomyositis accompanied by hypophysitis, lacrimal gland swelling, and hypertrophic pachymeningitis

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Conflict of interest: None

A 49-year-old woman was diagnosed as dermatomyositis (DM) because of fever, arthralgia, typical DM rash, creatine kinase elevation and muscle weakness 15 years ago, and treated by 20 mg/day of prednisolone (PSL). At August X (the onset year)-2, she was admitted to our Hospital because of arthralgia exacerbation and sclerodactyly despite of 10 mg/day of PSL. Diagnosis of DM / systemic sclerosis (SSc) overlap syndrome was made and 6 mg/week of methotrexate (MTX) was initiated with improvement of arthralgia. In August X, she noticed headache, dizziness, polyuria, eyelid edema, and left eye abduction disorder and re-admitted. Contrast-enhanced MRI revealed thick tentorium cerebelli and swelling of enhanced right lacrimal gland and pituitary gland. She had hyponatremia with intact pituitary hormone levels. Lacrimal gland biopsy showed neither infiltration of IgG4-posirive cells nor obvious malignancy. We diagnosed as hypophysitis associated with autoimmune disorder and started 50 mg/day of PSL. As for hyponatremia, diagnosis of central diabetes insipidus was made based on saline load test. Her symptoms were improved with PSL and vasopressin nasal spray along with the disappearance of the abnormality findings of MRI. This case was very rare case of DM accompanied by hypophysitis.

P43-44

Dramatic efficacy of high-dose intravenous gammaglobulin therapy in a patient with steroid-resistant polymyositis

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Conflict of interest: None

[Case] A 78-year-old man developed muscular pain that gradually worsened from March 202X. He had a blood test and had elevated CK. He was referred to our department for further examination and treatment. Laboratory studies revealed CK level of 4841 U /l, CRP level of 0.48 mg/dl, positive anti-SRP antibody, and positive anti-OJ antibody. MRI revealed T2 high signal on STIR at thigh muscles on both sides. Thigh muscle biopsy showed infiltration of inflammatory cells in the endomysium. Oral administration of PSL 60 mg and TAC 2 mg was started, but muscular pain and CK did not improve. Steroid pulse therapy (mPSL 1000 mg/day, 3 days) was also ineffective. After that, high-dose gamma globulin therapy (IVIG 25 g/day, 5 days) was performed, and the muscular pain improved dramatically, and elevated level of CK (6420 U/L) decreased to 3449 U/L. Afterwards, after the treatment of cyclophosphamide pulse therapy (IVCY 500 mg/every 2 weeks, 3 times), CK normalized and the patient was discharged with PSL 12.5 mg and TAC 3 mg. Currently, he is fine with PSL 9 mg and TAC 3 mg. [Consideration] We report successful treatment of high-dose intravenous gammaglobulin therapy in a patient with steroid-resistant polymyositis. Moreover, I would like to review the effectiveness of IVIG for polymyositis from the literature.

P44-1

A case of Takayasu arteritis complicated with pulmonary infarction

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Conflict of interest: None

A 48-year-old woman had a cough from October X-1. In February X, she had a fever. Chest CT showed a consolidation in the left lower lobe. Antibiotics did not improve her symptoms. There were no specific findings in the bronchoscopic cytology and bacteriological examination. In April X, she visited our hospital. Contrast-enhanced CT revealed thickening of arterial wall and stenosis of the pulmonary artery in the left lower lobe and indicated pulmonary infarction. In PET-CT, FDG accumulation was observed in the left subclavian artery, left pulmonary artery, and aorta. Finally, she was diagnosed with Takayasu arteritis (TA). Prednisolone (PSL) 1 mg/kg was started and her symptoms disappeared. At one month after treatment, the thickening of arterial wall in the left subclavian artery and pulmonary artery improved and the pulmonary infarction lesion tended to become smaller. Pulmonary infarction is reported to cause in 2% of TA with pulmonary artery involvement. In our hospital, two of 101 patients with TA had pulmonary infarction during the past five years. Although the frequency of pulmonary infarction with TA is very low, it is important to distinguish TA as the cause of pulmonary infarction because it causes an irreversible arterial stenosis if left untreated.

P44-2

Bilateral femoral nerve palsy (FNP): a rare complication of Takayasu arteritis (TA) mimicking adult-onset Still's disease (AOSD)

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Conflict of interest: None

A 44-year-old woman was admitted to our hospital because of fever, sore throat, rash and arthritis. 22 days before admission, rash on the left forearm developed. 6 days later, she began to have a fever, sore throat and arthritis. On examination, the temperature was 39.0°C and erythematous lesions were seen throughout her body. Laboratory test results were notable for an elevated WBC count, AST, ALT and ferritin. Blood tests for RF, ACPA and ANCA were reportedly negative. A CT scan showed systemic lymphadenopathy, and fat stranding around bilateral femoral arteries. AOSD and TA were suspected, and a skin biopsy showed no finding of vasculitis. The diagnosis of AOSD was established, and steroids and tocilizumab were administered, which worked. After discharge, weakness of

bilateral thighs progressed, and livedo reticularis appeared on her lower legs. Bilateral FNP due to invasion of inflammation from the vasculitis was suspected. The diagnosis was reviewed and changed into TA. We experienced a case of bilateral FNP due to TA mimicking AOSD. It was difficult to distinguish TA from AOSD at the time of onset, but findings of vasculitis became apparent during the treatment. FNP due to direct inflammatory invasion from TA has not been reported and is considered to be a rare case.

P44-3

Reversible improvement of arterial stenosis and wall thickness in aortitis by the early combination therapy of tocilizumab

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Conflict of interest: None

[Case] A 39-year old female who had a bruit in the cervical artery visited our hospital in 2019. Her blood examination was CRP 0.48 mg/dL, blood sedimentation (60 min) 35 mm. Her carotid artery showed 40% over rate vascular stenosis (wall thickness: 2.3 mm) on echo examination. Ascending aorta, aortic arch, brachiocephalic artery, subclavian artery, and carotid artery showed stenosis and vascular thickness on CT scan. She was diagnosed aortitis (type II a). PET/CT showed a high accumulation at the artery, and we considered active vasculitis. We started the treatment by 30 mg/day of prednisolone (PSL). The dose was gradually reduced to 20 mg/day in 4 weeks, and started the combined therapy of tocilizumab (TCZ 162 mg s.c. /week). Carotid echo examination was followed after 3, 6, 12 months. Carotid artery stenosis and wall thickness were improving gradually (wall thickness 1.0 mm). PET/CT showed a marked less accumulation in the blood vessels after 10 months. CT scan showed the improvement of aortic stenosis and wall thickness after 12 months. Carotid bruit was also improving gradually. [Discussion] To the best of our knowledge, there are few reports that artery stenosis and vascular thickness were improved reversibly by the early combination therapy of tocilizumab.

P44-4

Successful bronchial artery embolization in a case of Takayasu arteritis with hemoptysis

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Conflict of interest: None

[Case] A 60-year-old woman was admitted to our hospital because of sudden onset of cough, hemoptysis, and dyspnea. She had been diagnosed with Takayasu arteritis (TAK) 6 years earlier. Two years before this admission, valve replacement surgery had been performed for aortic and mitral valve insufficiency and warfarin therapy had been initiated. TAK had been stable on tocilizumab alone. Chest CT revealed widespread bilateral pulmonary infiltration and a suspected blood clot in the right main bronchus. She was conservatively treated with hemostatic agents. Chest CT performed 5 days later showed improvement of infiltration especially on the left lung and the mildly dilated right bronchial artery. Thus, airway bleeding from the right bronchial artery was suspected. Angiography showed abnormal poolings of the contrast medium in the right bronchial and intercostal arteries, and transcatheter embolization was performed in both arteries. [Clinical significance] Hemoptysis is a complication in TAK. It can be due to abnormal anastomoses caused by inflammation between e.g. bronchial and pulmonary arteries. Transcatheter embolization was effective in controlling the bleeding. Being also relatively less invasive, it can be recommended as a treatment of choice in such cases.

P45-1

Giant cell arteritis involving posterior auricular artery

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Conflict of interest: None

A 69-year-old woman presented to our department with bilateral scleritis. She had left posterior auricular, both shoulder and jaw pain 8 months earlier. Ultrasonography showed wall thickening of her left posterior auricular artery, and tenosynovitis of her both long head of biceps. Contrast-enhanced computed tomography (CT) and T2-weighted magnetic resonance imaging also indicated wall thickening of her left posterior auricular artery. ^{18}F-fluorodeoxyglucose uptake was increased in the wall of brachiocephalic artery with positron emission tomography combined with CT. She was diagnosed with giant cell arteritis (GCA) and polymyalgia rheumatica, and oral prednisolone 50 mg per day swiftly improved her symptoms. Posterior auricular artery is branched from the external carotid artery, and anastomose with branches of the superficial temporal artery. GCA can affect posterior auricular artery, and posterior auricular pain may be a clinical clue for early diagnosing GCA.

P45-2

Giant cell arthritis involving symptomatic lower leg vasculitis demonstrated by Fluorodeoxyglucose positron emission tomography computed tomography scan

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Conflict of interest: Yes

[Case] A 79-year-old woman was admitted to our hospital with a three-month history of worsening lower leg pain and intermittent claudication. Her laboratory revealed CRP 10.42 mg/dL, ESR 84 mm/h and negative results for ANCA. PET-CT showed FDG accumulation in vascular walls of aorta, bilateralcommon cervical, external cervical, vertebral, subclavian, axillary, common illiac, deep femoral, superficial femoral, popliteal, anterior tibial, posterior tibial arteries and right temporal artery. According to the positive results of the left temporal artery biopsy, she was diagnosed with giant cell arteritis (GCA), and started on prednisolone 45 mg/day. Her symtoms improved rapidly, and 2 months after PET-CT showed a decreased FDG accumulation in vascular walls. [Discussion] Vascular involvement in lower leg is not usually concerned, however symptomatic lower extremity vasculitis of GCA have been reported to be ranging from 0.003 to 0.18% (Medicine (Baltimore) 2011;90:40-51, J Rheumatol 2009;36:2277-83). In our case, PET-CT demonstrated the involvement of lower leg vasculitis. Some cases may require additional immunosuppressant drugs, endovascular treatment or amputation. [Conclusion] We report this case to emphasize the importance of lower leg involvement in GCA.

P45-3

Analysis of four cases of Giant cell arteritis

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Conflict of interest: None

[Objective] In order to clarify the interrelationship between clinical features and images of ultrasound and PET-CT [Methods] Four cases of GCA which satisfy the classification criteria recommended from American College of Rheumatology (1990) were recruited. [Results] The average age of the four cases was 79.75 years old (74 to 83 years old). The chief complaints with headache were head tumor palpation, loss of appetite, malaise, and uncomfortable of the face. Mean body temperature was 37.2 degrees (37 to 37.6 degrees). Complicated polymyalgia rheumatica were 2 cases. Ultrasound at temporal artery showed wall thickening in all cases. Accumulations of PET-CT not only in the temporal artery but also in the aortic arch and other sites were observed. Oral prednisolone followed by

three days intravenous methylprednisolone administration in 3 cases and oral prednisolone in 1 case were treated, respectively. Tocilizumab injections with prednisolone were introduced in 2 cases who were complicated with arteritis progression to the aortic arch and with MDS. [Conclusions] Ultrasound imaging was less invasive and useful for a screening test. PET-CT is considered to be useful for clearing interrelationship between prednisolone responsiveness and invasion of arteritis in patients with GCA.

P45-4

A case in which vascular ultrasound and MRA were negative, with abnormal uptake in the temporal artery on FDG-PET CT, and with a diagnosis of cranial giant cell arteritis

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Conflict of interest: None

A 84-year old male patient presented with head and neck pain persisted for 6 months and jaw claudication and pain in both upper and both lower extremities without fever. The temporal artery showed no swelling or tenderness. Laboratory tests showed the following results: CRP 6.0 md/dl and ESR ≧120 mm/h. Rheumatoid factor and anti-cyclic citrullinated peptide antibody were negative. No abnormal findings were found on head MRI, MRA, or temporal artery ultrasonography. He was diagnosed with polymyalgia rheumatica (PMR). Oral prednisolone (PSL) 20 mg/day was started to treat the PMR. However, FDG-PET showed inflammation in the temporal arteries on (SUVmax 2.2), the right sternoclavicular joint, right wrist joint, right shoulder joint, both hip joints, cervical spine and lumbar spine. No inflammation was observed in large blood vessels other than the temporal arteries. He was diagnosed with giant cell arteritis (GCA). There were no findings of malignant disease. A temporal artery biopsy confirmed the diagnosis for GCA. [Discussion] This case is a case of GCA in which FDG-PET was useful for diagnosis of GCA. There are few cases that FDG-PET showed inflammation in the temporal arteries; the usefulness of FDG-PET in the diagnosis of GCA is investigated.

P45-5

3 cases of glucocorticoid-resistant giant cell arteries over 80 years old improved with tocilizumab, leading to discontinue glucocorticoid

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Conflict of interest: None

Case 1. A 79-year-old woman was diagnosed with giant cell arteritis (GCA) and treated with prednisolone (PSL). GCA repeated to relapse with additional immunosuppressants after tapering PSL. But adding tocilizumab (TCZ) improved GCA at 87, leading to discontinuing PSL. Case 2. An 84-year-old woman was diagnosed with polymyalgia rheumatica and improved with PSL. Reducing PSL caused fever and joint pain. GCA was diagnosed by an increased vessel wall thickness of the carotid and the axillary artery in vascular ultrasound. GCA improved with PSL 40 mg/day but relapsed again by tapering PSL. Additional TCZ improved GCA and discontinued PSL. Case 3. An 83-year-old woman was diagnosed with cryptogenic organizing pneumonia and improved with PSL. Reducing PSL caused fever, headache at 87. PET/CT showed the intense FDG uptake in the bilateral subclavian and the femoral artery. GCA was diagnosed by a superficial temporal artery biopsy and improved with PSL 30 mg/day. Additional TCZ discontinued PSL. In all cases, PSL was discontinued within 1 year after adding TCZ without any serious adverse events. TCZ could be one of the treatment options for people over 80 years with glucocorticoid-resistant GCA because TCZ could reduce and discontinue PSL, safely and quickly. No conflict of interest.

P45-6

Successful tocilizumab treatment for giant cell arteritis complicated with hypertrophic pachymeningitis

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Conflict of interest: None

Case: A 88-year-old man was diagnosed with polymyalgia rheumatica 12 years ago. He was treated with prednisolone (PSL) 10 mg/day. His symptoms improved, PSL dose was tapered to 4 mg/day. He was admitted to our hospital with fever, headache, and loss of appetite. On clinical examination, he suffered from right temporal headache and fever. Ultrasound findings revealed halo sign and compression sign positive. Enhanced Brain MRI revealed partially thickened of the dura mater with enhancement. He was diagnosed with giant cell arteritis complicated with hypertrophic pachymeningitis, then he was treated with PSL 30 mg/day. However, his clinical symptoms were not improved, then he was treated with tocilizumab (TCZ). After treated with TCZ, his symptoms were improved, and ultrasound and MRI findings were improved. Clinical significance: There is rarely reported that TCZ was effective for both clinical conditions, and we report that it has clinical significance.

P45-7

A case of giant cell arteritis with a huge dissecting aortic aneurysm

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Conflict of interest: None

[Case] A 78-year-old female. X-18 years ago, she pointed out a thoracic aortic aneurysm. The aortic aneurysm continued to increase. She had a fever from January X year. In mid-June X year, she consulted a previous doctor with a fever of 38°C and cough. Although the heat source was not clear, CRP had risen to 17 mg/dL. She was hospitalized in the same hospital. She was referred to the Department of Rheumatology and was suspected of having giant cell arteritis (GCA) for having mild headache and right jaw claudication. She was transferred to our hospital in early July X year. A temporal artery biopsy was performed, and granulomatosis vasculitis with giant cells was found. FDG-PET/CT showed a high degree of FDG accumulation in the thoracoabdominal aorta including the aortic aneurysm, bilateral common carotid arteries, subclavian arteries, and common iliac arteries. She was diagnosed with GCA and started taking PSL 30 mg/day. She was discharged in early August X year, as her fever, headache, and jaw claudication disappeared and CRP decreased. [Clinical significance] A case of GCA with a huge dissecting aortic aneurysm and high accumulation of FDG-PET/CT in the aortic aneurysm. We report with some literature review.

P46-1

A case of breast cancer patient who developed large vessel vasculitis after administration of Pegfilgrastim

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Conflict of interest: None

The patient was a 61-year-old woman with breast cancer. Hormone therapy after mastectomy was started at the age of 45. Three years before admission, metastatic lesions were found and chemotherapy was started. Five months before admission, because of an increase in metastatic lesions, another chemotherapy was started and filgrastim was used for neutropenia. After the second course of chemotherapy, 8 days ago, pegfilgrastim was used for preventing neutropenia. And she admitted to the hospital with a 1 week history of fever and general malaise. Laboratory studies revealed CRP of 33 mg / dl. CT scan showed a new thickening of the descending aorta, and FDG-PET scan showed FDG accumulation at the same site. Pegfilgrastim-associated aortitis was considered and was followed up without treatment, then symptoms were disappeared and the CRP was decreased to normal. [Discussion] In the classification of CHCC

2012, ANCA-related vasculitis and immune complex-deposited small vessel vasculitis are presented as representatives of drug-induced vasculitis. However, in G-CSF associated vasculitis, many case reports of large vessel vasculitis have existed. Since the chances of using G-CSF will not decrease, we would like to deepen our understanding of this side effect while presenting this case.

P46-2

A case report of localized vasculitis in the lower limbs found to be refractory to catheterization

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Conflict of interest: None

[Intro] Vasculitis is often detected by fever, pulmonary hemorrhage, renal damage, and skin symptoms. However, we here report a case of vasculitis diagnosed in the absence of any symptoms of these, but with the difficulty of catheterization. [Case] The patient was a 69-year-old man. He was a non-smoker and had no history. He suffered from 1-year intermittent claudication and numbness of lower limbs. Since he was diagnosed as peripheral artery disease (PAD) by contrast induced CT, he was referred to the department of the radiology in our hospital. He was performed endovascular treatment (EVT), but he developed multiple thrombi during EVT, which made it difficulty. Both lower limbs became worse again, he was referred to our department due to PAD refractory to EVT. Since there were no coagulopathies or malignant diseases that could cause thrombosis, we suspected he had vasculitis and performed a PET-CT, which showed accumulation along the artery in the lower limbs. This led to the diagnosis of localized large vasculitis, which was confirmed by intravascular ultrasound. After treatment with corticosteroid and tocilizumab, the accumulation in the artery on PET had disappeared. [Conclusions] Vasculitis should be considered in cases of PAD where EVT is difficult due to multiple thrombi.

P46-3

G-CSF-induced vasculitis with cytotoxic agent chemotherapy for castration-resistant prostate cancer

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Conflict of interest: None

[Case] A 72-year old man was treated with docetaxel for castration-resistant prostate cancer. 8 days after administration of docetaxel, He showed neutropenia and G-CSF (Pegfilgrastim) had been administered for febrile neutropenia. He shows a fever and high C-reactive protein (CRP) on the 16th day. Contrast-enhanced CT scan showed fat stranding, edema in upper mediastinum and minimal amounts of left side pleural fluid, which led to suspicion of mediastinitis and treatment with antibiotics. In second course of docetaxel, G-CSF was again given to him prophylactically on the 2nd day. He complains of a slight fever and epigastrium pain on the 10th day. CT scan revealed thickening of the wall surrounding by thoracoabdomina junction aotra. He began prednisolone (PSL) 60 mg/day as a diagnostic treatment for major vasculitis. His fever and the CRP levels decreased rapidly next day. CT scan showed that the thickening of the wall improved in 2 week. The dose of PSL is now tapered down to 5 mg/day and continues with hormone therapy. [Discussion] Little has been reported on G-CSF-induced vasculitis, which is rarely. This desease often occurs around one week after the first G-CSF administration and generally has good response to PSL. We report a case with a review of the literature.

P46-4

Three cases of temporal arteritis with positive MPO-ANCA

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Conflict of interest: None

In rare instances, patients with temporal arteritis (TA) test positive for ANCA. We have experienced 3 cases of MPO-ANCA posive TA. We report the cases with literature review. Case 1. An 84 y.o. male with a fever of unknown origin (FUO), morning stiffness, jaw claudication, and positive MPO-ANCA underwent right temporal artery biopsy. The biopsy showed TA. He had no signs of SVV, and was diagnosed as GCA. He received 30 mg of prednisolone (PSL) and achieved remission. Though ANCA remained elevated, he did not develop SVV. Case 2. A 78 y.o. male with FUO, polyarthralgia, an induration with tenderness in left temoral area, and positive MPO-ANCA underwent left temporal artery biopsy. The biopsy showed TA. He had no signs of SVV, and he was diagnosed as GCA. He received 50 mg PSL, and achieved a remission. Case 3. A 68 y.o. female with FUO, neuropathy, and glomerulonephritis, and positive MPO-ANCA under went temporal artery biopsy, because she had temporal headache and tenderness on the temporal artery. Biopsy showed arteritis in a small artery. Based on the presence of neuritis, glomerulonephritis, and positive MPO-ANCA, she was diagnosed as microscopic polyangitiis, with temporal arteritis. She received 60 mg of PSL and intravenous cyclophosphamide (IVCY). Her condition improved.

P46-5

A case of GCS-F-induced large-vessel vasculitis

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Conflict of interest: None

(Case) 80-year-old Japanese man (Chief complaint) Fever (Present illness) A 80-year-old patient presented with a history of myelodysplastic syndromes and was observed without treatment. The patient presented with fever 2 days before and chest computed tomography (CT) revealed consolidation and ground glass opacity at the left lower lobe of lung. He was suspected of bacterial pneumonia and was treated with intravenous antibiotics. After admission granulocyte-colony stimulating factor (G-CSF) was administered due to leukopenia. Because fever continued for 2 weeks after initiating treatment, whole trunk contrast-enhanced CT was performed and revealed a newly established thickening of the brachiocephalic artery, left subclavian artery, and superior mesenteric artery. He was referred for evaluation of large-vessel vasculitis by rheumatologist. (Clinical course) The clinical examination revealed no abnormalities other than fever. Considering GCS-F-induced large-vessel vasculitis, we only stopped G-CSF and did not initiate glucocorticoid or immunosuppressants. His fever was subsided and CRP decreased from 8.86 mg/dl to 0.06 mg/dl three months after discontinuation of G-CSF. (Summary) We report a case of GCS-F-induced large-vessel vasculitis with some literature review.

P46-6

A case of aortitis that rapidly developed after administration of G-CSF

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Conflict of interest: None

A 58-year-old woman with cervical cancer which had been treated with docetaxel and carboplatin presented with fever 5 days prior to admission. PEG-G-CSF (polyethylen glycol-granulocyte-colony stimulating factor) was administered for the prevention of febrile neutropenia 8 days prior to admission. On admission, physical examination and whole body CT scan revealed no significant findings. As her fever persisted under treated with antibiotics, whole body CT scan was performed again on admission day 5, which revealed wall thickening of aorta. Her fever subsided in two weeks without any treatment. There has been no relapse of aortitis since then. Finally, she was diagnosed with G-CSF induced aortitis.

G-CSF is known as a cause of rapid onset aortitis. It is known that the onset of the disease is more common 6 to 15 days after G-CSF administration. Repeated imaging study should be considered even though the initial assessment was negative for aortitis.

P47-1

Infliximab-resistant Crohn's disease complicated with Takayasu arteritis successfully treated with tocilizumab

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Conflict of interest: None

[Case] 21-year-old man. [Chief complaint] Fever [Current medical history] The patient presented with frequent diarrhea from X-9. He was diagnosed with Crohn's disease (CD) at A hospital in X-3. Bloody stools persisted despite treatment with mesalazine, so he was introduced to our hospital. Then 40 mg adalimumab every 2 weeks was started; however, sigmoid colon stenosis revealed, so infliximab (IFX) was administered from October X-1. From June X, he had fever and pains in both inguinal regions. Contrast-enhanced CT revealed thickening and contrast effect in the walls of the superior mesenteric artery and the bilateral femoral arteries, so we considered to be complicating Takayasu arteritis (TKA). We changed treatment from IFX to 1 mg/kg PSL + tocilizumab (TCZ). Since then, the dose was reduced to PSL 5 mg with TCZ as of September X+1 without relapse of TKA and CD. [Discussion] TKA is known as a complications with CD. Although TCZ is effective against TKA, its use for CD is not common due to risks like intestinal perforation. We used TCZ with reference to previously reported RCTs and the ANDANTE trial that showed the efficacy of IL-6 inhibitors on IFX-resistant CD. [Conclusion] We experienced a case in which IFX-resistant CD complicated with TKA was treated with TCZ successfully.

P47-2

A case of ischemic optic neuropathy developed during the course of treatment for aortitis syndrome

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Conflict of interest: None

[Case presentation] An 80-year-old woman. She was diagnosed with aortitis syndrome at 28 years old. She has been treated by steroid and she finished taking steroid at 67 years old. She got aware of pain in the right eye and visual field impairment and visited our hospital the next day. Visual field defects were observed only in the lower half of the right eye, and the critical flicker Frequency (C.F.F.) was markedly decreased in the right eye at 10 Hz. He was admitted for suspicion of optic neuritis. Contrast-enhanced head MRI showed high intensity in the right optic nerve. The laboratory test did not detect an increase in antibodies related to demyelinating or autoimmune diseases, so we diagnosed arteritic ischemic optic neuropathy (AION) associated with aortitis syndrome. She was given steroid pulse therapy and oral steroids and tocilizumab (TCZ), after that visual field impairment and the C.F.F. of the right eye improved. [Discussion] We experienced a case of AION that developed during the course of treatment for aortitis syndrome. We diagnosed AION associated with aortitis syndrome, but it is atypical in many points and there are no reports in which TCZ is used for AION. we report this case as a valuable case with the subsequent treatment course.

P47-3

Juvenile temporal arteritis with nephrotic syndrome

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Conflict of interest: None

We experienced a rare case of 55 year old female with Juvenile temporal arteritis with nephrotic syndrome. She had Raynaud's phenomenon since a year ago and swelling of both temporal arteries from 6 months ago. At the first visit, the chordal induration with no pulsation or pain on bilateral heads and mild pitting edema on both lower legs were observed. MRI STIR images showed a high signal area along the bilateral superficial temporal arteries. Oral administration of beraprost and sarpogrelate was started for Raynaud. The histology of the left superficial temporal artery showed the marked eosinophil infiltration in every layer of the arterial wall without giant cells infiltration or granulomas, and she was diagnosed with juvenile temporal arteritis. At 17 days after the initial visit, eosinophilia (1056/mm3), serum albumin 2.4 g/dL, LDL 314 mg/dL, and urinary protein 8.46 g/g·Cr were shown, and the nephrotic syndrome was accompanied. The renal biopsy revealed minimal glomerular abnormalities. After 11 weeks, the swelling of the left temporal artery spontaneously disappeared. After 18w, oral PSL 40 mg/day was started for nephrotic syndrome. After 26w, the swelling disappeared on right temporal artery. After 38w, urinary protein maintained negative and PSL was decreased to 10 mg.

P47-4

A case of the large vessel vasculitis that cannot be diagnosed definitely histologically

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Conflict of interest: None

We report a 53-year-old man with large vessel vasculitis. In September, 2019, he noticed the right neck pain. The symptom gradually aggravated and came to detect the swelling. To exclude malignancy, (18) FDG PET-CT imaging was performed. The images demonstrated significant FDG uptake in a circumferential fashion along the right common carotid artery and weak FDG uptake in his abdominal aorta. Laboratory data revealed C-reactive protein level (2.744 mg/dL) elevated, complement level, IgG and IgG4 were normal. Anti-double-stranded deoxyribonucleic acid, anti-neutrophil cytoplasmic antibodies, interferon-gamma release assays and ACE were all negative. A physical examination revealed the redness and swelling, the tenderness of his right neck. He had no adenopathy or rash. The histological findings of the right common carotid artery revealed invasion of a neutrophil, lymphocytes, plasma cells and the myofibroblast. Plasmocytic IgG4 which invaded was negative. We were not able to obtain diagnosis depending on a biopsy. Because a symptom was strong, we started the treatment in PSL 15 mg/day, and remarkable improvement was found. We were treated without getting histologic proof. Fortunately, treatment succeeded. we reported it including histologic discussion.

P48-1

A case of microscopic polyangiitis with subarachnoid hemorrhage from cervical dural arteriovenous fistula

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Conflict of interest: None

[Case] A 74-year old woman presented with bilateral fever, ear closure and decreased sensation of bilateral legs. She was admitted to our hospital on suspicion of ANCA-related vasculitis. Microscopic polyangiitis (MPA) was diagnosed based on positive MPO-ANCA (266.4 mg/dL), mononeuritis multiplex and skin biopsy results. She was treated with steroid pulse

and cyclophosphamide pulse therapy. On the 7th day, sudden back pain and hypertension were observed, and cerebrospinal fluid (CSF) was studied. Subarachnoid hemorrhage was diagnosed based on the findings of xanthochromia in the CSF, and 3DCT revealed hemorrhage from the cervical spinal cord dural arteriovenous fistula. On the 8th day, she presented alveolar hemorrhage. Vasculitis-induced vascular wall damage and malformation were suspected, and treatment with plasma exchange and steroid pulse resulted in subsiding of clinical manifestations with the gradual improvement of laboratory data (MPO-ANCA: 5.4 mg/dl) and imaging findings. [Discussion] MPA is known to mainly damage small blood vessels, but vascular malformation and bleeding of medium-sized blood vessels rarely occur. [Conclusion] If MPA shows sudden back pain or hypertension, the need for angiographic CT including the neck should be considered. Conflict of interest: None

P48-2

Three cases of Rituximab induced acute thrombocytopenia in patients with ANCA-associated vasculitis

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Conflict of interest: None

[Introduction] Rituximab (RTX) was approved for GPA and MPA in 2013 in Japan. RTX -induced acute thrombocytopenia (RIAT) has not been sufficiently recognized. [Case Presentation] Case 1. A 52-year-old man with initial GPA presenting pancreatic mass, rapidly progressive glomerulonephritis and alveolar hemorrhage was treated with RTX. However, after the first RTX infusion, the PLT decreased to 14,000/μl. Case 2. A 61-year-old man with recurrent GPA showing hypertrophic pachymeningitis was administered RTX. Subsequently, after the third RTX infusion, the PLT decreased to 7,000/μl. Case 3. A 80-year-old man with initial MPA presenting optic perineuritis began RTX treatment. Then, after the fourth RTX infusion, the PLT decreased to 32,000/μl. In each case, the PLT spontaneously recovered after discontinuation of RTX. After we excluded the other reasons which may cause thrombocytopenia, we diagnosed each of them as RIAT. Although the precise mechanism of RIAT remains unclear, the way that platelets get involved in the antibody dependent cell-mediated cytotoxicity induced by RTX is speculated. [Conclusion] We treated three cases of RIAT in patients with ANCA-associated vasculitis. As RIAT may be underestimated and could compel to change treatment, clinicians should be aware of RIAT.

P48-3

Clinical Characteristics of two Microscopic Polyangiitis (MPA) Patients with myalgia complicated with Type 1 Diabetes (T1D)

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Conflict of interest: None

[Objective] A recent study demonstrated that an HLA haplotype is common in MPA and T1D. We report the clinical characteristics of MPA complicated with T1D. [Methods] MPA admitted for remission induction from January 2019 to September 2020 were retrospectively reviewed. [Results] Among the MPA patients (N=20), 11 patients were complicated with diabetes, 2 were complicated with T1D (69 y.o. male, 79 y.o. female). Common findings were, diffuse edematous lower limbs with severe tenderness, interstitial pneumonia, neuritis and purpura. CRP (15.52 and 11.22 mg/dL) was increased with low positive MPO-ANCA (15.7 and 21.5 U/mL) with anti-glutamic acid decarboxylase antibody positive. MRI revealed subcutaneous tissue edema and enhanced muscles in the lower limb where muscle biopsy revealed lymphocytic and histiocytic infiltration among the muscular fibers without rupture nor necrosis, compatible with myositis without finding of arteritis. There findings were not observed in MPA patients without diabetes or those complicated with T2D or steroid induced diabetes. [Clinical significance] We experienced 2 MPA patients with prominent myalgia diagnosed as myositis complicated with T1D. In consideration of subtype of MPA we will discuss the clinical difference with other MPA and also polymyositis.

P48-4

Rituximab-related late-onset neutropenia in a patient with microscopic polyangiitis

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Conflict of interest: None

[Case report] A 85-year-old woman presented to the hospital experiencing malaise, worsening of renal function, proteinuria and hematuria. She was hospitalized due to rapidly progressive glomerulonephritis. The chest CT showed interstitial lung disease. Blood test was positive for anti MPO antibody and she was diagnosed as microscopic polyangiitis (MPA). We started methylprednisolone pulse, rituximab (RTX) at 375 mg/m^2/week for 4 weeks and plasma exchange. One month later, her serum creatinine level improved, and she was discharged. Seven weeks after the last RTX administration, she developed leukopenia of 1,310/μL, with neutrophiles count of 144/μL. She was asymptomatic and there were no clinical signs of infection. She was hospitalized and treated with prophylactic antibiotics. White blood cell count returned to normal after 4 days without any other treatment. [Discussion] There are few reports about RTX-related late-onset neutropenia (LON) in a rheumatologic setting. Among patients at our hospital and identified from a review of the literature, RTX-related LON usually occurs after a few weeks after the RTX administration and follows a benign course. Our report suggest that we need to consider RTX-related LON when we see agranulocytosis after RTX therapy.

P48-5

A case of ANCA-associated vasculitis in whom desensitization therapy enabled continuation of rituximab treatment after anaphylaxis

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Conflict of interest: None

A 77-year-old male who was admitted 5 years ago with acute renal failure with fever and hematuria proteinuria. A renal biopsy revealed fibrinoid necrosis of the imported and exported fibrinous arterioles and cellular crescent formation in about 50% of the glomeruli, with MPO-ANCA: 313EU and elevated MPO-ANCA, which led to the diagnosis of microscopic polyangiitis (MPA). The patient was in remission after administration of rituximab and steroids, and thereafter, rituximab 500 mg was administered approximately every year while the MPO-ANCA level was monitored, and maintenance therapy was continued. After the normal administration of rituximab, he developed respiratory distress with swelling within 5 minutes of the start of treatment. After 3 months. When rituximab was re-administered with desensitization therapy, no allergic symptoms appeared. In the MAINRISTAN study, maintenance therapy with MPA was associated with a lower risk of recurrence in the rituximab group than in the azathioprine group, suggesting that rituximab is effective in maintenance therapy. This is a case in which rituximab was re-administered using desensitization therapy and the patient was able to continue treatment. We report this case based on the literature review.

P48-6

Association between body mass index and severe infection in anti-neutrophil cytoplasmic antibody-associated vasculitis: A retrospective cohort in Japan

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Conflict of interest: None

Background: Although previous studies have evaluated risk factors for the incidence of severe infection in patients with antineutrophil cytoplasmic antibody-associated vasculitis (AAV), the relationship between body mass index (BMI) and severe infection in AAV has not been elucidated. **Methods:** This single-center retrospective cohort study included 98 consecutive elderly AAV patients treated at the Aichi Medical University Hospital in Japan between 2004 and 2018. The relationships between BMI at diagnosis and subsequent first severe infection were assessed using multivariate Cox proportional hazards models. **Results:** During the entire follow-up period (median 22 months, IQR 7-52 months), 32 (32.7%) patients developed at least one severe infection. Low BMI (<18.5 kg/m^2 compared with normal BMI [18.5-23.0 kg/m^2], adjusted HR 2.70, 95%CI: 1.18-6.17, *P*=0.018) was the significant predictor of severe infection. **Conclusions:** Low BMI was associated with a higher risk of severe infection in elderly AAV patients, suggesting that careful management may be required to prevent the development of infection in patients with a low BMI. Further studies are needed to elucidate the optimal treatment strategy for these patients.

P48-7

Availability of BAFF measurement in induction therapy by Rituximab for ANCA-related vasculitis

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Conflict of interest: None

[Background] There is no definition of achievement a remission in induction therapy by Rituximab for ANCA-related vasculitis. BAFF (B cell activating factor belonging to the tumor necrosis factor family) is a molecule belonging to the TNF superfamily, and has been reported to be associated with AAV pathology. We examined whether serum BAFF is useful for predicting remission of AAV by RTX treatment. [Methods] We use BVAS (Birmingham Vasculitis Activity Score 2008 version 3) at 6 months after RTX treatment in 27 AAV patients (9 MPA, 18 GPA). [BVAS = 0] was achieved a remission, and [BVAS > 0] was not achieved. We considered changes of serum BAFF before RTX treatment, 1 month after treatment, and 6 months after treatment. [Results] In the remission group, serum BAFF increased consistently. In contrast, in the unachieved group, serum BAFF was within the normal range. In addition, there was no statistically significant difference in serum BAFF before and 1 month after RTX between two groups, but the serum BAFF in 6 months after RTX. [Conclusions] We suspected that B cells in the unachieved group were not completely depleted by RTX and remained in tissues. We considered that re-administration by RTX or other treatments should be needed if serum BAFF in six months after RTX is normal range.

P48-8

Clinical aspect of PTU-induced ANCA associated Vasculitis

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Conflict of interest: None

Background: Anti-thyroid drug is known as a causing for ANCA related vasculitis (AAV). We were experienced 3 cases of AAV complicated with PTU-treated Basedow's disase. To examine their clinical aspects, we compare them to other AAV examples. Case 1: 58 year female treated with PTU before two years. She showed the mass with granuloma around the orbit, peripheral nervous disturbance, lung nodules, and glomerulonephritis. L/E data showed MPO-ANCA 224 U/ml and PR3-ANCA 8.1 U/ml. Case 2: 44 year female lady treated with PTU before five years. She showed arthritis and sinusitis, associated with tighter of ANCA value (MPO-ANCA 300 U/ml and PR3-ANCA 350 U/ml). Case 3: 45 year female treated with PTU before two years. She showed fever, scleritis, glomerulonephritis, and high tighter of ANCA value (MPO-ANCA 81 U/ml and PR3-ANCA 112 U/ml). Total number of 15 cases of newly onset AAV (including previous 3 cases) were experienced for two years. Twelve cases of non-Basedow's AAV (5 men and 7 female, and 72.6±11.8 years old) were 9 cases of MPA and 3 cases GPA. Disucussion: Our Basedow's-AAV cases were younger and higher value tighter than non-Basedow's-AAV. All cases were double positive ANCA in Basedow's AAV. However, disease activity and target organs were not different in both groups.

P48-9

A case of microscopic polyangiitis resulting in multiple aneurysms in the abdominal cavity

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Conflict of interest: None

[Case] A 77-year-old female with a history of hypertension. She had never been diagnosed with kidney disease. One month before admission, she had worsening respiratory distress. A CT scan showed nodules and consolidations in both lungs, and severe renal dysfunction was also noted. She was diagnosed with microscopic polyangiitis because of rapidly progressive renal dysfunction, lung lesions, and MPO-ANCA positivity. Treatment with glucocorticoids was started. On the 5th day of hospitalization, she had severe epigastric pain. Contrast-enhanced CT scan showed bleeding due to a ruptured aneurysm of the right gastroepiploic artery, and embolization was performed. Rituximab was introduced as induction therapy and maintenance dialysis was started. A muscle biopsy showed small vessel vasculitis consistent with ANCA-associated vasculitis (AAV). [Discussion] AAV is mainly caused by systemic small vessel inflammation, and other sizes of vessels may also be involved, although this is very rare. Aneurysms in intraperitoneal arteries have been reported in only a few cases and sometimes it is a multiple case such as the present case. Medium-sized vascular aneurysms in the abdominal cavity often caused by polyarteritis nodosa, and it is important to differentiate between them.

P48-10

A case study of antithyroid drugs (ATD)-induced ANCA-associated vasculitis (AAV)

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Conflict of interest: None

[Objective] We sometimes experience ATD-induced AAV. We retrospectively reviewed medical records of ATD-induced AAV patients in our hospital in our hospital from October 2015 to September 2020. [Case 1] A 42-year-old woman with Graves' disease was taking Propylthiouracil (PTU). After diagnosed as ATD-induced AAV, she stopped taking PTU and the symptoms improved. [Case 2] A 67-year-old woman with Graves' disease was taking thiamazole (MMI) after subtotal thyroidectomy. After diagnosed as ATD-induced AAV, she stopped taking MMI and the symptoms improved. [Case 3] A 44-year-old man with Graves' disease was taking MMI. After diagnosed as EGPA, he stopped taking MMI. Little improvement was seen until PSL was started. [Case 4] A 57-year-old woman with Graves' disease was taking MMI. After diagnosed as ATD-induced AAV, she stopped taking MMI. However, the symptoms did not improve until PSL was started in March. Abdominal pain recurred, and CT scans showed multiple aneurysms in April. [Conclusion] Most of the patients diagnosed as drug-induced AAV were taking PTU and showed MPO-ANCA positive. In our study, some patients didn't improve after quitting ATD. Therefore coincidence of Graves' disease and vasculitis couldn't be ruled out. We report this case study, along with some literature review.

P48-11

A case of ANCA associated vasculitis (AAV) with intercostal arteritis presenting as rib pain and paravertebral fluid collection

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Conflict of interest: None

A 75-year-old man was admitted with a 2-month history of pain in the bilateral rib and scalp. He was complicated with exudative pleural effusion and the posterior mediastinal fluid collection at the Th6-8 level. A biopsy to exclude paravertebral abscess could not be performed due to its location. However, cultures of blood and pleural effusion were both negative. On the other hand, elevated sIL-2R levels and weakly positive MPO-ANCA were found while no definitive findings of lymphoma or AAV were observed. A PET-CT scan showed increased uptake of 18F-FDG in the spleen and in the paravertebral lesion. Splenectomy was performed to confirm lymphoma, but unexpectedly, necrotizing vasculitis of medium-sized arteries was revealed. Moreover, MPO-ANCA levels were elevated along with his clinical progression, which led us to diagnose him with AAV. Remission induction therapy with methylprednisolone pulse therapy and rituximab ameliorated his disease activity promptly. In our case, bilateral rib pain and paravertebral fluid collection were most likely caused by inflammation of intercostal arteries. His scalp pain was considered to be occipital neuralgia. We herein report a case of AAV, which predominantly affected medium-sized arteries, successfully treated with glucocorticoid and rituximab.

P48-12

Maintenance therapy with Rituximab in ANCA-associated vasculitis

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Conflict of interest: None

[Objectives] Rituximab (RTX) is recommended to use for the management of ANCA-associated vasculitis (AAV), both remission-induction and maintenance therapy. The purpose of this study is to investigate the efficacy and safety of RTX as maintenance therapy. [Methods] We retrospectively investigated 4 patients with AAV who have been treated with RTX in our center (2 male, 2 female) from 2016 to 2020. [Results] The average age at started with RTX was 60 years old. One patient was MPA, 2 were GPA and 1 was EGPA. RTX was used for remission-induction therapy at recurrence of AAV (2 renal damage, 2 peripheral nerve damage). The average CRP was 1.19 mg/dl, all patients showed MPO-ANCA positive; the average 174.3 IU/l, the average BVAS was 12. All of them were treated with high dose of GC and RTX 500 mg weekly (One patient was twice, 3 were 4 times). The interval of maintenance therapy of RTX was 6~12 months. Three patients were finished 4 courses, the data revealed average CRP 0.2 mg/dl, average MPO-ANCA 10 IU/l, low levels of B cell (<1%). The BVAS was 0, the average VDI was 3. There was no relapse, allergy reaction and infection. [Conclusion] Our data indicated maintenance therapy with RTX in AAV was effective and safety. Further study is needed for the appropriate treatment interval and period.

P48-13

A case of rheumatoid arthritis complicated with microscopic polyangiitis during therapy with golimumab

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Conflict of interest: None

[Introduction] It is known that anti-TNF-α therapy induces autoantibodies and autoimmune disorders. ANCA-associated vasculitis (AAV) were rarely reported. [Case] 84 year-old female had developed pain in multiple joints in December 2014. She was diagnosed as having rheumatoid arthritis from positive RF and anti-CCP antibodies. She had been successfully treated with golimumab since August 2016. However, because of a fever, she was referred to our hospital at the end of July 2020. A CT scan revealed infiltration shadows in the right upper and left lower lobe, and usual interstitial pneumonia pattern was detected. Because of positive for MPO-ANCA, proteinuria, occult hematuria and granular cast, she was suspected to have AAV. Renal biopsy showed crescentic glomerulonephritis, which confirmed the diagnosis of microscopic polyangiitis. The infiltration shadows were considered as organized pneumonia, because antibiotic therapy was ineffective. Golimumab was discontinued and steroid treatment was started, which improved her conditions and she was discharged from the hospital. [Conclusion] Anti-TNF-α therapy occasionally induces ANCA. AAV should be considered when faced with a fever, interstitial pneumonia, abnormal urinalysis results and so on, during the therapy with the drugs.

P48-14

A case of microscopic polyangiitis with rapidly progressive glomerulonephritis after positive conversion of MPO-ANCA during follow-up as idiopathic pulmonary fibrosis

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Conflict of interest: None

A 67-year-old man was pointed out of the ground glass opacity by the chest X-ray one year ago. Various autoantibodies were negative and he was followed up as idiopathic pulmonary fibrosis. He visited orthopedic surgery for bilateral lower thigh pain and took NSAIDs under diagonosis of lumbar spinal stenosis. After that he visited internal medicine for a slight fever and loss of appetite. Laboratory test results showed renal dysfunction and urinary test abnormalities, and he was admitted to our hospital for examination. The level of MPO-ANCA was highly elevated at 24.4 U/mL. Chest CT showed no increase in lung lesions, but rapidly progressive glomerulonephritis, polyarthritis, and myositis were observed. Under the diagnosis of microscopic polyangiitis, methylprednisolone pulse therapy was done, followed by high-dose prednisolone, and plasma exchanges, and intravenous cyclophosphamide. Renal biopsy showed necrotizing crescentic glomerulonephritis. Now the renal function is improved and the patient could avoid the introduction of hemodyalysis. In cases of idiopathic pulmonary fibrosis regular measurement of ANCA and confirmation of urine test may help with early therapeutic intervention.

P49-1

A case report of Granulomatosis with Polyangiitis with hypertrophic pachymeningitis in the lumber spinal canal

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Conflict of interest: None

[Case report] A 60-years-old woman developed a fever and cough. A month later, she admitted to our hospital due to the elevated C-related protein 15.6 mg/dL and white blood cells 16,400/μL. In the immunological studies, MPO-ANCA was positive at 22 IU/mL. PET/CT showed a mass with 18F-FDG uptake in lumber spinal canal at the levels of L4/L5. In the pathological examination, there was the invasion of the lymphocyte of the diffusion in dura mater and dura mater outside organization, and the formation of epithelioid granuloma with Langhans type giant cell in great numbers was recognized. Administration of prednisolone 30 mg/day was started as a diagnostic treatment, and the fever and inflammatory reaction were rapidly improved. It was diagnosed as granulomatosis with polyangiitis (GPA) which combined the hypertrophic pachymeningitis. [consideration] Hypertrophic pachymeningitis is known as a neurological lesion frequently secondary to ANCA-associated vasculitis, but there are few reports of cases occurring in the spinal cord compared to the head. In this case, the lesion as a candidate of the biopsy method was not recognized in other organs, and histopathology of hypertrophic pachymeningitis was recognized in the spinal cord lesion became a conclusive factor of the diagnosis of GPA.

P49-2

A Case of Granulomatosis with polyangiitis with repeated rupture of hepatic aneurysms

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Fumie Ohta, Yoshito Tsukada
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Conflict of interest: None

A 76-year-old Japanese woman was admitted to our hospital with numbness in her arms and legs. Laboratory data were as follows: blood urea nitrogen, 34.2 mg/dL; serum creatinine, 2.0 mg/dL; C-reactive protein 25.8 mg/dL; MPO-ANCA 213 IU/mL; while PR3-ANCA was negative. CT showed multiple nodular lesions in both lungs. The patient was diagnosed with GPA and given pulse therapy with methylprednisolone at 500 mg/day for 3 days followed by maintenance with prednisolone at 40 mg/day. Four days after steroid introduction, she complained of sudden-onset epigastric pain. CT showed extravasation within the liver. Angiography showed many aneurysms in the peripheral sites of the hepatic, mesenteric, and renal artery. Bleeding from the aneurysm in the posterior segment of the liver was suspected, and selective hepatic arterial embolization was performed. The next day, hemodialysis was started. During the hemodialysis, a sudden drop in blood pressure occurred. CT showed an increase of hematoma in the liver, and hepatic arterial embolization of the anterior segment branch was performed. As additional treatment, plasmapheresis was performed twice. MPO-ANCA became negative and multiple nodular lesions in both lungs disappeared. It is necessary to be careful about complication of aneurysms in GPA.

P49-3

A Case of localized granulomatosis with polyangiitis complicated with complete atrioventricular block

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Conflict of interest: None

A 54-year-old man was admitted to our hospital due to a 3-month history of left conjunctive congestion and polyarthralgia. Anti-neutrophil cytoplasmic antibody specific for proteinase-3 (PR3-ANCA) was positive at the previous clinic. Before 8 days admission to our hospital, he was hospitalized at another hospital due to an episode of syncope and fever. Then, electrocardiogram (ECG) showed complete atrioventricular block, and temporary pacemaker was implanted immediately. Computed tomography demonstrated multiple pulmonary and nasopharyngeal nodules. He was transferred to our hospital. Based on these findings, he was diagnosed with granulomatosis with polyangiitis (GPA). The patient was treated with 1 mg/kg/day of prednisolone and intermittent intravenous infusion of cyclophosphamide. ECG showed a sinus rhythm with first degree atrioventricular block, and the temporary pacemaker was removed on the 23rd days after the treatment for GPA. He was discharged at our hospital 2 months after admission. Cardiac complications are much less common in localized GPA than in systemic GPA. We believe it is worth to report this case, along with a review of the literature.

P49-4

Report of eosinophilic granulomatosis with polyangiitis with cholangitis at our hospital

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Conflict of interest: None

[Case] 58 year old female. 2018, Because the diagnostic criteria were met, eosinophilic granulomatosis with polyangiitis (EGPA) was diagnosed and treatment was introduced. Since May 2019, maintenance therapy had been performed only with prednisolone 5 mg / day. On May 21, 2020, she was hospitalized for elevated hepatobiliary enzymes. After admission, a CT scan revealed pericardial fluid retention and she was diagnosed with pericarditis. NSAIDs eliminated pericardial fluid and improved the inflammatory response on June 4, but she had a fever again on June 15. On June 18, she was diagnosed with acute cholangitis on contrast-enhanced CT and ENBD was placed. And the fever improved again. However, just before discharge, chest pain recurred on June 25, and pericardial adhesions were pointed out. She was diagnosed with EGPA-related pericarditis and was given prednisolone 55 mg / day, which also improved hepatobiliary enzymes. A CT scan 3 months after the introduction of treatment showed reduction of bile duct dilatation. [Discussion] It is estimated that this cholangitis is caused by EGPA based on the time series of onset and the course of treatment. EGPA is generally associated with small vasculitis, but cholangitis is not. This is an interesting case and I will report it here.

P49-5

A case of refractory hypertrophic pachymeningitis complicated with granulomatosis with polyangiitis effectively treated with rituximab and methotrexate

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Conflict of interest: None

[Case] Female in 70s [Medical history] She developed hearing loss on the left side in June X-1. In December X-1, based on elevated MPO-ANCA and findings of granuloma formation with inflammatory cell infiltration in biopsy sample of left middle ear mucosa, she was diagnosed with granulomatosis with polyangiitis (GPA). Oral prednisolone (PSL) 25 mg/day was started, and her hearing improved. After PSL tapering, symptoms did not recur. However, in April X, hearing loss reappeared, accompanied by left-sided headache and right facial paralysis. Contrast-enhanced MRI showed high-intensity area in the left-sided predominant cerebral dura mater. she was diagnosed with hypertrophic pachymeningitis (HP) complicated with GPA. In addition to increasing dose of PSL, two courses of steroid pulse and cyclophosphamide pulse therapy were administered. she was transferred to our hospital and two additional courses of steroid pulse therapy were administered. Nevertheless, the headache and inflammatory findings worsened and IgG index in cerebrospinal fluid was still high. Therefore, rituximab (RTX) and methotrexate (MTX) was added. After the therapy, symptoms and the inflammatory findings improved. [Conclusion] We experienced a case of refractory HP associated with GPA responded well with RTX and MTX.

P49-6

A case of the granulomatous polyangiitis diagnosed due to dysuria

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Conflict of interest: None

A 51-year-old man began to complain macro hematuria from May 20XX and then, pollakiuria and urge urinary incontinence. Later, he developed high fever and polyarthralgia. He visited the hospital for a secondary medical examination and was hospitalized after multiple nodular shadows in the lungs were pointed out by an X-ray. Although he was diagnosed as bacterial pneumonia and taken antibiotics, neither his symptoms nor examination was improved. However, laboratory exam showed high titer of PR3-ANCA and otorhinolaryngologist pointed out sinusitism. Biopsy of lung, kidney, and nasal mucosa failed to point to granulomatous polyangiitis (GPA). Computed tomography showed suspicion of mucinous adenocarcinoma of prostate. Prostate biopsy revealed that bilateral normal prostate tissue disappeared and severe neutrophil infiltration and angiitis. He was treated with corticosteroid and cyclophosphamide, which improved his subjective symptoms, including dysuria and laboratory and imaging findings. Conclusion: In GPA, prostatitis rarely occurred, but no case of severe loss of prostate tissue such as our case has been reported. So we have to pay attention to GPA if a patient with dysuria was accompanied by respiratory symptoms or abnormal findings by chest X ray.

P49-7

A prompt initiation of extracorporeal membrance oxygenation as an adjuctivetherapy rescued severe lung injury related to granulomatosis with polyangiitis: a case report

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Conflict of interest: None

A 49 years old man was admitted to our hospital because of respiratory failure. He regularly visited our hospital for granulomatosis with polyangiitis (GPA) that developed eight years ago. Two days before admission, dyspnea developed. The day before admission, he visited A hospital. Respiratory failure, hypotension and fever was observed. He was transported to our hospital and endotracheally intubated. A CT scan showed infiltrative shadows and antibiotic was administerd. On the 2nd hospital day, extracorporeal membrane oxygenation (ECMO) was initiated. We diagnosed his lung injury was related GPA. From the 4th day, methylprednisolone pulse therapy was administered for three days. On the 7th day, continuous renal replacement therapy was started due to drug-induced impairment of renal function. On the 8th day, tacrolimus was started. On the 9th day, the dialyzer membrane AN69ST was used to adsorb serum proinflammatory cytokines. His condition was improved and he was weaned off from ECMO. He was extubated and eventually discharged. Because it may be rare that GPA-induced rapid and severe lung disorder was rescued by immunosuppressants with the adjunctive therapy using prompt ECMO and cytokine removal, we believe it worth to report and discuss this case with a review of literature.

P49-8

A case of granulomatosis with polyangiitis with thoracic spine lesions

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Conflict of interest: None

[Medical history] A man in his 60s presented with muscle pain and malaise in his back from a month ago. Thereafter, the temperature was repeatedly in the 38°C range. Simple CT scan revealed multiple nodules in both lungs, and a contrast-enhanced MRI scan showed soft shadows on the ventral side of the thoracic vertebrae. His renal function was normal, and urinalysis revealed microscopic hematuria. MPO-ANCA was elevated to 308.0 IU/ml. A CT-guided biopsy of the lung nodule revealed a granulomatous lesion. A renal biopsy was revealed crescentic nephritis. The diagnosis of granulomatosis with polyangiitis (GPA) was made and we started prednisolone 50 mg/day. Intravenous cyclophosphamide was performed. The patient's fever was quickly relieved. MRI studies showed a trend toward improvement in the ventral aspect of the thoracic vertebrae. A CT scan showed that the pulmonary nodules had disappeared. The patient did not relapse. [Summary] GPA is a disease of systemic necrotizing granulomatous vasculitis involving the upper airway, lungs, and kidneys, and presents with a variety of clinical manifestations. We report here a case of GPA complicated by thoracic spine lesions, which was improved by standard treatment.

P50-1

Abdominal periaortitis with eosinophilic granulomatosis with polyangiitis: a case report

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Conflict of interest: None

[Background] Eosinophilic granulomatosis with polyangiitis (EGPA) is rarely complicated by large vessel involvement. Here we report a case of EGPA complicated by abdominal periaortitis. [Case] A 72-year old woman had a history of asthma and presented with fever and numbness in the lower legs. Eosinophilia (WBC 18400 /μL with 55.6 % eosinophils) and the high titer of myeloperoxidase (MPO)-ANCA (≧ 134.0 IU/mL) were revealed. After the diagnosis of EGPA, steroid therapy including intravenous pulse steroids was started and the above symptoms were temporarily improved. However, we found recurrences of EGPA symptoms such as fever, numbness and elevation of C-reactive protein at the point of tapering prednisolone to 15 mg/day. Furthermore back pain newly emerged. CT revealed a soft tissue mass around the abdominal aorta and FDG-PET revealed high FDG uptakes in the above mass. Although a biopsy of the periaortic lesion was not conducted, we diagnosed periaortitis associated with EGPA after the careful differential diagnosis. We treated her with intravenous cyclophosphamide (IVCY) in addition to steroid therapy. Reduction of the periaortic mass was confirmed within a month of treatment. [Conclusion] We suggest that IVCY may be effective for periaortitis with EGPA.

P50-2

Dose tapering of mepolizumab in Eosinophilic Granulomatosis with Polyangiitis (EGPA)

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Conflict of interest: None

[Objective] Mepolizumab has approved for EGPA at a dose of 300 mg/4 weeks but there is little evidence about dose tapering. Here, we report the efficacy of dose tapering of mepolizumab. [Methods] We retrospectively analyzed the medical records of 7 EGPA patients who have continued for more than 1 year. The extension of the administration was judged for each visit. [Results] Median age was 64 years and 6 cases experienced recurrences, had 4 years disease duration. 3 cases were ANCA positive, PSL was prescribed in all cases, and the dose was 4.5 mg, immunosuppressive drugs were co-administrated for 5 cases, eosinophil count was 421 / μl, the CRP levels was 0.06 mg / dl. The average duration of mepolizumab administration was 79 weeks, and the spacing of the dosing started at an average of 18 weeks, with the final dosing interval was 5 weeks 1 patient, 6 weeks 2 patients, 7 weeks 2 patients, and 8 weeks 1 patient. During the course, 6 patients (86%) could be reduced steroid dose and immunosuppressive drugs in 3 patients (43%), and no patients had any relapse or adverse events. [Conclusions] Mepolizumab for EGPA can be expected as a drug that enables further dose reduction of steroids and immunosuppressants without relapse even if the spacing of dosing.

P50-3

Five cases of eosinophilic polyangiitis granulomatosis who received the biologic mepolizumab

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Conflict of interest: None

Eosinophilic polyangiitis granulomatosis has preceding allergic disease such as asthma. It is said that genetic factors and environmental factors such as infection are related to the etiology, and about half of the cases are negative for anti-neutrophil cytoplasmic antibody (ANCA). The biologic mepolizumab is used in refractory and relapsed cases of eosinophilic polyangiitis granulomatosis, but is said to be particularly effective in ANCA-negative cases. The biologic mepolizumab is originally indicated for refractory bronchial asthma, and the cutoff for therapeutic indication is known according to the number of eosinophils. Unlike bronchial asthma, eosinophilic polyangiitis granulomatosis, which is an additional indication for the biologic mepolizumab, has no clear cut-off value such as eosinophil count. This time, we experienced 5 patients who received mepolizumab. The problematic symptoms of each case were different. The progress of improvement of the symptoms and the onset of eosinophilic polyangiitis granulomatosis, the transition of eosinophil levels, rheumatic factor levels, and ANCA values from before to the introduction of the biologic mepoli-

zumab were evaluated and some literature I will also report with consideration.

P50-4

An atypical case of eosinophilic granulomatosis with polyangiitis diagnosed by submaxillary gland biopsy

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Conflict of interest: None

A 55-year-old woman was referred to our hospital complaining of right submandibular gland enlargement (that started in February 2020), and hoarseness and dysphagia (that started in March 2020). She had a curtain sign, a left deviation of the tongue, and paresthesia of the right tongue. Therefore, she was suspected to have a disability of the right trigeminal nerve, left glossopharyngeal nerve, right vagus nerve, and left hypoglossal nerve. Contrast-enhanced MRI of the brain showed no obvious abnormal findings. A chest CT scan showed ground-glass shadows in the lower lobes of both lungs. Laboratory examinations revealed an elevated eosinophilic count, but both PR3-ANCA and MPO-ANCA were negative. In addition, there was no history of bronchial asthma or sinusitis. A histological examination of her submaxillary gland revealed characteristic findings of eosinophilic granulomatosis with polyangiitis. Both the enlargement of the submaxillary gland and the absence of a history of asthma or sinusitis in this patient are atypical features of eosinophilic granulomatosis with polyangiitis.

P50-5

Relapse of eosinophilic granulomatosis with polyangiitis (EGPA) during mepolizumab treatment: A case report

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Conflict of interest: None

[Case] A 67-year-old male. Fever and numbness of the extremities developed with multiple raised purpura on the dorsal sides of the hands and feet. Blood tests showed eosinophil-predominant leukocytosis, and chest CT revealed faint ground-glass opacities in both lungs. MPO-ANCA was 58.5 U/mL. After a skin biopsy, the patient was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). The symptoms were rapidly improved with prednisolone (PSL) at 60 mg/day. However, as the joint pain relapsed, mepolizumab (anti-IL-5 antibody drug) was administered. One year later, the skin eruption observed at the first medical examination relapsed, and MPO-ANCA, which had become negative, increased again to 13.4 U/mL, although there was no increase in the blood eosinophil count. A skin biopsy revealed vasculitis more severe than the initial form, although the infiltration mainly consisted of neutrophils with a few eosinophils. [Discussion] In the present case, EGPA relapsed during mepolizumab treatment. Mepolizumab treatment may allow dose reduction or even discontinuation of PSL treatment. However, there was no increase in the serum eosinophil count during mepolizumab treatment, suggesting that the relapse may have been mainly associated with immune cells other than eosinophils.

P50-6

A case of eosinophilia in which IL-5 was useful in differentiating from EGPA

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Conflict of interest: None

Case: 27 year-old female. Progress: She was in remission attending a gastroenterologist for ulcerative colitis. There was no history of bronchial asthma, but blood tests showed CRP 5.64 mg/dl, leucocyte 16010/μl, eosinophil fraction 58.5%, and IgE 1147 IU/ml, EGPA was suspected and admitted to the hospital. Bone marrow examination showed eosinophilia but no atypical cells or FIP1L1-PDGFRα fusion gene. An echocardiography and contrast CT showed a mural thrombus in the left ventricle, and suggested endocardial myocarditis due to EGPA, but the serum IL-5 level was found to be low. Based on these findings, EGPA was denyed and Löffler's endocarditis associated with eosinophilia was diagnosed and steroid and antithrombotic therapy were started. Discussion: This case was suspected EGPA based on the process. However, a discrepancy was bronchial asthma are almost inevitable in EGPA, but were absent in this case and there was no renal impairment. The IL-5 suggested that Löffler's endocarditis due to secondary eosinophilia caused symptoms with similar of EGPA, including thrombus-derived fever and increased inflammatory response. Since IL-5 is generally elevated in active EGPA, we report a case in which the measurement of IL-5 helped in the diagnosis, including a discussion of the literature.

P50-7

A case of eosinophilic granulomatosis with polyangiitis (EGPA) with pulmonary alveolar hemorrhage successfully treated with rituximab (RTX)

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Conflict of interest: None

A 66-year-old man, Bloody sputum emerged on day X-6, On day X for increased bloody sputum, On the same day, the patient was hospitalized in our department on an emergency basis for aggravated anemia and respiratory condition. The patient was diagnosed with EGPA with pulmonary alveolar hemorrhage. The patient was intubated and started undergoing mechanical ventilation for hemorrhagic shock due to pulmonary alveolar hemorrhage and respiratory failure and was admitted to an ICU for treatment. Following mPSL pulse therapy administered, IVCY, and plasma exchange therapy to which he did not respond, RTX was initiated and turned out to be effective. The patient was extubated, weaned from mechanical ventilation, and discharged from the ICU on day X + 39. In EGPA patients, pulmonary alveolar hemorrhage is a rare but very severe complication with a high mortality. In general, pulmonary alveolar hemorrhage and glomerulonephritis are often found in ANCA-positive cases, while cardiac lesions are common in ANCA-negative cases. Here we report a case of EGPA with pulmonary alveolar hemorrhage that was nonresponsive to various treatments but successfully treated with RTX, with a literature review.

P50-8

A case of refractory eosinophilic granulomatosis with polyangiitis successfully treated with cyclophosphamide, rituximab, and mepolizumab

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Conflict of interest: None

[Case] 45-year-old male [Past history] Asthma (X-5) [Present history] He developed right putamen bleeding at August X-2, and suffered from fever and rash of limbs. Laboratory data showed eosinophilia, elevated CRP and MPO-ANCA. He was diagnosed with EGPA, treated with PSL 80 mg/day after mPSL 1 g/day, and administered with IVCY and mepolizumab (MEP), which improved symptoms. PSL was tapered to 20 mg/day, but headache and polyneuropathy occurred with increased CRP. He was treated with PSL 60 mg/day after mPSL 1 g/day, which induced remission, but as it was difficult to taper PSL to less than 32.5 mg/day, at July X-1 he was treated with PSL 80 mg/day after mPSL 1 g/day, and RTX, which induced remission. After PSL was tapered to 32.5 mg/day, he developed cough, dyspnea, and bloody sputum, with hilar centrality consolidation on CT, and UCG showed decrease of EF from 68% to 8%. [Hospitalization

course] Coronary stenosis, eosinophil infiltration and vasculitis on myocardial biopsy were not found. MRI revealed post-enhancement of myocardium, suggesting cardiac involvement. PSL 60 mg/day after mPSL 1 g/day was started with IVCY and RTX, which induced remission. MEP was restarted at February X. PSL could be tapered to 20 mg/day without relapse. [Conclusion] We discussed this case through literature review.

P50-9

A case of eosinophilic granulomatosis with polyangitiis complicated by perforations of the small intestine and the colon

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Conflict of interest: None

A 64-year-old man was diagnosed with eosinophilic granulomatosis with polyangitiis (EGPA) based on bronchial asthma, mononeuritis multiplex, purpura and hypereosinophilia. Because he was suffered from abdominal pain due to gastric duodenal and colon ulcers and difficulty of walking due to mononeuritis multiplex, he was admitted to our hospital. Prednisolone (50 mg/day) and IVCY was initiated. Nevertheless, his condition did not improve. After IVIG was added, his physical and endoscopic findings improved gradually. But at 30 days after admission, he underwent an emergency surgery for transverse colon repair due to perforation. And two more days later, he underwent partial resection of the small intestine due to perforation. After that, a new perforation was speculated again, but he did not want to undergo reoperation. At 45 days after admission, he suddenly lost consciousness, and thereafter died. The surgical specimen revealed inflammatory cells infiltration in inner wall of the intestine. Multiple perforation of small intestine and colon is a rare complication of EGPA.

P50-10

A case of eosinophilic granulomatosis presented with polyangiitis with multiple cerebral infarction

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Conflict of interest: None

[Case] A 61-year-old man with allergic rhinitis and bronchial asthma had a fever, sensory disorders and purpura of both legs. C-reactive protein was high, and an echocardiography showed pericardial effusion and hypokinesia of the apex wall. He was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) due to asthma, eosinophilia, fever, mononeuritis multiplex, purpura, and myocardial damage. The neurological symptoms were mainly sensory disorders and there was no paralysis, but multiple cerebral infarctions were observed on head MRI. We considered cerebral infarctions to be a central nervous system lesion associated with EGPA. We started steroid pulse therapy (500 mg/day for 3 days), followed by PSL 70 mg (1 mg/kg) and cyclophosphamide pulse therapy. Numbness, pleuritis, pericarditis, and hypokinesia of the apex wall improved after these treatments. No new cerebral infarctions were observed in the following head MRI one month later. [Discussion] Cerebral infarction is occasionally reported in ANCA-associated vasculitis, but extremely rare with EGPA.

P51-1

A case of nodular polyarteritis diagnosed from biliary stasis liver disease as initial symptom

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Conflict of interest: None

The patient was 73-year-old man. A week before admission he realized a high fever and was prescribed with cold medicine. General malaise and the fever didn't improve and because of the blood test results T-Bil: 3.3 mg/dl, D-Bil: 2.4 mg/dl, AST/ALT=55/56 IU/L, CRP 34 mg/dl, he was diagnosed as cholangitis despite no abdominal symptoms. He was referred to our department for unknown fever with absence of gallstones on ERCP, negative bile and other cultures and no response to antibiotics. There was no evidence of infection, malignancy on CT, upper and lower endoscope and prostate tumor markers. No immunological abnormality was found. Primary vasculitis was suspected based on persistent fever, weight loss, malaise, anemia and low Alb. Angiography revealed hepatic aneurysms and caliber irregularities in the left and right renal arteries, which led to the diagnosis of PN. IVCY therapy in addition to high-dose PSL was used to induce remission. We experienced a case of PN with no major symptoms other than fever, which could be diagnosed by angiography. There were some reports of PN diagnosed by angiography following cholangitis or cholecystitis. We also discussed choice of radiographic test to diagnose PN because this case was able to detect aneurysms by CT angiography in thin slice.

P51-2

Minocycline-induced cutaneous polyarteritis nodosa

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Conflict of interest: None

A 25-year-old man presented with fever and rash that developed one day after taking minocycline for acne vulgaris. He had been taking minocycline intermittently for five years. The patient also had a history of fever, arthralgia, and tingling sensation on the bilateral forearms and legs, which subsided with the discontinuation of minocycline five months before. Physical examination revealed facial acne and multiple subcutaneous nodules on his lower extremities. Laboratory results showed positivity for myeloperoxidase-anti-neutrophil cytoplasmic antibody (MPO-ANCA). Antinuclear antibodies and urinalysis were unremarkable. A skin biopsy showed necrotizing vasculitis of the medium-sized artery and intravascular thrombi of the dermis. Based on these findings, he was diagnosed with minocycline-induced cutaneous polyarteritis nodosa (PAN). Cessation of minocycline and a short-course treatment with prednisolone (starting from 25 mg every other day and tapered off after 2 weeks) alleviated his symptoms. The characteristic signs of minocycline-induced vasculitis are PAN-like symptoms, although ANCA is often positive. Clinicians should review the patient's medication list when the patient has medium vessel vasculitis with positive ANCA serology.

P51-3

A case of microscopic polyangitis (MPA) with refractory multiple gastrointestinal ulcers due to median-size arteritis

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Conflict of interest: None

[Background] MPA is defined as necrotizing vasculitis mainly in small vessels including anti-neutrophil cytoplasmic antibody (ANCA) positive, and is rarely complicated by gastrointestinal ulcer due to medium-sized arteritis. [Case] A 70-year-old man developed cerebral infarction and duodenal ulcer, and interstitial pneumonia at the age of 64. From 2 months before admission, he had continuous diarrhea and fever. Colonoscopy showed multiple ulcers in the whole large intestine, suggesting a possibility of systemic vasculitis. Blood tests showed PR-3ANCA positive, minor renal damage, and angiography showed small aneurysms and irregularities in the diameter of many artery. We diagnosed and started treatment as MPA. After that, gastrointestinal bleeding were repeated, although we able to save his life without perforation. [Conclusion] This case is highly suggestive in terms of classification of vasculitis and treatment of refractory gastrointestinal ulcer. we report our experience of MPA with medium-sized vasculitis, with some literature reviews.

P52-1

A case of eosinophilic fasciitis successfully treated with mepolizumab

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Conflict of interest: None

[Introduction] We describe the case of a 36-year-old female who was treated successfully with mepolizumab monotherapy in a case of MPO-ANCA-positive eosinophilic fasciitis. [Case presentation] She presented swelling and pain appeared from the elbow on the ulnar side of the forearm to the wrist joint. Her white blood cell count was 13600 / μL with 58% eosinophils, aldolase was 26.4 U/L, and IgG was 2208 mg/dL, and MPO-ANCA was 15.3 IU/mL. En bloc biopsy from the forearm showed fibrosis of the subcutaneous connective tissue accompanied by fascia thickening and cell infiltration of eosinophils and mononuclear cells and no evidence of vasculitis. Finally, a diagnosis of EF was established from these clinical and laboratory findings. Because she requested not to underwent corticosteroids therapy, mepolizumab monotherapy, 300 mg every 4 weeks, was initiated. After the first administration of mepolizumab, the pain and sclerosis of the forearm improved rapidly, the eosinophil count was normalized after 4 weeks, and the serum aldolase level was normalized after 8 weeks. [Discussion] To our knowledge, this is the first case of EF to be treated with mepolizumab. Among EF, there is a group of diseases in which mepolizumab is highly effective.

P52-2

A case of enterocolic lymphocytic phlebitis (ELP) with fever of unknown origin

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Conflict of interest: None

A 66-year-old women developed fever and increased CRP. Empiric antibiotic therapy was ineffective and she was referred to our department. On admission, she presented with abdominal pain and vomiting. Contrast-enhanced abdominal CT demonstrated small nodules and high-density mesentery fat weaving. Hyaluronic acid levels in the ascetic fluid were high. Biopsy of the sigmoid colon revealed venous vasculitis, which suggested malignancy or vasculitis. Laparoscopic biopsy of the omentum was performed, and a diagnosis of ELP was made based on the presence of lymphocytic and granulomatous phlebitis. In general, vasculitis in the gastrointestinal tract is a focal lesion of arteritis and systemic vasculitis, and it is rarely confined to the veins of the gastrointestinal tract alone. The only reported cases of ELP were treated by surgery and there are no reports of treatment using medication, making it difficult to decide on a treatment plan.

P52-3

A case of peripheral neuropathy due to HCV-associated vasculitis improved by antiviral therapy of HCV

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Conflict of interest: None

[Background] hepatitis C virus (HCV) is known to cause cirrhosis and liver cancer due to parsistent infection. Moreover, it is reported that HCV causes vasculitis. [Case] A 49-year-pld man, whose chief complaint was gait disorder. He had purpura and edema of both lower legs and hyperalgesia of the distal extremities. Neurological findings were multiple mononeuropathy. HCV antibody werw positive and serum HCV levels were high, but cryoglobulin was negative. CRP was negative and there was no increased erythrocyte sedimentation rate. Antinuclear antibodies, MPO-ANCA, PR3-ANCA were all negative. Perineural nerve biopsy showed findings of vasculitis with axonal depletion and fibrinoid necrosis with variability per nerve bundle. The patient's symptoms were refractory, but after treatment with glecaprevir hydrate/pibrentasvie tablets, the vasculitis improved markedly with a decrease in serum HCV lexels. [Conclusions] We experienced a case of peripheral neuropathy due to HCV-associated vasculitis. This case suggests that elimination of hepatitis virus and reducation of viral load by antiviral therapy are important in the treatment of hepatitis virus-associated vasculitis. Histological examination with biopsy was also important, even if the inflammatory response and autoantibodies were negative.

P52-4

A case of localized vasculitis of the gastrointestinal tract with anorexia and weight loss as initial symptom

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Conflict of interest: None

[Case] A 82-year-old woman developed anorexia and weight loss, and referred to family clinic. No abnormalities were found in laboratory test and upper gastrointestinal endoscopy. The symptoms had persisted and she revealed weight-loss of 20 kg. Four months later, she was referred to our hospital. Her Laboratory data showed elevated levels of ESR (17 mm/h), but CRP, ANA and ANCA were all negative. Contrast-enhanced CT demonstrated vascular wall thickening with contrast effect in trunk of celiac and superior mesenteric artery. FDG-PET/CT showed abnormal uptake (SUV max 3.8) at the same part. We diagnosed was localized vasculitis of the gastrointestinal tract (LVGT) after exclusion of infective and malignant diseases. Prednisolone 0.6 mg/kg/day was initiated, and then all symptoms and ESR level markedly improved. [Conclusions] LVGT is rare vasculitic disorder, however, we need to consider as one of differential diagnosis when the patient developed anorexia and weight loss. We present this case with one more past case and discuss under some literature review.

P52-5

A case of rheumatoid vasculitis presenting rapidly progressive glomerulonephritis during rheumatoid arthritis treatment

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Conflict of interest: None

The patient was a woman in the 80's, who was diagnosed with rheumatoid arthritis (RA) 6 years ago. RA was refractory despite the use of several biologics. Moderate activity continued with abatacept, prednisolone (PSL) 6 mg, and salazosulfasalazine 1 g. She presented with a 1-month history of dyspepsia, diarrhea and leg edema. Proteinuria, occult blood, and renal dysfunction were observed. Rapidly progressive glomerulonephritis (RPGN) was suspected and renal biopsy was performed. Diagnosis of RPGN was made based on cellular crescent formation. Since ANCA was negative, a history of treatment-resistant RA, hypocomplementemia, elevated immune complexes, and livedo reticularis in the lower extremities were observed, the cause of RPGN was considered to be rheumatoid vasculitis (RV). Amyloid deposits were found in the glomeruli and arterioles, and renal amyloidosis was diagnosed. Complications of gastrointestinal amyloidosis was also diagnosed by random biopsy. The dose of PSL was increased to 15 mg, and laboratory findings have been tended to improve. RV should be differentiated if RPGN findings are present during the course of treatment in refractory RA patients. There are few reports of renal lesions as organ lesions of RV, and we report this experience.

P52-6

Certolizumab Pegol-induced Immunoglobulin A Vasculitis in a Patient with Rheumatoid Arthritis

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Conflict of interest: None

[Introduction] Certolizumab pegol (CZP) is a TNF inhibitor with the unique characteristic of being a humanized Fab' fragment. IgA vasculitis has been reported as an adverse event associated with the use of TNF inhibitors, including infliximab, etanercept, and adalimumab. Here, we describe the first case of IgA vasculitis which was presumably induced by CZP. [Case] The case was a 34-year-old woman with rheumatoid arthritis who had been treated with CZP for 3 years. She had delivered a child 5 months earlier. On presentation, she had a 2-day history of abdominal pain and purpura on the lower extremities. Histological analyses of a skin specimen revealed inflammatory cell infiltrates and IgA deposits in the vessel walls of the upper dermis. Computed tomography showed ileitis. The diagnosis was IgA vasculitis, presumably associated with use of CZP. CZP was discontinued and prednisolone was administered, which promptly improved the abdominal pain and purpura. [Discussion] The cumulative immunomodulatory effects of the TNF inhibitor and the patient's postpartum status were considered to be involved in inducing IgA vasculitis. Clinicians should be aware of IgA vasculitis-related symptoms as a possible adverse effect of TNF inhibitors to ensure prompt diagnosis and appropriate treatment.

P52-7

A cases of cryoglobulinemia vasculitis (CV) suffered from rapid spread of ischemic necrosis of foot during treatment by RTX

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Conflict of interest: None

Two years ago a 66-year-old woman was diagnosed with CV because of Raynaud's phenomenon, purpura, peripheral nerve neuropathy, low serum C4, positive RF and cryoglobulin. Treatment with PSL 45 mg/day and RTX 500 mg/body improved her symptoms. PSL was tapered and discontinued while RTX was continued as a maintenance therapy. After 6 months of stopping PSL, CV relapsed with the foot drop and the dose of PSL was increased to 30 mg/day. PSL was again tapered to 6 mg/day over 1 year as symptoms improved. But motor and sensory disorders of her limbs worsened, so she was hospitalized for further treatment. CV relapse was determined based on the exclusion of other diseases, mononeuritis multiplex, positive cryoglobulin, high IgG/M and low serum C4. She was treated with steroid pulse, PSL 45 mg/day and RTX 500 mg/body. While the neurological symptoms improved, ischemia and purpura appeared on the right foot. Endovascular treatment for ischemia was performed at another hospital. The obstructed blood vessel opened temporarily but reoccluded. The cause of ischemia and necrosis in this case was thought to be thrombus formation due to vascular endothelial cell damage by immune complex deposition in the small blood vessels of the CV or increased blood viscosity caused by the contrast medium.

P52-8

Treatment of primary angiitis of the central nervous system by Mycophenolate Mofetil

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Conflict of interest: None

She is a 70-year-old female with history of polymyalgia rheumatica who presented dizziness. Head MRI showed vessel wall thickening and marked stenosis from the distal left internal carotid artery to the left middle cerebral artery with a contrast effect, and the patient was referred us for examination. Blood and cerebrospinal fluid culture were negative and there was no evidence of vasculitis on FDG-PET/CT, temporal artery biopsy or ophthalmological examination. The patient was treated with PSL 50 mg/day for primary angiitis of the central nervous system (PACNS), but a new vascular stenosis appeared in the right anterior cerebral artery. Acyclovir and minocycline were initiated to rule out vasculitis caused by herpes zoster virus (VZV) and chlamydia. Subsequently, VZV PCR and IgG antibody negativity were found and there was no change in the MRI findings, so mycophenolate mofetil (MMF) was started as an intensified treatment. 2 months after starting MMF, there was an improvement in the head MRI findings. The diagnosis of PACNS often needs exclusion diagnosis because histopathological examination cannot be performed on lesions close to the central intracranial region. It is necessary to exclude infections, especially VSV vasculitis.

P52-9

A case of adult-onset streptococcal infection-related polyarteritis nodosa with peripheral neuropathy

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Conflict of interest: None

A 55-year-old man was referred to our hospital because of numbness and weakness of the right hand. Three weeks before the admission, sore throat, fever, purpura of lower extremeties appeared. Antistreptolysin-O (ASO) titer was 1,000 IU/mL, whereas no disease-specific autoantibodies were positive. A biopsy of the skin revealed rupture of blood vessle walls and fibrinoid necrosis mainly in the muscular arteries. Nerve conduction study (NCS) showed axonal damage in the right median nerve. He was diagnosed as polyarteritis nodosa (PN) triggered by streptococcal infection. The fever and purpura disappeared promptly after high-dose corticosteroid treatment. Neurological symptoms partially relieved by high-dose intravenous immunoglobulin therapy. Although there have been some pediatric case reports of PN associated with streptococcal infection, adult case reports are rare. Only five of those cases had peripheral neuropathy, three of which reported detailed clinical courses. All these three cases were suspected of streptococcal infection on the basis of preceding upper respiratory tract symptoms or eleveted ASO, and NCS was performed in one case. Since the current case is highly rare, we will report on its clinical course with reference to the previous reports.

P52-10

A case of Buerger's disease with upper limb ischemia in anti-CCP antibody-positive woman who needed to be differentiated from rheumatic diseases

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Conflict of interest: None

[Case] 49 years old, female [Chief complaint] Cold feeling of fingers, gangrene and ulcer of fingers [Clinical course] Nine months ago, she felt coldness on left 4th and 5th fingers. 4 months ago, her condition of fingers got worse and she was diagnosed as rheumatoid arthritis (RA) due to finger stiffness and positivity of anti-CCP antibody (18.9 IU/mL), and started methotrexate (MTX) and vasodilator. Finger ulcer appeared 2 months later. Prednisolone (PSL) 7.5 mg/day was added, but ulcer progressed to gangrene. On admission to our hospital, we stopped MTX and reduced PSL because she had no arthritis. Although she had diabetes, dyslipidemia, hypertension and were a heavy-smoker, we considered ASO less likely because she did not have atherosclerotic lesions proximal to elbow and knee joints. She was diagnosed as having Buerger's disease as she was under 50 years old, and had smoking history and arterial occlusion peripheral to elbow and knee joints. We continued follow-up for natural amputation of her right 2nd finger. [Clinical significance] Buerger's disease is rare inflammatory and obstructive vascular disease and commonly affected in

young men. We report a case of middle-aged woman with Buerger's disease that required differentiation from other rheumatic diseases and ASO.

P52-11

A case of IgA vasculitis and nephrotic syndrome triggered by cytomegalovirus enteritis

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Conflict of interest: None

He has palmoplantar pustulosis arthritis and was treated with MTX 12 mg, PSL 7.5 mg, ADA 40 mg biweekly. He was treated for pneumocystis pneumonia in May. On 2nd day of discharge, abdominal pain appeared. On 3rd day bloody stool appeared and he took an OTC medicine. On 4th day, fever and purpura appeared. On 6th day, he visited us and the dermatology dept. After discontinuation of some medicines, he returned home. However, due to further worsening of symptoms, he admitted to our hospital on 7th day. We suspected IgA vasculitis and started mPSL 1000 mg pulse. The aftertreatment was sPSL 60 mg (0.8 mg/kg). He has cytomegalovirus (CMV) antigenemia. colonoscopy was performed to stop bleeding. The ileocecal inflammation was found, biopsy was consistent with CMV enteritis. A skin biopsy showed vasculitis but no IgA deposition. During the course of hospitalization, nephrotic syndrome occurred. A renal biopsy showed IgA deposition in the loop wall and the mesangium. On the other hand, intraductal proliferation was observed, which was considered atypical for IgA nephropathy. We diagnosed of IgA vasculitis and nephrotic syndrome triggered by CMV enteritis, CMV reactivated by drug induced hypersensitivity syndrome. The causes of this case are discussed and reported with literature findings.

P52-12

A case of medium-sized arterial occlusion of the left lower limbwith Sjogren's syndrome

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Conflict of interest: None

A 66-year-old woman had caused the swelling of left ankle joint since X-3 and small ulcers since X-2. She was diagnosed with lymphedema because of no detection of ANCA, Anti-phospholipid antibody, and venous thrombosis in the lower limbs. The ulcers worsened and she was admitted to our hospital in X. Anti-SS-A/B antibodies were positive and she was diagnosed with Sjogren's syndrome (SjS) based on the ophthalmological findings. Deep skin ulcers were found in her left foot. Skin biopsy revealed the infiltration of inflammatory cells in small and medium-sized vessels. Vasculitis was considered and prednisolone 1 mg/kg was started after steroid pulse. Contrast-enhanced computed tomography showed occlusion from the left anterior tibial artery to dorsal pedis artery. Although balloon dilatation was performed, blood flow in the toes was not improvedand amputation was performed at the proximal Lisfranc's joint. Cyclophosphamide pulse and balloon dilation of the posterior tibial artery was performed. These treatments were successful and she was discharged. Although about 5% of patients with SjS had small and medium-sized vasculitis, it is rare to experience patients with obstruction of a medium-sized artery based on SjS. This was a rare case in which SjS was suspected to have caused arterial occlusion.

P53-1

Twenty-five years of observation in a woman with hypocomplementemic urticarial vasculitis complicated with Jaccoud's arthropathy and valvular heart disease

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Conflict of interest: None

[Case] 50-year-old woman [History] At age of 26, she developed urticarial-like papules on her extremities, then she suffered from pain and swelling of fingers. Blood tests showed hypocomplementemia, and a biopsy of the skin rash showed leukocytoclastic vasculitis. PSL 30 mg/day was started and joint and skin symptoms improved. But with steroid reduction, symptoms relapsed, and arthritis progressed to Jaccoud's arthropathy (JA). At age of 35, she developed congestive heart failure by severe mitral regurgitation. She was transferred to our hospital for mitral valvuloplasty, but 3 years later, mitral regurgitation recurred. She underwent prosthetic valve replacement at age 40. Symptoms were then stable, but JA deformity progressed. [Discussion] 5 cases of concomitant HUVS, JA, and valvular heart disease have been reported. This case occurred with HUVS and arthritis, which led to JA and valvular heart disease over a 9 years. Although skin rash and arthritis were controlled, she required a heart valve replacement, and JA deformity progressed. When HUVS is associated with JA, regular evaluation of cardiac function is recommended. The control of JA is the future agenda. [Clinical significance] We present the first case of 25 years observation with HUVS, JA and valvular heart disease in Japan.

P53-2

A case of ANCA-associated vasculitis (AAV) complicated with jugular foramen syndrome

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Conflict of interest: None

70 years old, woman had developed hearing loss of right ear. She was referred to the department of Otorhinolaryngology in our hospital and diagnosed as otitis media with AAV. She was referred to our department, however she did not have other organ manifestations. She was treated by eardrum tube placement. Then she had developed right ear pain, hearing loss, head and neck pain, hoarseness, since next year and treated by antiviral drugs as herpes virus infection. Her symptoms had not improved. On admission, she had developed fever, weight loss, muscle weakness of right face, pharyngeal dyskinesia, dysphagia. These symptoms suggested multiple cranial nerve paralyses on of VII to XI nerves. Enhanced MRI showed no evidence of pachymeningitis, but ^{18}FDG-PET showed uptake on jugular foramen. We diagnosed jugular foramen syndrome by necrotizing granulomatous lesion of AAV and started administration of high dose glucocorticoid and intravenous cyclophosphamide. Her symptom improved gradually. Cranial nerve (CN) palsy is rare manifestation in AAV. Some cases of CN palsy were reported as necrotizing granulomatous lesion of cranial base, and our case seems to be caused by a similar mechanism. We report a rare case of AAV complicated with jugular foramen syndrome.

P53-3

A case of systemic scleroderma complicated by microscopic polyangiitis (MPA) resulting in intraperitoneal hemorrhage from the upper pancreaticoduodenal artery

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Conflict of interest: None

A 69-year-old woman diagnosed systemic scleroderma in X-7, due to Raynaud's and skin sclerosis and anti-centromere and anti-RNA poly-

merase III antibodies positive. On March in X, she was referred to our hospital for fever, dyspnea, exacerbation of IP and MPO-ANCA positivity. We diagnosed MPA due to rapid decline in renal function and occult urine, and treat by steroid pulse therapy and cyclophosphamide pulse therapy, slowly improved. However, on 10th day abdominal pain and hypotension occurred suddenly, and contrast-enhanced CT showed bleeding with extravasation around the pancreatic head. Angiography showed multiple caliber irregularities and extravasation in superior pancreaticoduodenal artery and thromboembolization was performed. It was thought to be due to MPA and a steroid pulse was administered again. She was later complicated by opportunistic infections and other complications, but she was in remission after PSL tapering and the addition of azathioprine, and was transferred to the hospital on 124th day. ANCA-associated vasculitis is a small form of vasculitis that rarely causes inflammatory changes in medium-sized vessels. This is a valuable case, and we report the case with reviews of the literatures.

P53-4

A case of variable size vasculitis showing left gastric arterial aneurysm rupture and left subclavian artery stenosis accompanied by microscopic polyangiitis

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Conflict of interest: None

A 74-year-old man was presented with lower extremity weakness. His laboratory data showed high C reactive protein, low albumin, proteinuria, and hematuria. He was diagnosed as microscopic polyangiitis (MPA) from MPO-ANCA positivity, progressive renal insufficiency, interstitial pneumonia, and lower leg livedo reticularis. Prednisolone (PSL) 60 mg/day was given. Although he had positive anti-nuclear antibody (Speckled x640, Nucleolar x160), and positive anti-RNA polymerase 3, he had no connective tissue disease other than MPA. On day 14, he was suffered by sudden epigastric pain. Contrast enhanced CT revealed that his left gastric arterial aneurysm ruptured. Bleeding was stopped by intravascular treatment. PSL was rapidly tapered, and intravenous cyclophosphamide was added. On day 52, he realized blood pressure difference between his left and right arm. Magnetic resonance angiography showed severe stenosis at beginning of left subclavian artery. Additional treatment, such as mycophenolate mofetil or azathioprine, caused adverse events and had to be withdrawn. The difference of left-right blood pressure has been deteriorating. MPA's medium- and large-size vessel lesions are rare. We report this case, which is meaningful about MPA with medium- and large-size vasculitis.

P53-5

A case of ANCA-associated vasculitis with perihepatitis

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Conflict of interest: None

[Case] A 72-year-old woman had a persistent fever and right hypochondrial pain. However she received antibiotic treatment at a nearby medical clinic, high inflammatory response was continued. She visited our hospital. We suspected ANCA-associated vasculitis (AAV) because she had findings of lower purpura and left interstitial pneumonia, with CRP 7.9 mg/dL and MPO-ANCA 22520 IU /mL. We found leukocytoclastic vasculitis by skin biopsy and pauci-immune-type crescetic glomerulonephritis by renal biopsy. We diagnosed with systemic AAV. A contrast-enhanced CT scan showed an early enhanced area along the surface of the right lobe of the liver, suspected of perihepatitis. We started treatment with PSL 30 mg /day. After starting treatment, physical findings and MPO-ANCA titer was improved. 40 days after treatment, CT scan examination also showed improvement. [Discussion] We presume that the perihepatitis was due to AAV because her perihepatitis was improved by steroid treatment alone without antibiotics. AAV is a necrotizing vasculitis of small blood vessels and is known to cause various symptoms throughout the body such as peritonitis, but there were no reports of perihepatitis due to AAV in the past. We report this case as a suggestive case for considering the pathophysiology of AAV.

P53-6

A case of peripheral T/NK cell lymphoma with multiple skin ulcers and skin vasculitis

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Conflict of interest: None

A case report: A 67-year-old man with a diagnosis of MDS in 2011 developed painful erythema reticulata and purpura on his elbow, lower leg, left toe, and ear in February 2018, which became multiple ulcers. Non-specific peripheral T-cell lymphoma (PTCL-NOS) was suspected by a skin biopsy and treatment with 30 mg/day of prednisolone (PSL) was successful, but 8 months later, intractable nasal bleeding appeared and multiple skin ulcers also flared up. Because the vasculitis was found by the second skin biopsy, the patient was referred to our hospital. Biopsies again from the skin and nasal mucosa showed small and medium vessel necrosis and thrombus occlusion in some areas. Combined with episodes of skin symptoms worsening in winter and improving slightly in spring, he was suspected with cryoglobulinemic vasculitis. He was treated with PSL 55 mg/day (1 mg/kg) but the skin symptoms did not improve and additional skin biopsies showed no evidence of vasculitis. Upon re-evaluation of his previous pathology, flow cytometry showed a predominance of CD56+ expression but negative for EBER, the diagnosis was made as peripheral NK/T-cell lymphoma (unclassifiable). He was subsequently treated with CHOP and GDP therapy, and his skin ulcers improved.

P53-7

Our experience of mononeuritis multiplex of ANCA-associated vasculitis

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Conflict of interest: None

[Objective] Mononeuritis multiplex is a common manifestation in ANCA-associated vasculitis (AAV). [Methods] This study enrolled AAV patients with the clinical records including the mononeuritis multiple between April 2014 and September 2019. We collected the date about the dysfunction and the course of treatment. [Results] Of five patients enrolled in this study, four were female and the mean age was 67.6 years old. MPO-ANCA was present in three patients. Two patients were diagnosed with microscopic polyangiitis and four with eosinophilic polyangiogenic granulomatosis. Mean BVAS was 23.8, all presenting with peripheral neuropathy. Two patients each had pulmonary involvement or gastrointestinal involvement. The mean interval between the onset of mononeuritis multiplex and the start of the treatment was 12.4 days. In combination with glucocorticoids, 3 patients received cyclophosphamide (CY), one patient each was treated with azathioprine (AZA) or rituximab (RTX), four patients with intravenous immunoglobulin therapy (IVIG). The mean of number of muscles with MMT scores of three or less decreased from 5.8 to 3.2 after the treatment. [Conclusions] Early treatment combined with glucocorticoids and immunosuppressants was effective for mononeuritis multiplex of ANCA-associated vasculitis.

P53-8

A Case of Hypertrophic Pachymenigitis Possibly Derived from Granulomatous Vasculitis

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Conflict of interest: None

[Case] A man in his 30s presented with a 1-month history of left side headache. Brain MRI revealed supratentorial diffuse linear pachymeningeal thickening with contrast enhancement as well as the findings consistent with mastoiditis. He was initially treated with antibiotics, but his headache deteriorated. An open pachymeningeal biopsy was performed and showed extensive fibrosis of the dura and inflammatory infiltrate but no evidence of IgG4-related disease. A vasculitis-related hypertrophic pachymeningitis (HP) was suspected, and he was referred to our hospital. Because he had no other manifestations suggesting vasculitis or serum ANCA, the biopsy specimen was sent to the "JPVAS vasculitis pathological diagnosis consultation". In addition to the fibrous thickening of dura, perivascular lymphocytic and histiocytic infiltrate with some multinucleated giant cells were the predominant features, which implied granulomatous vasculitis. However, they lacked clear features of necrotizing vasculitis. He was treated with prednisolone, and his headache immediately disappeared. [Clinical significance] Although this case was considered most possibly ANCA-negative granulomatosis with polyangiitis, decisive evidence was not obtained. Similar cases might have been diagnosed as idiopathic HP.

P53-9

Two cases of Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis with orbital tip syndrome

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Conflict of interest: None

(Case 1) A 92-year-old man. One year prior to admission, the patient had been treated with prednisolone (PSL) for granulomatosis with polyangiitis (GPA). One month prior to admission, the patient developed right eye vision loss and right eyelid ptosis. Upon admission and further investigation, the patient's physical examination revealed that the right eye has a visual acuity of only light perception, eyelid ptosis, eye movement disorder, and light reflex loss. (Case 2) An 87-year-old woman. A few months prior to admission, the patient experienced numbness in the left upper and lower limbs with developing right eyelid ptosis and diplopia. Upon admission and further investigation, the patient's physical examination revealed right eyelid ptosis, eye movement disorder, mydriasis, and light reflex loss. She was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). (Discussion) Orbital apical syndrome is a syndrome in which the cranial nerves running through the optic nerve tract and the upper orbital fissure are easily affected resulting to visual impairment, ptosis, diplopia, and facial pain. It should be taken into consideration that ANCA-associated vasculitis is one of the causes of orbital tip syndrome.

P53-10

A case of Otitis Media with ANCA-Associated Vasculitis presented with severe bilateral hearing loss

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Conflict of interest: None

A 81 year-old woman presented with progressive bilateral hearing loss and ear pain. She was diagnosed as otitis media and treated with antibiotics and ventilation tubes; however, she was not improved. At another hospital, she was diagnosed with otitis media with ANCA associated vasculitis because serum P-ANCA was elevated. Her otitis media was improved by glucocorticoids treatment but relapsed after discontinuing glucocorticoids. When she was admitted to our hospital due to refractory otitis media, temporal bone CT scan presented soft shadows in the bilateral middle ear and mastoid cavity. Pure tone audiometry showed mixed hearing loss of about 100 dB on both sides. We started immunosuppressive therapy with glucocorticoid and cyclophosphamide. After the treatment, the pure sound hearing test showed the improvement of her hearing loss up to 60 dB on both sides. Temporal bone CT scan also showed the improvement in bilateral middle ear and mastoid cavity. In this case, her hearing loss was improved by early combined therapy with glucocorticoids and immunosuppressants for otitis media with ANCA associated vasculitis and the disease is considered to be important differential diagnosis in case of refractory otitis media.

P53-11

Central retinal artery occlusion in an eosinophilic polyangiitis granulomatosis patient

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Conflict of interest: None

[Case presentation] 61-year-old woman [Chief complaint] rash, drop feet and right vision loss [Current medical history] In 2018, she developed bronchial asthma. In June 2020, she admitted to our hospital with complaints of numbness in both feet and drop feet. Physical examination revealed erythema in both palms and right vision loss (10 cm index valve). Blood tests showed an elevation of eosinophils (9700/μL), CRP, IgE, and IgG4. A skin biopsy of palm showed extravascular granuloma and the diagnosis of eosinophilic polyangiitis granulomatosis (EGPA) was made. Vision loss was diagnosed as central retinal artery occlusion (CRAO). She was treated with steroid pulse, prednisolone, cyclophosphamide pulses, intravenous immunoglobulin, and azathioprine. Her symptoms and blood tests improved. Her right visual acuity improved to 0.02. Her bilateral drop foots remained. [Discussion] Ocular manifestations of EGPA were categorized into two groups: idiopathic orbital inflammation-type and ischemic vasculitis-type. There are some case reports of effective early aggressive immunosuppressive treatment of ocular manifestations. We report a case of an ischemic type patient with improvement in vision loss with early immunosuppressive treatment.

P54-1

A Case of Primary Sjögren's Syndrome with Pulmonary Hypertension

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Conflict of interest: None

[Case] A 55-year-old woman presented with Raynaud's phenomenon from 20 years ago, and dryness of the mouth and eyes from 17 years ago. She has had dyspnea during exertion from 1 year ago. Abnormal hypertension, proteinuria and X-ray abnormality were pointed out in the medical check-up and she was admitted to our hospital. Increased second heart sound and fine crackles were heard on auscultation. Chest X-ray showed cardiac enlargement, left second arch protrusion, and diffuse ground-glass appearance. Lymphopenia, hypoalbuminemia, hypergamma globulinemia were observed. A definitive diagnosis of Sjogren's syndrome was made based on labial gland biopsy, decreased tear / saliva secretion, and positivity of anti-SS-A and anti-SS-B antibody. Echocardiography showed a high estimated right ventricular systolic pressure of 43 mmHg, and right heart catheterization revealed pulmonary arterial hypertension (meanPAP 44 mmHg). The treatment by oral prednisolone and intravenous cyclophosphamide was started. Tadalafil was initiated. The symptoms were alleviated. The estimated RVSP dropped to 32 mmHg, and proteinuria disappeared. [Discussion] It had been reported to be rare that primary Sjogren's syndrome is complicated by PAH. We report on its clinical features with review of the literature.

P54-2

CD127 expression in PBMCs and lymphocytes in Japanese and Caucasian populations healthy volunteers and primary Sjögren syndrome patients

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Conflict of interest: Yes

[Objective] IL-7 is produced by epithelial and stromal cells and regulates T cell proliferation and survival. IL-7 signals through the cell-surface IL-7 receptor (IL7R) formed by IL7Rα (CD127) and γ chain (CD132). Increased expression of IL-7 and IL7R is suggested to play critical role in salivary gland tissue of primary Sjögren's syndrome (pSS). We studied CD127 expression in PBMC in Japanese and Caucasian healthy volunteers (HV) and pSS patients. [Methods] PBMC in Japanese and Caucasian HV (n=30 and 33) and pSS patients (n=5 and 10) were isolated. Number of CD127 mAb per cell was assessed using indirect immunofluorescence assay (QIFIKIT®). [Results] The ratios of PBMC and lymphocytes were similar between Japanese and Caucasian HV. CD127 expression in PBMC of HV were similar and no difference between the races. CD127 expression in PBMC of pSS tended to be lower than HV, but no significant difference. [Conclusions] There've been reports of CD127 expression in salivary gland tissue of pSS, but no reports in peripheral blood lymphocytes. In this study, there was a trend of lower CD127 expression in pSS that may be linked to cell infiltration in the tissues. These results will help to develop future pSS treatment targeting IL7R. Dr Murakami of Sumida Hospital helped for sample collection.

P54-3

A case of primary Sjögren's syndrome (SjS) mimicking multicentric Castleman's disease (MCD)

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Conflict of interest: None

[Case Report] A 34 year-old woman visited a hospital due to intermittent fever and arthralgia in July 2017. Inguinal and axillary lymphadenopathy and hyperglobulinemia were found. Anti SS-A antibody was positive, but sicca symptom was unclear, so MCD was firstly suspected. A right axillary lymph node biopsy showed follicular hyperplasia without any of germinal central atrophy, hyaline vasucular proliferation, or interfollicular plasma cell proliferation. Five months later, she underwent re-biopsy at left axilla because of elevated serum IL-6 level, but there were the same findings. Her symptom once diminished, but recurred in February 2020. She was referred to us in July 2020. Rf and ACPA was negative. ANA was 40 X (Speckled). Anti SS-A antibody was 258 U/ml. Anti-Sm, ds-DNA, and RNP antibody was negative. IgG4 was 61 mg/dl. There was no evidence of dry eyes, but decreased saliva in gum test, low uptake at salivary glands in scintigram, and Greenspan grade 3 in lip biopsy made our diagnosed of SjS. [Discussion] Reports of SjS mimicking MCD are limited. We think poor sicca symptom is a cause of delayed diagnosis. In the differential diagnosis from MCD, this case suggests importance of a lymph node biopsy and tests for salivary or lacrimal glands regardless of sicca symptom.

P54-4

A case of Sjögren's syndrome with thrombotic thrombocytopenic purpura preceded by painful erythema

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Conflict of interest: None

[Case] 45-year-old woman. May X-11 year Sjogren's syndrome was diagnosed. August 19, X year Painful erythema was found on the lower leg. A skin biopsy was performed, but the diagnosis of erythema nodosum was not made due to insufficient adipose tissue, but it was clinically judged to be erythema nodosum, but there was no exacerbation. On September 19, epigastric pain, vomiting, hematuria, and oral bleeding were noted, and the patient visited the hospital outside the appointment. Plt 20,000 / μl, Hb11.1 g / dL, Tbil3.7 mg / dL, Dbil0.7 mg / dL, LDH3985 IU / l, Cre1.32 mg / dL, crushed red blood cells 1.3%, direct Coombs Test positive, ADAMTS13 activity 1%, ADAMTS13 inhibitor 1.9 BU / mL. The patient was diagnosed with thrombotic thrombocytopenic purpura based on the decrease in ADAMTS13 activity and the results of ADAMTS13 inhibitor. After steroid pulse (mPSL1g) and performing plasma exchange, platelets improved, so plasma exchange was completed on October 1, but decreased to Plt 19,000 / μl on October 4. Since it increased to LDH650 IU / l, RTX375 mg / m2 was administered 4 times from October 10, and plasma exchange was withdrawn. [Conclusion] We reported a case of Sjogren's syndrome in which painful erythema preceded thrombotic thrombocytopenic purpura.

P54-5

Childhood Sjögren's syndrome with decreased salivary production at diagnosis: a report of two cases

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Conflict of interest: None

[Background] Childhood Sjögren's syndrome tends to bepresent with no lack of subjective sicca symptoms. [Case report] Case 1 was that of a 15-year-old woman girl who was followed with thrombocytopenia followed-up for 16 months. Anti-SS-A/Ro antibody was detected 44 months before consultation. Anti-nuclear antibody titer was 1:80 (homogeneous, speckled), the Schirmer's test was 25 mm, Saxon' test result was 1.04 g/2 min, unstimulated salivary production was 1.2 ml/15 min, serum IgG level was 1617 mg/dl. Focus score on labial salivary gland biopsy showed 0.48. Case 2 was that of a 12-year-old woman girl who was diagnosed with aplastic anemia 8 years before consultation, and anti-SS-A/Ro antibody was first detected 4 months prior. Anti-nuclear antibody titer was 1:80 (homogeneous, speckled), the Schirmer's test was 8 mm, Saxon' test result was 2.12 g/2 min, unstimulated salivary production was 1.5 ml/15 min, serum IgG level was 1837 mg/dl. Focus score on labial salivary gland biopsy showed 0.68. [Conclusion] Both patients showed mild sicca symptoms subjectively. To diagnose childhood Sjögren's syndrome early, we should evaluate objective sicca symptoms for in patients who has with abnormal laboratory data including leukopenia and hypergammaglobulinemia.

P54-6

Association of peripheral T cell subsets with clinical features in patients with primary Sjögren's syndrome

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Conflict of interest: None

[Objective] To clarify the association of peripheral T cell subsets with clinical features in patients with primary Sjögren's syndrome (pSS). [Methods] 1) We compared the population of each peripheral memory $CD4^+$T cell subset ($CD45RA^-CD4^+$), including Th1 ($CXCR3^+CXCR5^-CCR6^-$), Th17 ($CXCR3^-CXCR5^-CCR6^+$), Th17.1 ($CXCR3^+CXCR5^-CCR6^+$), Tfh1 ($CXCR3^+CXCR5^+CCR6^-$), Tfh2 ($CXCR3^-CXCR5^+CCR6^-$), and Tfh17 ($CXCR3^-CXCR5^+CCR6^+$), between 20 pSS patients (56.7±19.2 years old, Male 3/Female 17, no immunosuppressive therapy) and 10 healthy controls (HCs) (41.7±11.2 years old, M3/F7). 2) Correlation between clinical parameters and each peripheral T cell subset population was analyzed in pSS patients. [Results] 1) Peripheral Th1 cells were significantly decreased ($p=0.004$), while Tfh1 ($p=0.007$) and Tfh17 ($p<0.0001$) cells were significantly increased in pSS patients than in HCs. 2) Among 20 pSS patients, ESSDAI score was 5.3±3.5, the positivity of anti-SS-A antibody was 80%, and serum IgG was 2007.5±710.2 mg/dl. The population of peripheral Th1 cells significantly and negatively correlated with serum IgG ($p=0.03$). [Conclusions] We found that the population of peripheral Th1, Tfh1, and Tfh17 cells differed between pSS patients and HCs, and that decreased Th1 cells negatively correlated with serum IgG in pSS.

P54-7

A case of Sjögren's syndrome with brainstem encephalitis

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Conflict of interest: None

[Objective] Neuropathy caused by SS develops with variety of symptoms. The diagnosis of SS must be made with caution because there are cases with preceding neurological symptoms. We report a case of SS with brainstem encephalitis that was preceded by acute neurological symptoms that improved with immunosuppressive therapy. [Case] 50-year old man [History of present illness] He became aware of diplopia, lightheadedness, and numbness in his right upper extremity since May 2020. MRI scan showed a contrast effect in the brainstem area. Examination ruled out infection, malignancy, and stroke. Autoimmune-mediated encephalitis was suspected and intravenous methylprednisolone and oral prednisolone were started, but he was transferred to our department due to worsening symptoms. [Passage] The diagnosis of Sjögren's syndrome (SS) was made based on positive anti-SS-A and anti-SS-B antibodies, positive Saxon test, and findings of hyposalivation of the salivary glands. We increased the prednisolone dose and administered intermittent intravenous cyclophosphamide therapy. The neurological symptoms and imaging findings improved after intensified treatment, and the patient progressed without worsening of symptoms in the taper of prednisolone.

P54-8

Successful treatment with hydroxychloroquine for refractory interstitial lung disease associated with primary Sjogren syndrome

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Conflict of interest: None

[Case] A 53-year-old female had been followed by our department under the diagnosis of Sjogren syndrome (SjS) and autoimmune hepatitis for 2 years, and had been treated with prednisolone (PSL) at 4 mg/day. She suffered exertional dyspnea and was diagnosed with SjS-associated interstitial lung disease (ILD), based on the elevated levels of KL-6 and diffuse ground glass opacity revealed by a chest CT scan. Because her symptoms and hypoxemia worsened even after increasing the PSL dosage to 35 mg/day, she was admitted to our department and was treated with methylprednisolone pulse, intravenous cyclophosphamide (IVCY) and tacrolimus. However, her state was further exacerbated, and she was complicated with cytomegalovirus infection during the treatment. Therefore, IVCY and tacrolimus were discontinued and hydroxychloroquine (HCQ) was added along with PSL. This treatment resulted in marked improvement of her symptoms and lung shadows. She was discharged after the introduction of home oxygen therapy. [Discussion] The overproduction of type 1 interferon (IFN) by plasmacytoid dendritic cells (pDCs) involves in the pathogenesis of SjS. HCQs, acting on pDC endosome and nucleic acids to suppress type 1 IFN production, may have a potential to improve refractory SjS-associated ILD.

P54-9

Three cases of pulmonary hypertension associated with Sjögren's syndrome treated with immunosuppressive therapy

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Conflict of interest: None

We report 3 patients with Sjögren's syndrome treated with immunosuppressive therapy due to complications of pulmonary hypertension. [Case 1] 46 years old female. She had a 6 years history of Sjögren's syndrome with Raynaud phenomenon, skin rash, dry eyes, dry mouth, positive anti SS-A antibody, and positive RF. She was diagnosed with group 1 pulmonary hypertension. PSL and macitentan were initiated and responded well. [Case 2] 80 years old female. She was diagnosed as Sjögren's syndrome and systemic sclerosis with dry eyes, dry mouth, interstitial pneumonia, Raynaud phenomenon, positive anti SS-A/B antibodies, anti centromere antibody, anti Scl-70 antibody 2 years and 3 months ago. Pulmonary hypertension in groups 1, 2, and 3 was noticed and upfront combination therapy was initiated but did not respond well. So we started steroid therapy which had a good effect. [Case 3] 63 years old female. She had a 15 years history of Sjögren's syndrome and systemic sclerosis with Raynaud phenomenon, dry eyes, dry mouth, skin sclerosis, interstitial pneumonia, positive RF and anti centromere antibody. She was diagnosed with pulmonary hypertension in group 1 and 3, and PSL and MMF were started but did not respond well. We report 3 cases with a literature review.

P54-10

A case of Sjögren's syndrome with systemic lupus erythematosus that developed various autonomic neuropathy including segmental anhidrosis

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Conflict of interest: None

The case was a 68-year-old man. He had SLE for 40 years, and his condition was stable for more than 20 years after administration of PSL 5 mg every other day. Urinary retention due to neurogenic bladder developed from early July X, and anhidrosis developed from mid-July of the same year. In the end of July, dry mouth appeared, anti-SS-A antibody was positive, and strong monocyte infiltration into the minor salivary glands was confirmed by lip biopsy, and a definitive diagnosis of Sjogren's syndrome was made. Although there was a cutaneous vascular reaction, the sympathetic skin sweating reaction had disappeared. Skin biopsy showed mild sweat gland atrophy but no lymphocyte infiltration. The thermal sweating test showed segmental sweating. The tendon reflex was normal. Nerve conduction studies showed normal MCAP and SNAP. No organic abnormalities were found in the bladder or urethra. From the above, it was suggested that this case had a disorder of the autonomic ganglion preganglionic fibers. Steroidal pulse therapy was effective, and anhidrosis and urinary retention improved. In this case, it is suggested that the disorder is different from the previously reported one, and we report it together with the literature review.

P54-11

Two cases of Sjögren's syndrome (SS) complained with rapid systemic edema due to capillary leak syndrome

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Conflict of interest: None

[Case 1] 57 y.o., male. Diagnosed with dermatomyositis (DM) 5 years ago. Clinical remission was achieved and daily 1 mg of prednisolone (PSL) was continued during 5 years. One week after emergency cholecystectomy, systemic edema, ascites and eruption were appeared. Worsening of DM was suspected, PSL dose was increased up to 1 mg/kg/day, however, his condition was getting worse. According to clinical history and anti ss-A antibody, association of SS was suspected. Steroid pulse therapy was initiated, but it did not work well. Further immunosuppressive therapy could not be performed because of opportunistic infection. At day 60, he was died. [Case 2] 76 year old male was admitted to hospital for systemic edema, pleural effusion and dyspnea 4 months before. Administration of diuretics made his condition better temporally, however, his symptoms flared up again. According to the biopsy of pleura revealed aggregates of lymphocytes and anti ss-A antibody, he was diagnosed as SS. Fifty mg of prednisolone was administered and intravenous cyclophosphamide (IVCY) was initiated. After 4 courses of IVCY, pleural effusion was diminished. [Discussion] From our experience of these cases, insufficient immunosuppression lead to a poor outcome. Early assessment of critical condition will be required.

P54-12

A Case of Sjögren's syndrome with deletion of the Long Arm of Chromosome 20

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Conflict of interest: None

[Case] 65-year-old woman who complained swelling of the eyelids [Current medical history] From around X-1, Swelling of the eyelids were noticed. From June X, slight fever, dry mouth, and dry eye appeared. Laboratory data showed CRP 0.13 mg/dL, IgG 2634 mg/dL, IgG4 6.1 mg/dL, antinuclear antibody 320 times (speckled pattern). Autoantibodies such as Anti-SS-B/La antibody were positive. Lip biopsy showed infiltration of lymphocytes and plasma cells around the salivary glands. Sjögren 's syndrome was confirmed. Meanwhile, immunoelectrophoresis was performed, which revealed IgG-λ type M protein. Bone marrow examination revealed non-IgM monoclonal gammopathy of undetermined significance (MGUS). Chromosome examination revealed a deletion of the long arm of chromosome 20 (Del (20q)). [Clinical Significance] We experienced a case of MGUS with chromosomal abnormalities and autoimmune disease. Del (20q) has been reported in myelodysplastic syndrome and multiple myeloma. The deletion site contains molecules related to immune diseases such as adenosine deaminase, Serine/Threonine Kinase 4. There are few reports on the comorbidity of a Del (20q) and autoimmune diseases. Going forward, it will be important to accumulate the information for autoimmune diseases with chromosomal abnormalities.

P55-1

The significance of serum cholinesterase activity in IgG4-related disease

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Conflict of interest: None

[Objective] We often experience the cases of IgG4-related disease (IgG4RD) with low serum cholinesterase (ChE) activity. These cases demonstrated that the serum ChE activity before and after treatment changed in accordance with the improvement of organs' enlargement and serum IgG4 level. Therefore, we studied about the significance of serum ChE activity in IgG4RD cases. The objective is to clarify the significance of serum ChE activity in IgG4RD. [Methods] The clinical characteristics and number of organ involvements in 30 Japanese patients with IgG4RD were retrospectively assessed and also compared with healthy subjects. [Results] Fourteen of 30 IgG4RD cases had significantly lower levels of serum ChE activity (131.9±42.7 U/L) than those of other 16 IgG4RD cases (328.2±61.7 U/L) and healthy subjects ($p<0.05$). Moreover, IgG4RD group with low ChE activity (4.3±1.3) had more number of organ involvements than IgG4RD group with normal ChE activity (1.9±1.3) ($p<0.05$). In IgG4RD group with low ChE activity, ChE levels all improved after steroid treatment and correlated with disease activity. [Conclusions] Serum ChE activity might be a potential novel predictive markers of the extension of the lesions and the disease activity in IgG4RD.

P55-2

A case of IgG4-related disease with immune thrombocytopenic purpura and autoimmune neutropenia

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Conflict of interest: None

A 57-year-old man with pancytopenia was referred to our hospital. An computed tomography (CT) scan showed systemic lymphadenopathy, splenomegaly, masses in the bilateral renal pelvis, swollen kidneys, and multiple low-density lesions in the renal parenchyma. A positron emission tomography-CT scan revealed abnormal uptake in those lesions. We diagnosed him with autoimmune neutropenia (AIN) due to positive anti-neutrophil antibodies, and thrombocytopenia caused by immune thrombocytopenic purpura (ITP) based on the results of the bone marrow biopsy. He was treated with high-dose immunoglobulin, eltrombopag, and dexamethasone pulse therapy. However, none of them resulted in the improvement of cytopenia. He was treated with splenic irradiation and that was successful for recovering cytopenia. We performed a renal biopsy, and finally diagnosed IgG4-related interstitial nephritis. He was treated with prednisolone, thereby marked improvement in pancytopenia and imaging findings. As far as we searched, there have been 16 reports of IgG4-RD with ITP, and one report of IgG4-RD with ITP and AIN. Mass lesions in the renal pelvis have been described only in 12 reports. We here report a case of IgG4-RD with ITP that was successfully treated with splenic irradiation and confirmed by renal biopsy.

P55-3

A case of IgG4-related disease that caused splenomegaly and thrombocytopenia due to narrowing of the splenic vein caused by spreading of autoimmune pancreatitis

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Conflict of interest: None

[Introduction] IgG4-related disease is a systemic chronic inflammatory disease characterized by high serum IgG4 levels and infiltration of IgG4-positive plasma cells into some organs. However, reports of splenomegaly complicated by thrombocytopenia are rare. [Case] A 73-year-old woman became aware of a bimaxillary swelling and visited our hospital in March 2014. Submandibular gland biopsy revealed ≧50% IgG4-positive cells. Computed tomography (CT) showed swelling of the pancreatic tail, and the levels of IgG4 were high (195 mg/dl). Hence, the patient was diagnosed with IgG4-related disease. After 6 months, CT showed an increase in pancreatic tail swelling, as well as splenomegaly, caused by stenosis of the splenic vein; the platelet count also tended to decrease. The levels of platelet-associated-IgG were 133 ng/10^7 cells. Pancreatic tail swelling and splenomegaly improved following the administration of prednisolone 40 mg/day, and the platelet count also recovered. [Discussion] Through imaging, stenosis of the splenic vein associated with pancreatic swelling was considered the cause of splenic hyperactivity and thrombocytopenia. The spleen is a rare site of IgG4-related disease. However, attention is necessary for patients presenting with splenomegaly and thrombopenia.

P55-4

A case of IgG4-related disease with large and small vasculotides

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Conflict of interest: None

(Case) A 76-year-old male complained of fever, fatigue, and loss of appetite. Enlargement of bilateral lacrimal glands and pituitary swelling was detected on CT images. A blood test showed high serum IgG 2542 mg/dl and IgG4 616 mg/dl, suggesting IgG4-related disease (IgG4-RD). In addition, contrast-enhanced CT showed diffuse thickening of the abdominal aortic and coronary arterial wall, multiple poorly enhanced lesions of right renal cortex. Furthermore, contrast-enhanced MRI images showed a uniform contrast effect on the pituitary gland, and coronary CT angiography showed soft tissue swelling outside coronary artery. These findings were consistent with IgG4-related hypophysitis and coronary vasculotides. Right renal pathological findings showed tubular interstitial nephritis and massive infiltration by IgG4-positive plasma cells. So, we diagnosed

IgG4-RD with coronary and abdominal vasculotides from comprehensive diagnostic criteria of IgG4-RD 2011. (Clinical Significance) In this case, an accidentally detected pituitary swelling and intraorbital mass led to IgG4-related coronary vasculotide. Coronary vasculotide is found in about 5% of IgG4-RD. It was significant to search not only abdominal artery but also small blood vessels including coronary vasculotides in IgG4-RD.

P55-5

A case of IgG4-related disease with perineuritis

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Conflict of interest: None

A 78-year-old man was aware of blindness in his right eye when he got up. He visited an ophthalmologist, but cause didn't know. His right vision is down to 0.04. Peripheral visual stenosis and paracentral dark spots were observed. There were no abnormalities in the anterior and fundus findings. He was referred to our department for a high serum IgG4 212 mg/dL with low right vision. He was started with 30 mg in oral PSL for acute low vision, and viaspirin 100 mg/day for suspected ischemic optic neuropathy. Orbital MRI and abdominal CT revealed perineuritis and superior mesenteric periarteritis with IgG4-related disease (IgG4-RD). After PSL, right visual acuity improved from 0.04 to 0.80. Serum IgG4 decreased to 84 mg/dL. He started to combinate with azathioprine 50 mg/day. (Clinical Implications) Perineuritis causes inflammatory optic nerve sheath, and secondary perineuritis is caused by polyangiitis granulomatosis, IgG4-RD, Crohn's disease, and Behcet's disease, but perineuritis associated with IgG4-RD is very rare. Because of the high recurrence rate and the poor prognosis of delayed treatment, it is important to distinguish between optic neuritis and perineuritis. As in this case, perineuritis with only visual loss should be considered such as IgG4-RD.

P55-6

A case of a lumbar spine epidural mass requiring differentiation between plasmacytoma and IgG4-related disease

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Conflict of interest: None

Objective: IgG4-related diseases (IgG4-RD) are characterized by significant infiltration and fibrosis of lymphocytes and IgG4-positive plasma cells, resulting in swelling and nodal involvement of various organs throughout the body. In this article, we report a case of a rare IgG4-RD that formed an epidural mass and required differentiation from a plasmacytoma, with a discussion of the literature. Case: 40 years old, female. The patient presented with back pain from early June 2020. From June 25, the abnormal sensations moved up to the pericardial region; from June 30, electric doctor. A spinal MRI was performed, which revealed a mass lesion in the lumbar epidural, and the patient was admitted to the hospital on the same day; an epidural mass resection was performed on July 1. Pathological examination showed a number of IgG4-positive cells, and she was suspected to have an IgG4-RD. Additional immunostaining was performed at our hospital to differentiate it from plasmacytoma: the ratio of IgG4-positive cells to IgG-positive cells was 65%, the number of IgG4-positive cells was more than 10 cells per HPF, the kappa/lambda ratio of IgG4-positive cells was similar, no monoclonal cell proliferation was observed, and plasmacytoma was negative. The diagnosis of IgG4-RD was made.

P55-7

IgG4-Related Disease Complicated by Brain Parenchymal Lesions Successfully Treated with Corticosteroid Therapy: A Case Report

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Conflict of interest: Yes

A 62-year-old Japanese male was admitted to our hospital for abdominal discomfort and altered consciousness. He has shown no major neurologic abnormalities except for drowsiness, urinary retention, and fecal incontinence. The serum IgG4 levels were elevated and systemic lymph nodes were enlarged. Brain magnetic resonance imaging has shown scattered hyperintense signals in the brain parenchyma. Biopsy from inguinal lymph nodes has shown massive infiltration of IgG4-positive plasma cells: the ratio of IgG4-positive/IgG-positive plasma cells was nearly 100%. He was diagnosed as IgG4-related lymphadenopathy based on the laboratory and pathological findings. After steroid therapy, the remarkable clinical responses in the parallel with the decrease of serum IgG4 level. Moreover, brain MRI 1 month after the steroid therapy initiation has shown a complete disappearance of the hyperintense lesions in brain parenchyma. These findings supported the diagnosis of IgG4-RD that is related to the brain parenchymal lesions. Central nervous system lesions such as brain parenchymal lesions associated with IgG4-RD are scarce. However, IgG4-RD should be considered in patients with elevated serum IgG and IgG4 levels, accompanying brain parenchymal lesions as well as systemic symptoms.

P55-8

Two case of IgG4-related disease complicated by lung cancer

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Conflict of interest: None

Pulmonary lesions in patients with IgG4-related disease (IgG4-RD) are sometimes difficult to differentiate IgG4-related respiratory disease (IgG4-RRD) from malignancies. We have recently encountered two cases of IgG4-RD with pulmonary lesions, which proved to be malignant after resection. The first case is 79-year-old man diagnosed histologically as IgG4-RD from mediastinal enlarged lymph nodes. Five months later, pulmonary mass presented increase in size, and diagnosed as squamous cell carcinoma after resection. The second case is 72-year-old woman diagnosed as IgG4-RD histologically from the biopsied swelling submandibular gland, and had been followed up with no treatment. Five years later, growing grand glass opacity in her left lung was revealed, and diagnosed as adenocarcinoma after resection. By histopathological assessment, cancer cells occurred from atypical squamous metaplasia against a background of interstitial pneumonia with few lymphoplasmacytic infiltration in first case. On the other hand, IgG4-positive plasma cells around the lesion were shown in the second case, which suggest reaction to malignancy. Although IgG4-RD complicated by lung cancer is rare, pathological diagnosis should be required to differentiate malignancy from IgG4-RRD.

P55-9

Spontaneous remission of IgG4-related retroperitoneal fibrosis

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Conflict of interest: None

[Background] Some forms of retroperitoneal fibrosis (RPF) have been considered to be a part of the spectrum of IgG4-related disease (IgG4RD). We report a case of spontaneous resolution in IgG4-related RPF (IgG4-RPF). [Case presentation] A 79-year-old man presented abdominal discomfort and referred to our hospital. Abdominal US showed left hydronephrosis. Abdominal CT and MRI demonstrated retroperitoneal tumor lesion,

indicating a cause of hydronephrosis. Laboratory examination showed elevated levels of IgG (1958 mg/dL), IgG4 (292 mg/dL), IgE (542 IU/mL), soluble IL-2 receptor (1075 U/mL). Biopsy specimen revealed significant infiltration of IgG4-positive plasma cells and storiform fibrosis without malignancy. Therefore, we diagnosed as IgG4-RPF. Because the patient caused few symptoms, a careful 'watch-and-wait' approach was initially taken. Three months later, CT showed complete resolution of IgG4-RPF and serological findings all normalized. Long-term spontaneous remission is maintained. [Conclusion] IgG4RD is rarely reported to be long-term spontaneous remission. A careful 'watch-and-wait' approach could be considered as an alternative to immune suppression for IgG4-RPF, especially if they are not causing symptoms or organ compromise.

P55-10

A case of IgG4-related Mikulitz's disease associated with giant ovarian cystic tumor with significant infiltration of IgG4-positive plasma cells

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Conflict of interest: None

[Case] A 50s-year-old Japanese woman had swollen eyelids and submandibular glands for 10 years. She gradually developed body weight gain and progressive abdominal distention for recent 3 years. Under clinical diagnosis of giant ovarian cystic tumor, the bilateral salpingo-oophorectomy was demonstrated. Swollen bilateral lacrimal glands, hard palate and submandibular glands, and elevated level of serum IgG4 (319 mg/dL) were recognized on preoperative examinations. She was referred to our hospital for further examinations and treatment for suspicion of IgG4-related disease (IgG4RD). Biopsy from hard palate lesion showed significant infiltration of IgG4-positive plasma cells (IgG4/IgG 68%, IgG4 >100/HPF) and storiform fibrosis, and therefore we diagnosed as IgG4-related Mikulitz's disease (IgG4MD) and initiated prednisolone 0.6 mg/kg/day. Furthermore, resected giant ovarian mucinous cystadenoma revealed significant infiltration of IgG4-positive plasma cells (IgG4/IgG 69%, IgG4 114/HPF).

P55-11

Characteristics of IgG4-Related Dacryoadenitis and Sialadenitis

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Conflict of interest: None

[Objective] IgG4-related disease (IgG4-RD) is recognized as a systemic disease that may affect various organs. Dacryoadenitis and sialadenitis (DS) are one of the main disease features of IgG4-RD. In this study, we examined the characteristics of DS in IgG4-RD. [Methods] We analyzed IgG4-RD patients diagnosed from 2008 in our facility. The diagnosis for IgG4-RD was based on comprehensive diagnostic criteria 2011. Laboratory data, image findings and clinical course were analyzed from their medical records retrospectively. [Results] Twenty six patients had DS lesions (DS group) and 20 patients did not have (non-DS group). Compared to the non-DS group, the DS group had higher serum IgG4 and lower CRP, serum IgA, and complement level. The number of organ involvements was significantly higher in the DS group. During the course, 7 patients had relapsed in the DS group and 8 patients in the non-DS group. In addition, 10 cases of the DS group had no other organ involvements, and 9 out of 10 were followed up without treatment, [Conclusions] We showed the characteristics of serum biomarkers for IgG4-related dacryoadenitis and sialadenitis. This study suggest the patients of IgG4-RD localized DS involvements may be able to follow-up without intervention.

P55-12

A case of IgG4-related hypertrophic pachymenigitis, which was diagnosed five years after the onset

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Conflict of interest: None

[Case] 5 years ago, A woman in her 60s noticed anosmia and was consulted to a neurosurgeon. MRI showed a hypertrophic pachymeningitis (HP). She refused craniotomy biopsy and was followed up. 3 years ago, she came to our hospital for second opinion and underwent a craniotomy. The pathology showed significant plasma cell infiltration, and IgG4-positive cell infiltration of more than 10/HPF, but it was hard to evaluate the IgG4/IgG ratio and the serum IgG4 level was only 96.2 mg/dL. 1 year ago, she was admitted because of suspicion of IgG4-related disease (IgG-4RD), the worsening of thickening of cerebral falx on MRI and elevated serum IgG4 level (167 mg/dL). There were no organ involvement other than HP. The ratio of IgG4/IgG-positive cells was 60%. In addition, she met the 2019 ACR/EULAR classification criteria with the score of 22 points and was diagnosed with IgG4-RD. Treatment was started with 0.6 mg/kg/day of prednisolone, MRI findings and serum IgG4 level improved. But anosmia did not improve. [Clinical significance] HP caused by IgG4-RD generally occurs in isolation with a mildly elevated serum IgG4 level. Pathological examination is important to confirm the diagnosis because of the wide variety of causes of HP. This case reaffirmed these characteristics.

P55-13

A report of two cases of IgG4-related disease with swelling of extraocular muscles

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Conflict of interest: None

[Case 1] The patient was a 79-year-old man with a 3-months history of right visual loss. He was admitted to our hospital with high serum level of IgG4 (433 mg/dL). MRI demonstrated right inferior extraocular muscle hypertrophy. CT scan showed bilateral ureter wall thickening and right hydronephrosis. He was diagnosed with IgG4-related disease (IgG4-RD). We treated him with high-dose glucocorticoid therapy and rituximab, which improved his visual acuity and findings of retroperitoneal fibrosis. [Case 2] The patient was a 51-year-old man with right eyelid swelling. He was hospitalized due to high serum level of IgG4 (1960 mg/dL). CT scan showed swelling of the right extraocular muscles, right lacrimal gland and right infraorbital nerve, and retroperitoneal fibrosis, including soft tissue around the abdominal aorta and retroperitoneal mass. We diagnosed him with IgG4-RD and initiated high-dose glucocorticoid therapy, and his orbital disease and other findings disappeared. It has been reported that 17 to 23% of IgG4-RD patients have ocular lesions, but swelling of the extraocular muscles is rare because it accounts for 5 to 35%. We present two cases of IgG4-RD with swelling of the extraocular muscles and report the clinical characteristics of them with a review of the literature.

P55-14

The disease activity of IgG4-related Disease is evaluated by DWIBS; A case report

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Conflict of interest: None

A 68-year-old man was referred for examination and treatment of bi-

lateral submandibular gland. He was diagnosed as Immunoglobulin G4-related disease (IgG4-RD), Mikulitz's disease because of elevated serum level of IgG4 and increased ratio of IgG4/IgG positive cells in submandibular gland biopsy. In addition, his full physical examination revealed kidney disease, autoimmune pancreatitis and retroperitoneal fibromatosis. Diffusion-weighted imaging with background body signal suppression (DWIBS), newly established whole-body oncological imaging revealed signal enhancement of the submandibular gland, pancreas, surrounding tissue of abdominal aortic wall and kidney. The patient received *55 mg/day of prednisone.* The swelling of bilateral submandibular gland reduced. And also abnormal levels of *pancreatic* enzymes and renal dysfunction were improved. Two months later, the follow up DWIBS revealed the significant improvement of signal intensity of the submandibular gland, pancreas and surrounding tissue of abdominal aortic wall. Because IgG4-RD affects multiple organ systems, full physical examination is important for evaluate disease activity. Here we reported the case that single DWIBS image had been evaluated the whole body distribution of IgG4-RD.

P55-15

A case of rheumatoid arthritis that led to the diagnosis of B-cell lymphoma during the treatment of IgG4-related disease

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Conflict of interest: None

A 79-year-old-man was diagnosed with rheumatoid arthritis (RA) in X-24, but he was not treated. In June X-5, he was treated with prednisolone (PSL) and salazosulfapyridine (SASP). In July X-5, he showed lymphadenopathy and mild splenomegaly. He was diagnosed with reactive lymphadenopathy by a biopsy of the right axillary lymph node and treated with 4 mg/week of methotrexate (MTX) in July X-5, with the dosage gradually increased to 12 mg/week by October X-5. We ceased the administration of MTX in January X-4. In December X-1, he showed exacerbation of splenomegaly and was diagnosed with IgG4-related disease (IgG4-RD) by a rebiopsy of the right axillary lymph node. The pathological findings were marked plasma cell infiltration with ≧100 IgG4-positive plasma cells/HPF and an IgG4/IgG-positive cell ratio of ≧80%. His IgG4 level was 902 mg/dl, and his SIL2R level was 9067 mg/dl. In January X, he was treated with 0.6 mg/kg of PSL. Although his IgG4 level decreased, his SIL2R level increased and his splenomegaly was further exacerbated. In April X, he was diagnosed with B-cell lymphoma by an EUS-FNA biopsy of the pancreatic tail tumors. IgG4-RD often merge with malignant lymphoma. We should consider performing a rebiopsy in cases of IgG4-RD that show a poor response to steroid therapy.

P55-16

A case of IgG4-related disease with a localized steroid-refractory skin rash on the right side of the body

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Conflict of interest: None

A 41-year-old man was started on prednisolone (PSL) 40 mg/day at A Hospital for right eyelid swelling since X-17. Infiltrative erythema and papules appeared on the right frontal area, right chest and abdomen, and from the back to the lumbar region since X-15. He underwent a right orbital mass excision and skin biopsy at B Hospital. However, a definite diagnosis could not be made. Since X-1, the right eye protrusion flared up again, with nodules in the abdomen and pain at the skin rash site. Blood sampling revealed an elevated serum IgG4 level (1413 mg/dL), and CT showed right maxillary sinus to ethmoid sinus sinus sinusitis with right orbital continuity, and head MRI showed a right intra-orbital mass and dural thickening with contrast effects. A biopsy of a pseudo-tumor removed from the right orbit and a biopsy of a right abdominal subcutaneous node revealed significant lymphocyte and plasma cell infiltration, fibrosis and IgG4-positive plasma cell infiltration, which led to the diagnosis of IgG4-related disease. PSL 45 mg/day (0.8 mg/kg) was started and rituximab 620 mg/body (375 mg/m^2) was started for four courses. We report here a case of IgG4-related disease with non-specific skin rash and neuralgia, based on a review of the literature.

P55-17

A case of IgG4-related disease along with taste and smell disorders

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Conflict of interest: None

A 70-year-old male presented with bilateral upper eyelid swelling from October 20XX-1, and abnormalities in the sense of smell and taste from December 20XX. Cervical US showed a right submandibular mass and he was referred to our clinic. Although, there were no abnormal findings in the oral cavity or tongue, CT showed bilateral lacrimal, right submandibular gland and generalized lymph node swelling, thickening of the iliac artery vessel wall, retroperitoneal fibrosis, and granular shadows in both lungs. Pathology of the right submandibular gland revealed numerous IgG-positive plasma cell infiltrates with fibrosis, of which approximately 50% were IgG4-stained positive cells. Serum IgG4 2570 mg/dL, which led to the diagnosis of IgG4-related disease. After the treatment with prednisolone 55 mg/day, and the lesions disappeared and his olfactory and taste abnormalities improved. Although the etiology and pathogenesis of IgG4-related diseases remain unclear, an association between IL-4 and IL-10 and IgG4 production has been reported. Olfactory deficits in IgG4-related diseases have been frequently reported, the same possibility for taste disorders was estimated in this patient.

P55-18

A case of IgG4-related cholangitis that took time to diagnose

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Conflict of interest: None

[Case] 54-year-old man. Liver damage was found in a medical test in May X, and then he had fever and malaise. A blood test showed elevated hepatobiliary enzymes. He was hospitalized for cholangitis, but MRCP showed no biliary obstruction, and contrast CT showed systemic lymphadenopathy. Soluble IL-2 receptor increased to 6950 U/mL, and FDG accumulated to lymph nodes by PET-CT, so he was introduced to our hematology. Malignant lymphoma was negative by bone marrow puncture and inguinal lymph node biopsy, and blood tests showed IgG: 4929 mg/dL and IgG4: 4640 mg/dL, so he was introduced to us. Lacrimal gland and peripancreatic lymph node biopsy were performed, 50% or more of IgG4-positive cells were found, so he was diagnosed IgG4-RD. After biopsy, his symptoms were relieved, but fever, malaise, and jaundice appeared, and hepatobiliary enzymes elevated again in January X+1. PSC or AIP were negative by MRCP, but abdominal echo showed a gallbladder wall thickening, so he was diagnosed IgG4-related gallbladder. After he took prednisolone 1 mg/kg, hepatobiliary enzymes, inflammatory reaction, and gallbladder wall thickening gradually improved. [Discussion] It's important to list IgG4-related cholecystitis as a differential disease of cryptogenic hepatobiliary enzymes.

P56-1

Successful treatment with Baricitinib for para-colostomal ulceration in a patient with Behçet's disease

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Conflict of interest: None

A 70 years old female with past medical history of rheumatoid arthritis (RA) and intestinal Behçet's disease (BD) was admitted to our hospital because of para-colostomal ulceration. At the age of 61, she was diagnosed with intestinal BD by the presence of oral ulcerations, pseudofolliculitis, genital ulcers, and anal/rectal ulcers. She was treated with prednisolone, colchicine, cyclosporine, and anti-TNF-α amonoclonal antibody. But anal/rectal ulcers progressed to several anal and rectovaginal fistulas. Since she had repeated fistula infections, she underwent colorectal resection with colostomy to control infections. Few months after surgery, para-colostomal ulceration was noted, and gradually deepened. There are few reports showing para-ileostomal ulceration associated with BD. Therefor, we diagnosed the para-colostomal ulcer as cutaneous manifestation of BD. At the same time, her disease activity of RA was elevated. We decided to switch adalimumab to baricitinib. Responding to treatment with baricitinib, arhtiritis and para-colostomal ulcer ware improved. This is the first case of BD complicated with a para-colostomal ulcer that was successfully treated with baricitinib.

P56-2

Giant ulcer developing at the temporal artery biopsy site and periodic systemic inflammatory response syndrome in a case of myelodysplastic syndrome with trisomy 8

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Conflict of interest: None

[Case] A 70-year-old man, who had been diagnosed as having myelodysplastic syndrome (MDS) with trisomy 8 three months ago, presented with fever and thickening of the aortic wall. Because giant cell arteritis was suspected, temporal artery biopsy was performed. One week later, swelling and redness developed at the biopsy site. Antibiotics and local treatment were ineffective. The incision site was reopened, but there were no findings suggesting infection. It turned into a large ulcer. Periodic episodes of migratory and infiltrative round-shape erythema on the face, fever, hypotension, and nausea repeated 5 times; these episodes subsided within a few days. There was no evidence of septicemia. Despite treatment with glucocorticoids, periodic hypotension still persisted. He died of cerebral infarction and unresponsive hypotension the next month. [Discussion] Because the biopsy site turned into a large ulcer, Sweet syndrome (or pyoderma gangrenosum) was suspected. Systemic inflammatory response syndrome is reported in patients with malignancy-associated Sweet syndrome. Giant ulcer developing at the biopsy site can also be regarded as "Giant pathergy reaction". There may be a common pathophysiology between the present case and Behçet's -like disease associated with trisomy 8 MDS.

P56-3

Unilateral pleural effusion in a patient with Behçet's disease

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Conflict of interest: None

A 44-year-old woman was diagnosed as having Behçet's disease by oral ulcers, genital lesions, and erythema nodosum at other hospital. Her HLA was A2, A33, B44, and B46. Colchicine was effective against her symptoms, but she stopped her hospital visits. A few months later, she visited our hospital due to high fever, dyspnea, chest pain, cough, and arthralgia. The serum C-reactive protein (CRP) level was increased and the computed tomography showed right pleural effusion. The pleural effusion was exudative. Infection, malignancy and other collagen diseases were excluded by various examinations. After colchicine was re-administered, her symptoms and pleural effusion immediately disappeared and the CRP level decreased to the normal range. Although rarely reported, unilateral pleural effusion could be a complication of Behçet's disease.

P56-4

Evaluation of erythema nodosum associated with Behçet's disease by dermatologic ultrasound

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Conflict of interest: None

[Case] A 42-year-old female was admitted to our hospital for rashes on lower limbs, fever and right knee pain that worsened in 5 days. Her body temperature was 38.2 °C and she showed painful oral aphthae, a genital ulcer, erythema nodosum (EN)-like lesions on lower limbs, and swollen knees. Musculoskeletal ultrasound of the knee demonstrated no synovitis but enthesitis at the quadriceps and infrapatellar ligament. Dermatologic ultrasound on EN showed thickening of the interlobular septa of the subcutaneous adipose tissue with hypoechogenicity and increased doppler flow consistent with septal panniculitis. A biopsy of EN revealed neutrophil-dominant septal panniculitis, micro-abscesses in the subcutaneous adipose tissue, and arterial vasculitis. She was diagnosed as Behçet's disease (BD) and received oral colchicine. Her symptoms improved 2 days later and dermatologic ultrasound showed disappearance of the doppler flow and improvement of thickening of the adipose tissue septa 6 days later. [Clinical significance] EN is a common cutaneous symptom of BD and pathologically presents with septal panniculitis. Since the ultrasound findings of septal panniculitis are characteristic, dermatologic ultrasound may be useful for diagnosing EN noninvasively and evaluating their activity in BD.

P57-1

A difficulty diagnosed case of systemic juvenile idiopathic arthritis treated with tocilizmab with macrophage activation syndrome triggered by infectious mononucleosis

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Conflict of interest: None

A 16 years-old woman was diagnosed systemic juvenile idiopathic arthritis (sJIA) and steroid therapy was started. Tocilizmab (TCZ) was added on and prednisolone (PSL) was tapered to 5 mg/day without flare. She was admitted because of fever. The laboratory tests showed hepatic disorder, leukocytopenia, thrombocytopenia, elevated ferritin, therefore we diagnosed as macrophage activation syndrome (MAS) with sJIA. Her symptoms were improved with steroid pulse therapy, PSL 50 mg/day with cyclosporin (CsA). On the contrary, laboratory data showed haptic disorder, leukocytosis, atypical lymphocyte. Both CMV-HRP and EB virus anti-body were negative, but EBV-PCR result was highly positive. She presented with fever and eyelid edema without either sore throat or cervical lymphadenopathy, therefore we diagnosed infectious mononucleosis (IM). CsA was stopped and PSL was tapered. Atypical lymphocyte was elevated and hepatic disorder was persisted, viral skin rash was appeared, but she was improved finally. As EB-VCA-IgM and IgG became positive, IL-18 was high elevated later, we considered MAS with IM. Early symptoms of infection were masked by TCZ, therefore atypical clinical course may be presented. Physicians should be aware of IM that may be trigger of MAS in sJIA.

P57-2

A case of systemic juvenile idiopathic arthritis treated with tocilizumab after improvement of the inflammatory response by cyclosporine and plasma exchange

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Conflict of interest: None

[Introduction] Macrophage activation syndrome (MAS) is a severe complication of systemic juvenile idiopathic arthritis (sJIA). Clinicians

should be aware of the risk for MAS during treatment with tocilizumab (TCZ), the indication for which in sJIA has not been established. [Case] A 5-year-old girl with arthralgias, erythema, fevers, and marked inflammation based on blood testing was diagnosed with sJIA. Because her fever recurred after pulse therapy, she was transferred to our hospital. The serum cytokine profile showed a marked elevation of serum IL-18 (92,179 pg/mL), suggesting a high risk for developing MAS triggered by TCZ. After a steroid pulse and treatment with prednisolone and cyclosporine (CyA), the fever resolved. Plasma exchange was performed, then TCZ was administered after confirming that the IL-18 level had decreased (10,374 pg/mL). Prednisolone was tapered without symptom recurrence. [Discussion] The usefulness of combined leukocyte apheresis and plasma exchange has been reported to prevent the development of MAS in patients with sJIA. We successfully administered TCZ using CyA and plasma exchange without leukocyte apheresis. Before TCZ administration, control of inflammation by CyA and plasma exchange is important to prevent MAS.

P57-3

A case of primary antiphospholipid syndrome presenting with autoimmune choreas as the first manifestation in a 13-year-old boy

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Conflict of interest: None

Three weeks before admission, a 13-year-old boy with no family history had tended to drop objects, and his heel began to hit another heel when he walked. Progressively, he developed involuntary movements such as chorea, tic, and myoclonus. At the time of admission, there are no physical findings other than involuntary movements. Blood tests showed mildly decreased platelet counts. MRI showed scattered lacunar infarctions in the deep white matter, but no vascular malformations or lesions in basal ganglia. There were no abnormalities in the ECG, EEG, CSF examination. Because of prolonged APTT, anti-cardiolipin IgG and lupus anticoagulant were tested and revealed positive. He was diagnosed as having antiphospholipid antibody syndrome (APS). Since he had no other autoimmune diseases, his chorea was assumed to be due to autoimmune chorea associated with APS. A few days after starting anticoagulation therapy and methylprednisolone (mPSL) pulse therapy, and his chorea rapidly resolved. Oral prednisolone, azathioprine, and warfarin were maintained without residual symptoms or recurrence. In this case, the pathogenesis of autoimmune chorea was not thrombosis, but direct damage to vascular endothelial cells and/or neurons mediated by antiphospholipid antibodies.

P57-4

A pediatric case of systemic lupus erythematosus with lupus anticoagulant hypoprothrombinemia syndrome developed with epistaxis

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Conflict of interest: None

Lupus anticoagulant hypoprothrombinemia syndrome (LAHPS) is developed in the patients with systemic lupus erythematosus (SLE) and the pediatric patients with viral infection. The definition of LAHPS is the hypoprothrombinemia due to anti-prothrombin antibody in the patients with lupus anticoagulant positive. Although the patients with antiphospholipid syndrome show thrombosis, LAHPS patients show bleeding symptom. A 12-year-old girl showed frequent nasal hemorrhage, and difficult to stop bleeding. She was referred to our hospital because of anemia, hematuria, proteinuria, and hypocomplimentemia, and diagnosed as having SLE. Laboratory data showed extended both APTT and PT, and cross-mixing test showed inhibitor pattern. Furthermore, it was revealed that activity of prothrombin was decreased, and anti-prothrombin antibody was positive, as well as positive lupus anticoagulant and anti-cardiolipin antibody. She was complicated LAHPS with SLE. After the treatment of two courses of methylprednisolone pulse therapy, extended PT were normalized, and recurrent nasal hemorrhage were improved. [Conclusions] LAHPS should be considered in the case of bleeding symptoms with extended PT in the patients with SLE.

P57-5

A case of juvenile SEL with prolonged hypophosphatemia due to inappropriate FGF23 secretion

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Conflict of interest: None

[Background] We treated a patient juvenile SEL prolonged hypophosphatemia due to inappropriate FGF23 secretion. [Case] An 11-year-old girl admitted to our hospital with malar rash. She was diagnosed with SLE by leukocytopenia, hypocomplementemia, positive antinuclear antibodies and high dsDNA antibodies. On admission, she had hypophosphatemia (1.7 mg/dL). She was treated with oral phosphorus, but hypophosphatemia did not improve. FGF23 was high value at 282 pg/mL (baseline 16-69 pg/mL), and continuous intravenous phosphorus was added with the diagnosis of hypophosphatemia due to high FGF23 levels. IVIG was added due to poor improvement in hypocomplementemia even after steroid pulse treatment. After IVIG, hypocomplementemia improved. The serum phosphorus level gradually improved and the patient was discharged after 2 months of hospitalization. FGF23 improved to 66 pg/mL 6 months after discharge. [Conclusion] Three cases of juvenile SLE with hypophosphatemia have been reported, but there are no adult cases. There are no underlying FGF23-related diseases, suggesting the involvement of proinflammatory cytokines, but the pathogenesis is unknown. This suggests that prolonged hypophosphatemia may be due to inappropriate FGF23 secretion in relation to the pathogenesis of SLE.

P57-6

A case of anti-MDA5 antibody positive juvenile dermatomyositis successfully treated with only steroid therapy

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Conflict of interest: None

A 2 years 8 months old girl visited our hospital due to redness, swelling, pain and red papules occurred on the left finger. At visit, she presented normal oxygen saturation under room air atmosphere, vasodilation and bleeding on both nail beds, swelling of both fingers, and no myalgia or muscle weakness. Blood test showed anti-MDA5 antibody 101. Chest CT and femoral MRI revealed no abnormality. She was diagnosed as anti-MDA5 antibody positive juvenile dermatomyositis (MDA5+JDM), and treated with methylprednisolon pulse therapy and oral prednisolon (PSL). After admission, no respiratory or muscular symptoms were occurred. She was discharged on day 19 after admission. Anti-MDA5 antibody became negative 6 months after discharge, and PSL was discontinued. For more than 2 years, no respiratory symptoms were occurred, anti-MDA5 antibody was negative, and imaging showed no signs of interstitial pneumonia (ILD). Japanese MDA5+JDM patients are frequently complicated with ILD. Some have rapid-progressive ILD, and have poor prognosis. So more potent immunosuppressive therapy is recommended from an early stage. However, this case was successfully treated with only steroid therapy. Even if anti-MDA5 antibody is positive, aggressive treatment might not be always necessary in some cases.

P57-7

A case of Graves' disease which developed during drug-free remission of juvenile dermatomyositis

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Conflict of interest: None

Graves' disease (GD) is an autoimmune hyperthyroidism caused by TSH receptor stimulating autoantibodies. GD often complicates connective tissue diseases but rarely with idiopathic inflammatory myopathies. We report a case of GD which developed during drug-free remission of juvenile dermatomyositis (JDM). The patient is a currently 13-year-old Japanese boy who had been diagnosed with JDM at 6-year-old. He was positive for anti-MDA5 antibodies but had no history of interstitial lung disease. Clinical remission was achieved by prednisolone (PSL) and MTX and maintained after the cessation of the medication at 10-year-old. However, serum levels of soluble interleukin-2 receptor (sIL-2R) gradually elevated and reached to a peak level of 3,185 U/mL at the age of 11 years when he presented with palpitation and goiter. The diagnosis of GD was made by hyperthyroidism associated with positive TSH receptor stimulating antibodies and increased uptake on 99m technetium scintigraphy. He was treated with 15 mg/day of methimazole (MMI), and is currently controlled on maintenance dose. To our knowledge, this is the 1st report of JDM complicated with GD. A serum sIL-2R level elevates in both JDM and GD. Thus, complication of GD could be a cause of unexpected elevation of sIL-2R in inactive JDM.

P57-8

A case of anti-NXP2 antibody-positive juvenile dermatomyositis with calcinosis preceding muscle weakness

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Conflict of interest: None

Calcinosis occurs as a symptom in 30-70% of all juvenile dermatomyositis (JDM) cases. Most cases appear after 1 year from the onset of JDM. [Case] A 10-year-old boy showed skin calcifications on both thighs 2 years before admission. He had erythema on both knuckles and knees, but was diagnosed as having atopic dermatitis. No symptoms of muscle weakness occurred at that time. Proximal muscle weakness appeared gradually from 1 year before admission. He visited our hospital because of difficulty in walking. At the first visit, his CMAS was 37. Both hands and ankles had joint contracture. The erythema in his knuckles and knees were considered Gottron papules. A heliothrope rash was also observed. He was diagnosed as having JDM and received 2 courses of mPSL pulse therapy, followed by oral PSL and MTX therapies. In addition, IVIG and bisphosphonate administration were started. Anti-NXP2 antibody was found to be positive later. [Discussion] The pathogenesis of calcinosis in JDM has not been clarified, but anti-NXP2 antibodies are associated with joint contracture and calcinosis. In this case, owing to the slow progression of the muscle weakness, JDM was diagnosed only 2 years after onset. In pediatric patients with calcinosis, dermatomyositis is a differential diagnosis.

P57-9

Clinical features of pediatric patients diagnosed with microgeodic disease

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Conflict of interest: None

[Objective] Microgeodic disease (MD) is a rare disease that causes spindle-shaped swelling, pain, and redness in the fingers and toes of children, and the clinical features of MD remain unclear. To report the clinical features of MD in childhood. [Methods] During the period from April 2018 to April 2020, 6 children with MD diagnosed at our hospital were retrospectively analyzed using the medical records. [Results] Four cases were girls. The median age at diagnosis was 13 years. It often occurred in winter, and almost all cases had coldness of limbs, chilblain-like rash, and peripheral circulatory insufficiency was observed. The affected areas were fingers in 3 cases and toes in 3 cases. Although there were 2 cases with abnormal findings on X-ray, there were 5 cases with abnormal findings on MRI images Three cases were treated Vasodilators. All cases improved by the summer. [Conclusions] MD is thought to be precipitated by peripheral circulatory insufficiency induced cooling. In this study, many cases developed in winter, and the presence of chilblain-like rash is considered to be a characteristic of this disease. MRI is easier to detect abnormal findings than X-ray and is useful for early diagnosis. I think that these characteristics are helpful in the differential diagnosis.

P58-1

Improved Treatment Responsiveness of TAFRO Syndrome by Shohangekabukuryoto: A Report of Two Cases

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Conflict of interest: None

TAFRO syndrome is a systemic inflammatory disease characterized by idiopathic thrombocytopenia, anasarca, myelofibrosis, renal dysfunction, and organomegaly. We here report two cases of TAFRO syndrome in which a combination therapy of Shohangekabukuryoto, known to have diuretic effect, improved not only anasarca but also treatment responsiveness. In both cases, the patients were admitted for the symptoms suggestive of TAFRO syndrome, including high inflammatory markers, thrombocytopenia, and anasarca. Both patients were diagnosed with TAFRO syndrome, including one that was classified as severe. This case was treated with steroid pulse therapy followed by PSL 60 mg and cyclosporine (CyA). Inflammatory markers and renal function improved, but anasarca-associated symptoms and thrombocytopenia persisted. The other case was treated with PSL 40 mg and CyA, which rapidly improved inflammatory response, but anasarca, weight gain, and thrombocytopenia persisted. In both cases, after Shohangekabukuryoto was started, not only the general condition improved due to increased diuretics, the platelet count also improved, and remission was achieved. Our cases demonstrated that treatment responsiveness as well as anasarca improved, indicating the significance of the use of Shohangekabukuryoto.

P58-2

A fulminant case of TAFRO syndrome that associated with rheumatoid arthritis

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Conflict of interest: None

A 81-year-old female patient presenting with polyarthralgia was diagnosed with rheumatoid arthritis based on the positivity for anti-cyclic citrullinated peptide antibody and rheumatoid factor. She was treated with sulfasalazine and corticosteroids because of renal dysfunction. Seven months later, she was hospitalized for dyspnea of exertion, pleural effusion. Imaging and pathological investigations did not show the evidence of vasculitis or malignancy. She was suspected of having TAFRO syndrome due to anasarca, thrombocytopenia, and high levels of serum IL-6, CRP and ALP. On the 10th day of hospitalization, she received high-dose glucocorticoids and tocilizumab. After the treatment, her anasarca ameliorated, but her renal function worsened. She died on the 18th day of hospitalization. Autopsy findings were consistent with TAFRO syndrome. No case of TAFRO syndrome associated rheumatoid arthritis has been reported so far. We herein report our case with the autopsy findings and a review of the literature.

P58-3

A case of TAFRO syndrome successfully treated with prednisolone, tocilizumab, and cyclosporine

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Conflict of interest: None

A thirty-nine female was admitted to a local hospital complaining fever, pitting edema, and oliguresis. She had past history of asthma. Blood test revealed thrombocytopenia, renal dysfunction, and elevated CRP level. She was transferred to our hospital for further treatment. Since her edema and kidney function rapidly worsened, hemodialysis was initiated. Chest and Abdominal plain CT revealed pleural effusion, ascites, splenomegaly and intra-abdominal lymphadenopathy. Bone marrow biopsy specimens revealed megakaryocyte proliferation without malignancy. Lymph node biopsy was not performed. Under the diagnosis of TAFRO syndrome, methylprednisolone pulse therapy was initiated followed by prednisolone 80 mg per day. Tocilizumab 720 mg per two weeks, cyclosporine 200 mg, and eltrombopag 50 mg were also administrated. Those treatment ameliorated her symptoms, and laboratory findings. She was withdrawn from hemodialysis, and dose of prednisolone was tapered. TAFRO syndrome is a systemic inflammatory disorder manifesting as thrombocytopenia, anasarca, fever, reticulin myelofibrosis or renal insufficiency, and organomegaly. Although the treatment strategy of TAFRO syndrome is not established, combination therapy of prednisolone, tocilizumab, and cyclosporine might be effective.

P58-4

Clinical features and treatment results of the patients with TAFRO syndrome in Ehime university hospital

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Conflict of interest: None

[Objective] TAFRO syndrome is a rare disease with thrombocytopenia, anasarca, fever, reticulin fibrosis/renal dysfunction and organomegaly. The disease show a various progress, and some patients exhibit a rapidly severe clinical course with multiple organ failure and died. We aim to analyze the clinical features of TAFRO syndrome in our hospital. [Methods] We analyzed 7 patients with TAFRO syndrome from January 2013 to October 2020 in our hospital. [Results] Seven patients (4 females, 3 males) were between 24- and 79-year-old (mean 54). There were many severe cases (grade 3: 2 cases, grade 4: 2 cases and grade 5: 3 cases). All cases were treated with high dose corticosteroid therapy, and 5 cases were treated by a steroid pulse therapy. However, steroids alone were inadequate in all cases, cyclosporine was used in 2 cases and tacrolimus in 1 case. Tocilizumab (TCZ) was administered to 5 cases, but 1 case required a change to rituximab (RTX). RTX was administered to 2 cases from the beginning. Among them, 3 cases were able to quit TCZ. [Conclusions] At our hospital there were many severe cases, and all cases required biologics. Three cases were admitted in which TCZ could be stopped. We report clinical features and treatment results in our hospital with a review of the literature.

P58-5

Two severe and refractory cases of TAFRO syndrome treated with Tacrolimus and Rituximab adding to glucocorticoids

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Conflict of interest: None

Case 1: A 53-year-old man developed fever, anasarca, bilateral pleural effusion, ascites, severe thrombocytopenia, and renal failure. Diagnosis of TAFRO syndrome was made according to the 2015 diagnostic criteria. We administered high-dose glucocorticoids and cyclosporine A (CsA). However, they were ineffective. Renal function worsened and hemodialysis had been administered temporarily. Though adding tocilizumab (TCZ) was partially effective, it was ceased due to sepsis. CsA was also discontinued with no effect. We added tacrolimus (TAC) resulting in remission. But the disease recurred in five months. He received rituximab (RTX) and increase in dosage of TAC and PSL, which resulted in remission again. Case 2: A 50-year-old man developed similar symptoms as the former. We diagnosed him as TAFRO syndrome. Though we administered high-dose glucocorticoids and CsA, renal function and thrombocytopenia were deteriorated. We replaced CsA with TAC. Subsequently, he became in remission. Conclusions: The guidelines for treatment has not been established yet, and reports of successfully treated severe cases in recurrence are scarce. In our cases adding TAC were effective. RTX was also effective in recurrence. We suggest the possibility of efficacy of TAC and/or RTX for refractory cases.

P58-6

A case of TAFRO syndrome with demyelinating polyneuropathy successfully treated with triple therapy of prednisolone, tocilizumab, and cyclosporine

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Conflict of interest: None

A 62-year-old woman presented to a local hospital with oliguria, and general malaise. Examination revealed anasarca, renal dysfunction, thrombocytopenia and high C-reactive protein level. Her symptoms were initially suspected to be caused by severe infection, and she was given antibiotics. However, she developed anasarca, acute kidney injury, high liver enzymes level and thrombocytopenia, and was transferred to our hospital for further care. Systemic lymphadenopathy was revealed, but biopsy was not possible due to general condition. Further, she developed polyneuropathy. Her symptoms except for polyneuropathy were similar to TAFRO syndrome. Her clinical symptoms and laboratory data improved with initiation of intravenous steroid pulse therapy and tocilizumab. However, as prednisolone was tapered, her symptoms worsened. After triple therapy of prednisolone, tocilizumab, and cyclosporine, her condition was improved. Polyneuropathy was poorly improved, and Examination findings suggestive of demyelinating disease. She was given two courses of intravenous immunoglobulin therapy, and polyneuropathy was improved. In this case, the typical clinical symptoms of TAFRO syndrome and demyelinating polyneuropathy were observed. In addition, triple therapy was remarkably successful.

P58-7

A case of angioimmunoblastic T-cell lymphoma that was difficult to differentiate from TAFRO syndrome

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Conflict of interest: None

In year X, the patient had vomiting, diarrhea, and fever, and gastrointestinal endoscopy showed no abnormalities. A pleural ascites was observed. She was started on steroid pulse therapy and referred to our department. In addition to marked pleural and abdominal effusion, multiple lymph node enlargement was noted; WBC 1400/μL, Hb 8.5 g/dL, PLT 48,000/μL, LDH 322 U/L, CRP 7.01 mg/dL, ferritin 410.5 ng/mL, IgG 513 mg/dL, soluble IL-2 receptor 2616 U/ml and suspected TAFRO syndrome and hematologic malignant disease. Bone marrow biopsy and random skin biopsy showed no malignant cells. Flow cytometry showed no abnormality, and the diagnosis of TAFRO syndrome was made, although the histopathological findings were undetermined. Lymph node histopathological diagnosis was made as Angioimmunoblastic T-cell lymphoma (AITL) and the patient was transferred to our hematology department. Since TAFRO syndrome progresses rapidly and early treatment is desirable, lymph node biopsy is not mandatory in its diagnostic criteria, but exclusion of the diagnosis, especially of malignant lymphoma, is important. In this case, the final diagnosis of AITL was made on lymph node histopathology after the initiation of TCZ. We report this case as a case in which a lymph node biopsy was clinically useful.

P58-8

Tocilizumab improved TAFRO syndrome with an inadequate response to conventional therapy; A case report

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Conflict of interest: None

TAFRO syndrome is a rare systemic inflammatory disease characterized by Thrombocytopenia, Anasarca, Fever, Reticulin fibrosis of the bone marrow, and Organomegaly. A 58-years old male was presented with severe anasarca, thrombocytopenia, renal dysfunction, and hepatosplenomegaly. His bone marrow examination revealed reticulin fibrosis, which was compatible with TAFRO syndrome. Because initial corticosteroid monotherapy failed, simultaneous combination therapy of corticosteroid and cyclosporine was performed. However, his serious anasarca and thrombocytopenia was not improved. Finally, he received the corticosteroid/cyclosporin A/tocilizumab triple combination therapy. Anasarca was significantly reduced within six weeks and his platelet counts were normalized immediately. Our report suggests the possible efficacy of tocilizumab in patients with TAFRO syndrome with an inadequate response to conventional combination therapy of corticosteroid and cyclosporine A. Upfront combination therapy of tocilizumab might be more beneficial than sequential escalation therapy of tocilizumab.

P59-1

SAPHO Syndrome Treated by Bisphosphonate: A Case Report

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Conflict of interest: None

A 62-year-old female visited our hospital with low back pain and fever despite she underwent antibiotic treatment for 1 month. Laboratory exam showed WBC: 5800/μL, CRP: 3.5 mg/dL and ESR (1h/2h): 59/79 mm. X-ray and CT images of lumbar spine showed bone destruction and sclerotic lesions on the corners of multiple vertebral bodies. She was suspected to have tuberculous spondylitis, she was taken CT scan of breast, and there was hyperplasia on the sternoclavicular joint. Bone marrow edema was shown on MRI of lumbar spine. Bone scintigram showed increased radioactivity on the sternoclavicular joint and thoracic and lumbar spine. Because we found that she was diagnosed as palmoplantar pustulosis five years ago, we diagnosed SAPHO syndrome. Monthly intravenous ibandronate administration was started. 3 months after treatment, her pain and fever were relieved and laboratory exam were improved. 1 year after treatment, vertebral destruction was not worsening. The diagnosis of SAPHO syndrome is difficult because radiographic images show bone destruction like infection or malignancy. Although no consensus has reached on the treatment of SAPHO syndrome, in this case, the patient treated by BP improved her symptom. Further evidence is needed to determine the treatment of SAPHO syndrome.

P59-2

A case of SAPHO syndrome with right abducens paralysis due to hypertrophic pachymeningitis

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Conflict of interest: None

[Case] A 54-year-old female, who was diagnosed with palmoplantar pustulosis, had swelling of her left mandible and was diagnosed chronic osteomyelitis of left mandible and right sphenoid bone by MRI. She underwent a biopsy and culture test of left mandibular bone, and was diagnosed with aseptic osteomyelitis. After that, she also had diplopia, and MRI showed hypertrophic pachymeningitis of the right middle cranial fossa. Based on these results, we diagnosed SAPHO syndrome with right abducens paralysis induced by hypertrophic pachymeningitis. We started administration of steroid and methotrexate, and she underwent tonsillectomy and smoking cessation guidance. Ocular symptoms improved over time after the start of treatment, and MRI also showed improvement in dural thickening. [Conclusion] In this case, aseptic osteomyelitis of the right sphenoid bone due to SAPHO syndrome caused localized hypertrophic pachymeningitis and abducens nerve disorder. We report the clinical course of this case with a review of the literature.

P59-3

Efficacy of Adalimumab in SAPHO syndrome associated with aseptic abscess: A case report

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Conflict of interest: None

A 67-year-old woman, who had been suffered from repeated pain in the sternoclavicular joint, was admitted for tenderness and swelling on both clavicles. Peripheral blood had remarkably high WBC over 50,000 and CRP over 40, but vital signs were stable. Hypertrophy of the clavicle and fusion of the sternoclavicular joint and sternocostal joint were observed. Subcutaneous abscess was spreading around the neck, the sternum, and the axilla. Puncture fluid was obtained, and monocytes and polynuclear cells were extremely increased, but only a small amount of P. acnes was detected. Although the abscess was reduced by subcutaneous irrigation, recurrence occurred in a short period despite treatment with various antibacterial agents. Serum TNF-α increased to 23.9 pg / mL, suggesting that autoinflammation is involved. Administration of adalimumab resulted in a negative inflammatory reaction and no recurrence of the abscess. Adalimumab reduced serum IL-6 from 34.7 pg / mL to below the detection limit. So far, SAPHO syndrome with aseptic abscess has been reported only in cases with IBD, and this case is not associated with IBD. This case is valuable because administration of adalimumab could suppress inflammatory cytokines and the recurrence of abscesses.

P60-1

The analysis of 6 patients with relapsing polychondritis

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Conflict of interest: None

[Objective] To analyze the clinical features of relapsing polychondritis (RP). [Methods] We retrospectively analyzed clinical features of 6 RP patients at our hospital from September 2017 to August 2020. [Results] Male-female ratio was 4:2 and median (min-max) age at diagnosis was 71 (34-83) years. At the time of diagnosis, auricular chondritis 83.3%, polyarthritis 66.7%, ocular lesions 50.0%, hearing impairment 50%, and vasculitis 33.3% were observed. In 5 cases with auricular cartilage inflammation, the disease duration at diagnosis was 2 (1-4) months, whereas in 1 case without auricular and ocular lesions, the duration was 24 months from the initial respiratory symptoms. In addition to polyarthritis, she had hearing impairment, granulomatous cutaneous panniculitis, and facial paralysis, and PET-CT showed continuous tracheal chondritis to the subsegmental bronchus accompanied by segmental bronchus stenosis, and aortitis. Initial treatment was prednisolone (0.5-1 mg/kg/day) in all cases, methotrexate in 3, calcineurin inhibitor in 2, cyclophosphamide pulse therapy in 1. Tocilizumab introduced in the case lacking auricular chondritis led to remission. [Conclusions] The cases lacking auricular chondritis may have different features from the cases with auricular involvement.

P60-2

Developing type 1 diabetes during treatment for relapsing polychondritis: Two case reports

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Conflict of interest: None

[Background] Relapsing polychondritis (RP) is known to be associated with various autoimmune diseases. We report 2 cases of RP with type 1 diabetes (T1DM). [Case 1] A 55-year-old woman received oral treatment for diabetes mellitus (DM). A few years before the onset of T1DM, she presented to a former doctor with auricular, nasal, respiratory symptoms, and RP was diagnosed. She was transferred to our hospital when she was stable, because of repeated relapse despite intensive treatment. At the time of RP onset, she was negative for anti-GAD antibody. However, the post-transfer testing at our hospital showed a high titer of anti-GAD antibody, suggesting that slowly progressive insulin-dependent DM (SPIDDM) has developed. [Case 2] A 35-year-old woman developed auricular, nasal, and respiratory symptoms 10 years before the onset of T1DM. She developed tracheal stenosis, and RP was diagnosed. Intensive treatment including infliximab did not result in remission, but tocilizumab did 7 years before the onset of T1DM. She had been stable, but she developed fulminant T1DM (FT1DM). [Discussion] In both cases, auricular, nasal, and respiratory lesions were affected, and they developed SPIDDM and FT1DM in stable condition. There are few reports on T1DM developed in RP patients.

P60-3

A case of relapsing polychondritis associated with optic perineuritis

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Conflict of interest: None

[Case] 72-year-old man presented fever and sinus headache. One month later, he developed general weakness. Subsequently, he developed diplopia, painful red eyes and nose pain, and referred to our hospital. He was clinically diagnosed as Guillain-Barre syndrome and improved by IVIG. Eye symptom was diagnosed as scleritis of unknown etiology. Two month later, he revealed central vision loss of left eye and redness of right eye. Then, he developed total blindness of left eye and admitted to our hospital. Laboratory data showed elevated WBC, ESR and CRP levels with negative tests of ANA and ANCAs. MRI T2-fat saturated and T1-Gd enhanced images demonstrated high intensity and positive Gd-enhancement along left optic nerve sheath. Then, the results of positive test of anti-type II collagen antibody and positive biopsy finding that degenerated nasal cartilage with lymphocytic infiltration around cartilage tissue caused the diagnosis of relapsing polychondritis (RP) associated with optic perineuritis. Steroid therapy was initiated and his visual symptom promptly improved. [Conclusion] Our message suggests that we should be careful for behind the eye in RP patients with visual symptoms.

P60-4

4 cases of relapsing polychondritis that swarmed in one summer

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Conflict of interest: None

Tokyo Women's Medical University Yachiyo Medical Center is a core hospital with about 500 beds. Although our facility has been open since 2008, as of the spring of 2018, there was only one patient with relapsing polychondritis (RP) who had developed in 2008. However, since the summer of 2018, four patients with RP have been treated, and all of them were onset in the summer of 2018. All 4 cases were male, 2 cases in their 40s, 2 cases in their 60s, 2 cases with hypertension, and 1 case with diabetes, and no complication of autoimmune comorbidity was observed. Swelling and redness of the auricle were observed in all cases, and saddle nose was observed in 2 cases. Scleritis was observed in 3 cases and sinusitis was complicated in 1 case, but no serious organ involvement was observed. Induction of remission with steroids was performed in 3 cases, and methotrexate was used in combination in 2 cases for steroid tapering. One case is treated with NSAIDS alone. RP is a rare disease and the number of patients in Japan is estimated to be 400-500. Sun exposure and chemical substances have been reported as external factors for the onset, and the form of swarm onset in summer suggests these external factors. We will analyze the patient background and report it based on the literature.

P60-5

A case of relapsing polychondritis in which FDG-PET was superior in diagnosis

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Conflict of interest: None

[Case] 64-year-old man [Chief complaint] Fever [Clinical course] In April X, pyrexia, chest pain, and respiratory discomfort developed. In July, he visited a hospital due to fatigue. Contrast-enhanced CT revealed bronchial thickening with contrast enhancement around the bronchus. He was admitted to our hospital for a detailed examination. Blood cultures were negative and bacterial infections were negative. Spirometry revealed a restrictive defect. Contrast-enhanced CT revealed only a bronchial lesion, but no other organ lesions were detected. Therefore, FDG-PET was performed for further examination. FDG-PET identified the multisystemic cartilaginous abnormalities that were recognized by an increased fluorine-18 deoxyglucose uptake on left auricle, laryngeal cartilages, tracheobronchial tree, and rib cartilages. He was diagnosed with relapsing polychondritis and prednisolone 65 mg/day was started. [Consideration] Relapsing polychondritis is a rare disease. In some cases, the disease progresses without long-term diagnosis. Diagnosis is difficult and requires demonstration of multiple organ damage and biopsy. In this case, contrast-enhanced CT showed a single organ disorder, but FDG-PET showed multiple organ disorders. We report a case in which FDG-PET was superior in diagnosis.

P60-6

A case of high-dose intravenous cyclophosphamide therapy for steroid-resistant organizing pneumonia caused by myelodysplastic syndrome associated with recurrent polychondritis

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Conflict of interest: None

A man in his 60s with 7-year history of relapsing polychondritis (RP). He was diagnosed as myelodysplastic syndrome (MDS) in year X-6 and organizing pneumonia (OP) in year X-4. After cyclophosphamide pulse therapy, the symptoms had not worsened. In year X, he was hospitalized in a near-by hospital due to fever and respiratory distress during exertion. The response to antibacterial treatment was poor, so he was transferred to our hospital with diagnosis of re-exacerbation of OP. Steroid pulse started on the 4th day of hospitalization. Fever had disappeared and oxygen satu-

ration had improved, but he was febrile again on the 16th day. Prednisolone was increased from 40 mg/day to 60 mg/day. The fever disappeared, but the case was considered to be steroid resistant, so cyclophosphamide pulse therapy was performed starting on the 19th day. There were no major complications, and he was discharged on the 39th day. Currently, he is treated with prednizolone 35 mg/day. There are some reports on OP in MDS patients, but there are very few on treatments other than steroids. We report here a case of steroid-resistant OP associated with MDS complicated by RP with some discussion of the effectiveness of cyclophosphamide.

P61-1

Characteristics of Patients whose Diagnosis Changed from Polymyalgia Rheumatica to Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We have experienced cases in which the diagnosis changed from polymyalgia rheumatica (PMR) to elderly-onset rheumatoid arthritis (EORA). This retrospective study aims to survey such cases. [Method] We studied 95 cases diagnosed with PMR. Treatment with prednisolone (PSL) was initiated between May 2010 and July 2020. In 12 cases, the diagnosis subsequently changed to EORA (EORA group). We compared baseline patient characteristics of these 12 cases with 83 cases maintaining a diagnosis of PMR (PMR group). We also investigated the PSL-free rate and its predictors. [Result] The mean patient age was 75 years, and 57 (60.0%) were female. The mean levels of CRP and MMP-3 were 7.7 mg/dL and 254.0 ng/mL, respectively. The RF-positive rate was 9.5%, and the ACPA-positive rate was 3.2%. Among the PMR group, 60.2% of patients achieved PSL-free remission. In the PMR and EORA groups, mean age, proportion of female patients, CRP, MMP-3, RF-positive rate, and ACPA-positive rate were 76/74 years ($p = 0.55$), 51 (61.4%)/6 (50.0%) ($p = 0.45$), 7.72/7.76 ($p = 0.89$), 237.7/370.8 ($p = 0.04$), 8.4/16.7% ($p = 0.36$), and 2.4/8.3% ($p = 0.27$), respectively. [Conclusion] The baseline MMP-3 level was higher in the EORA group than in the PMR group.

P61-2

A case of polymyalgia rheumatica complicated with ulcerative colitis

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Conflict of interest: None

A 50-year-old male presented with fever and watery diarrhea in August 201X. He was admitted to our hospital in November because of abdominal pain and bloody stool. Colonoscopy revealed continuous lesions from the rectum to the ascending colon. There was no visible vascular pattern and multiple erosions with adherent purulent mucus were observed. The diagnosis was pancolitis type of ulcerative colitis (UC). He was given mesalazine and the clinical symptoms improved. Significant pain and tenderness in both shoulders, upper arms and femoral regions occurred at the end of November. Abdominal symptoms showed no tendency to worsen. RF and anti-CCP Ab were both negative and he was diagnosed with polymyalgia rheumatica (PMR). He was treated with 20 mg of prednisolone and his symptoms were improved. Arthropathy is the most common extraintestinal manifestation of UC. Furthermore, various rheumatic diseases associated with UC have been reported. We present a rare case of PMR patient followed by the complication of UC with a literature review.

P61-3

Improvement of glycemic control ameliorated disease activity in three patients with polymyalgia rheumatica

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Conflict of interest: None

[Background] Polymyalgia rheumatica (PMR) is a chronic inflammatory condition of the elderly, characterized by severe pain and stiffness mostly affecting the shoulders, upper arms, and/or pelvic girdle. Subclinical inflammation in type II diabetes mellitus (DM) has been reported; however, the association between DM and PMR remains to be clarified. [Case Reports] Patient 1, 68-year-old man had PMR and DM. Although he had been taking metformin and dipeptidyl peptidase-4 (DPP-4) inhibitor for the treatment of DM, his glycemic control was still inadequate. Therefore, we added repaglinide before the treatment of PMR. Patient 2, 61-year-old man had suffered from diabetes and later developed PMR. We added repaglinide to DPP-4 inhibitor prior to glucocorticoid therapy. Patient 3, 82-year-old woman had PMR with DM. She received repaglinide for DM before the treatment of PMR. All three patients showed amelioration of PMR symptoms and laboratory findings after treatment for DM without addition of glucocorticoid. [Conclusions] The present case series suggests the possibility that glucocorticoid treatment can be avoided in a subset of patients with PMR. Clearer information is expected to be achieved with more extensive studies whether DM-related PMR as a new disease subtype exists.

P61-4

Treatment and clinical course of polymyalgia rheumatica in our clinic

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Yu Family Clinic

Conflict of interest: None

[Objective] To investigate the clinical course and prognosis of polymyalgia rheumatica (PMR) patients in our clinic. [Methods] Age at onset, treatment, clinical course and prognosis, and complications were studied in 45 patients with PMR. [Results] The onset age was 72.7 years. The CRP level was 4.9 mg/dL. Prednisolone (PSL) was given to all the patients at a dose of 12.8 mg/day. Healing was observed in 19 patients (the time to heal was 30.1 months). The CRP level decreased by 80.6% at 4 weeks of treatment in the patients who achieved healing. 21 patients were receiving PSL at $\leqq$2 mg/day, with an 82% decrease in CRP level at 4 weeks. Five patients were receiving PSL at $\geqq$5 mg/day, with a 48.2% decrease in CRP level at 4 weeks. Of the 5 patients, one later developed spondyloarthritis. Complications included vertebral compression fracture (2 cases), herpes zoster (1 case), and pneumocystis pneumonia (1 case). [Conclusions] The prognosis of PMR was thought to be good, but some patients require long-term treatment. Our study suggests that the decrease in CRP level after 4 weeks of PSL treatment may serve as a predictor of healing potential. As some patients with PMR require long-term oral PSL treatment, clinicians should be fully aware of the risks of osteoporosis and infections.

P61-5

Clinical characteristics of polymyalgia rheumatica

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is an inflammatory disease that affects the shoulder and pelvic girdles in aged persons. To clarify the clinical feature, ultrasonography (US) findings, and response to glucocorticoid (GC) and DMARDs, we reviewed PMR patients recently refered to our hospital. [Methods] Sixty nine patients (M/F=29/40) who were diagnosed as PMR were reviewed. Clinical symptoms including shoulder and pelvic pain, peripheral arthritis, and swelling of hands, bursitis (BS) / tenosynovitis (TS) of shoulders by US, and response to GC, and rate of GC-free were investigated. [Results] The mean age was 72.3 years. Seven patients with malignancy, but no giant cell arteritis was observed. Clinical features include shoulder pain 100%, pelvic pain 67.6%, peripheral arthritis 66.7%, and swelling of hands due to TS 30.4%. Either BS or TS was demonstrated by US in 36.4%. Mean dose of prednisolone was 12.6 mg/day at the start of therapy and was tapered to 4.4 mg/day at 1 year. Rate of GC-free patients was 30.4%. In the DMARD combination case, salazosulfapyridine was used most frequently and was effective. [Conclusions] In addition to typical shoulder pain, peripheral arthritis and swelling of hands was common in PMR patients.

P61-6

Examination of Polymyalgia rheumatica (PMR) cases at our hospital

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is an inflammatory disease of unknown cause that often occurs in elderly people aged 50 years or older and presents. This time, we examined the course of PMR cases experienced at our hospital. [Methods] 7 patients who were diagnosed with PMR at our hospital from January 2015 to January 2019 and were able to follow the progress for more than 1 year. The transition of disease activity including CRP and the dose change of prednisolone (PSL) were evaluated for 1 year after the start of treatment. [Results] The average of age was 74.4 years for 3 males and 4 females. Treatment was oral PSL in all cases. The average CRP at diagnosis was 3.9 mg / dL, and the initial dose of PSL was 9 mg / day on average. The average CRP at 1 year was 0.24 mg / dL, and all patients were in remission. In one case, PSL was able to discontinued and no recurrence was observed. In 6 patients, the average dose of PSL was reduced to 2.1 mg / day, but it continued, and in 2 patients, needed re-increase in steroids due to relapse during the course of dose reduction. [Conclusions] Most of the cases required long-term PSL treatment, and the risk-benefit balance needs to be reexamined in consideration of complications. There is an urgent need to establish new therapeutic strategies.

P62-1

Investigation of the diagnosis of high serum ferritin levels

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Conflict of interest: None

[Objectives] Serum ferritin levels (SFL) are reported to be elevated in inflammatory diseases. Some cases are suspected AOSD and other collagen diseases due to the presence of high SFL. The purpose of this study is to investigate the diagnosis in cases with high SFL. [Methods] Patients over 18 years-old who had SFL over 10000 ng/ml in our hospital between July 5, 2018 and July 4, 2019 were selected. The diagnosis was extracted from the medical records. When there are some diagnoses, the disease most likely to contribute to the increase SFL is identified as the main diagnosis. The other diagnoses were noted as complication. [Results] 46 cases were identified. The main diagnosis was malignancy in 17 cases, infection in 10, hepatocellular dysfunction in 10, collagen disease in 6, iron overload in 2, and other in 1. Among the collagen diseases, AOSD was found in 4 cases, SLE and GPA in 1 case. AOSD showed higher SFL compared to other collagen diseases. 7 had hemophagocytic syndrome, including 3 with collagen disease. These included 2 with AOSD and 1 with SLE. AOSD with hemophagocytic syndrome tended to have higher SFL than those without. [Conclusions] A small percentage of patients with high SFL had collagen disease. AOSD, especially with hemophagocytic syndrome, may have higher SFL.

P62-2

Hypocomplementemia and treatment responsiveness to adult onset Still's disease (AOSD)

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Conflict of interest: None

[Objective] To investigate the relationship between serum complement levels and treatment responsiveness in patients with AOSD. [Methods] Twenty one patients with AOSD (male; 4 cases, female; 17 cases) who were admitted to our hospital from 2011 to September 2020 were included, and were divided into two groups as follows; low CH50 and low C4 (low complement group; LCG) and high CH50 and high C4 (high complement group; HCG). The laboratory findings and treatments were compared between two groups. [Results] Eight patients were classified into LCG. There was no significant difference in sex ratio or age. In LCG, hemoglobin levels (10.9 (10.8-11.5) vs 12.1 (11.8-12.7) g/dL, p=0.016) and platelet counts (10.9 (8.4-25.3) vs 36.8 (20.6-48.2) ×104 /μL, p=0.004) were significantly lower, and serum ferritin (20180 (10214-47389) vs 3979 (2479-8844) ng/mL, p=0.008) was higher. All patients in LCG and 10 in HCG were treated with glucocorticoid pulse therapy. Glucocorticoid dose was more frequently increased again during treatment in LCG than HCG (2.5 (1.8-3.0) vs 1.0 (1.0-2.0) times, p=0.034). Two patients over 60 years and having low complement (C4 <5.0 mg/dL) needed to be added cyclophosphamide and plasma exchange. [Conclusions] Patients with hypocomplementemia showed refractory AOSD.

P62-3

Usefulness of tocilizumab for adult-onset Still's disease

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Conflict of interest: None

[Objective] To investigate the usefulness of tocilizumab (TCZ) for adult-onset Still's disease (AOSD). [Methods] Retrospective analysis of cases in which TCZ was introduced among AOSD patients who had medical treatment in our department by September 2020. [Results] The subjects were 18 cases. 9 (G+T group) who received additional TCZ after initial treatment with glucocorticoid (GC), and 9 (T alone group) who received initial treatment with TCZ alone. 7 of 9 patients in the G+T group improved after 4 weeks of the first TCZ administration (2 of the 7 patients had exacerbated hepatic disorder within 2 weeks of the first TCZ administration, but continued TCZ improved the hepatic disorder), and 2 patients did not. (Similarly, in both cases, the liver disorder worsened within 2 weeks, and TCZ was discontinued within 12 weeks. 6 of 9 patients in the T alone group improved after 4 weeks of the first administration of TCZ (4 patients had exacerbated liver damage within 2 weeks, but continued TCZ improved liver damage), and 3 patients did not improve (all exacerbated liver damage). TCZ was discontinued within 4 weeks. [Conclusions] It was suggested that clinical judgment for exacerbation of liver damage that may occur within 2 weeks of the first administration of TCZ is related to usefulness.

P62-4

Case series of adult-onset still disease treated with tocilizumab

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Conflict of interest: None

[Objective] The evaluation of efficacy of tocilizumab for adult onset still disease. [Methods] We have picked up 14 cases of adult-onset still disease treated with tocilizumab in our department and related facility. Additionally, we have analyzed their clinical background, clinical course during treatment, and discontinuation or reduction of glucocorticoid and other immunosuppressive agent. [Results] 14 cases were treated with tocilizumab, 4 male, 10 female patients. mean age was 57 year-old, disease duration was 4.8 years. 6 cases were treated with methotrexate, 7 Cyclosporine, 1 Tacrolimus, 1 Cyclophosphamide respectively. Glucocorticoid or immunosuppresive agent were reduced or discontinued, their disease activity was suppressed in all cases. Furthermore, glucocorticoid was discontinued in 4 cases. [Conclusions] According to our analysis, Tocilizumab is likely to be efficacy for steroid resistant or dependent adult onset still disease. Moreover, even glucocorticoid reduction might be possible in long-standing cases.

P62-5

Sjögren's syndrome with Still's disease like-symptoms; its existence and clinical features

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Conflict of interest: None

[Objective] We experience cases of Sjogren's syndrome (SS) with clinical features similar to those of Adult-Onset Still's Disease (AOSD). The purpose of this study is to show the existence of a subgroup of SS that had AOSD-like clinical features (SS-AOSD). [Methods] We reviewed medical records and examined clinical features of AOSD and SS-AOSD (who were admitted to our hospital). AOSD was diagnosed according to the criteria by Yamaguchi. SS-AOSD was diagnosed when patients met diagnostic criteria for Sjogren's syndrome (1999 Ministry of Health group) and Yamaguchi criteria for AOSD. [Results] Subjects were 40 cases of AOSD (M/F: 9/31, mean age; 49± 18.3) and 13 cases of SS-AOSD (M/F: 1/12, mean age; 43± 18.9) and there were no differences. No differences were found in frequencies of symptoms including fever, rheumatoid rash, and arthritis between AOSD and SS-AOSD groups. SS-AOSD showed organ involvement such as liver dysfunction similar to AOSD. There were no differences in CBC and serum levels of AST, ALT, LDH, CRP, ferritin C3/C4, IL-6, and Il-18 between 2 groups. Atypical rash frequently occurred in SS-AOSD. [Conclusions] There was a subgroup in Sjogren's syndrome which showed similar clinical features to AOSD.

P62-6

Successful reintroduction of tocilizumab in a patient with adult onset Still's disease complicating newly developed macrophage activation syndrome following first tocilizumab introduction

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Conflict of interest: None

[Case] 29 year-old female admitted to our hospital with fever, rash, lymphadenopathy, sore throat, myalgia and arthritis. She also revealed splenomegaly and pericarditis on CT, and an elevation of liver enzymes and leukocytosis. She was diagnosed as having AOSD. Since the initial therapy with methyl-prednisolone (mPSL) pulse and prednisolone 50 mg was partially effective, she was started on tocilizumab on day 19. Although her systemic symptoms had improved rapidly, her laboratory findings revealed ferritin 1298.3 ng/mL, platelet 11.7×10^4 /μL and fibrinogen 145 mg/dL on day 29. She was diagnosed as having MAS, which was successfully treated with mPSL pulse and prednisolone 60 mg. She was reintroduced tocilizumab on day 35 and discharged without recurrence. [Discussion] There have been 6 reports on MAS following tocilizumab therapy in AOSD of active phase. Five cases were reintroduced tocilizumab successfully without a relapse. The possible mechanism of MAS may be associated with an unfavorable imbalance in cytokine network caused by specific inhibition of IL-6. Since this may be transient, re-administration of tocilizumab can be considered. [Conclusion] Reporting this case is valuable in considering the optimal induction remission therapy with tocilizumab in active AOSD.

P62-7

Elderly-onset Still's disease with RS3PE syndrome-like symptoms; a case report

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Conflict of interest: None

[Case] A 75-year-old man developed fever and polyarthritis with pitting edema on the dorsum of the hands and feet from 9 weeks before admission. He had no rash or sore throat. The blood test 3 weeks before showed increased white blood cell count with neutrophil dominance and C-reactive protein but were negative for rheumatoid factor, anti-cyclic citrullinated peptide, and anti-nuclear antibodies. Joint ultrasonography showed synovitis and tenosynovitis in the fingers, toes, wrists, and ankles. He received prednisolone (PSL) 15 mg/day under the diagnosis of RS3PE syndrome, which improved the edema, but the other symptoms persisted. At the admission to our hospital, blood test showed liver dysfunction and elevated serum ferratin (9000 ng/mL) and IL-18 levels (>5000 pg/mL). No apparent malignancy or infection was found. Adult-onset Still's disease (AOSD) was diagnosed. He achieved remission with steroid pulse therapy, following by PSL and cyclosporine. [Discussion] Some cases with RS3PE syndrome-like symptoms, including rheumatoid arthritis, polymyalgia rheumatica, ankylosing spondylitis, sarcoidosis, and systemic lupus erythematosus, have been reported, but no AOSD ones have. [Conclusion] AOSD can occur in elderly patients and can present with RS3PE syndrome-like symptoms.

P63-1

Three cases of polyarthritis with palmoplantar pustulosis (PPP) which were difficult to distinguish from Pustulotic Arthro Osteitis (PAO) and other types of arthritis

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Conflict of interest: None

(Case 1) A 39-year-old woman, who had past and family history of PPP. After tonsillectomy, her cutaneous symptom completely improved. Six years after tonsillectomy, she presented with polyarthritis with elevated rheumatoid factor (RF) at 28 IU/ml but her anti-citrullinated protein antibody (ACPA) was negative. She was diagnosed with rheumatoid arthritis (RA) and treated with MTX successfully. (Case 2) A 58-year-old man, who was diagnosed with PPP four months ago, presented with polyarthralgia and non-infectious pleuritis with elevated RF (269 IU/ml) but his ACPA was negative. With the treatment of prednisolone (30 mg), the pleuritis and polyarthralgia improved. However, during tapering of prednisolone, an exacerbation of polyarthritis was observed. He was diagnosed with PAO and his joint symptom was resistant to MTX and TNF inhibitors. (Case 3) A 64-year-old woman, who had past history of ulcerative colitis (UC) and PPP. She presented with polyarthritis without exacervation of UC and PPP. Her RF was elevated at (142 IU/ml) but ACPA was negative. It was difficult to distinguish from PAO and inflammatory bowel disease-associated spondyloarthritis. We treated her with NSAIDs, prednisolone, SASP, MTX and TNF-inhibitor (Adalimumab) successfully.

P63-2

Two cases of polyarthritis developed during immune checkpoint inhibitor therapy

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Conflict of interest: None

[Case 1] A-48-year-old woman with advanced lung adenocarcinoma developed polyarthritis after the first administration of nivolumab. PET-CT images indicated that the primary and metastatic lesions of the lung adenocarcinoma were significantly reduced, and increased FDG uptake was instead seen in the bilateral shoulder and hip joints. Her arthritis promptly improved with the administration of prednisolone (15 mg/day). The prednisolone was tapered while the nivolumab therapy was continued. [Case 2] A 76-year-old man with advanced urothelial carcinoma developed polyarthritis with extensive swelling of both his hands and feet after 17 cycles of pembrolizumab. PET-CT images demonstrated increased FDG uptake in multiple joints and the lung metastatic lesion of the urothe-

lial carcinoma. RS3PE syndrome was diagnosed, and the administration of prednisolone (15 mg/day) dramatically improved his symptoms within 2 weeks. Clinical significance: A few cases of arthritis during anti-PD-1 antibody therapy were reported, but this “case 2” is the first report of RS3PE syndrome developed during pembrolizumab therapy. In order for oncologists to recognize arthritis as immune-related adverse events, rheumatologists should actively report these immune-related musculoskeletal toxicities.

P63-3

A case of idiopathic multicentric Castleman’s disease with autoimmune hemolytic anemia

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Conflict of interest: None

[Case] A 66-year-old woman was referred to our hospital for further examination of fever, arthralgia and anemia in May. The anemia was diagnosed as autoimmune hemolytic anemia (AIHA). Additional examination showed polyclonal elevated IgG, systemic multiple lymph node enlargement and hepatosplenomegaly, then she was admitted to our hospital in July. [Clinical course] A lymph node biopsy of the axilla revealed interfollicular plasmacytic infiltration and capillary hyperplasia. Human herpes virus 8 infection was excluded. We diagnosed her as idiopathic Castleman’s disease (iMCD). She was treated with prednisolone and tocilizumab. Her symptoms were significantly improved. [Clinical significance] iMCD is a disease with multi-regional lymphadenopathy and systemic symptoms with characteristic pathology. Excessive production of cytokines, mainly IL-6, has been reported to cause various symptoms. AIHA, on the other hand, is a condition in which autoantibodies against red blood cells are produced, resulting in hemolysis. The involvement of Th17 differentiated by IL-6 has been reported in AIHA, suggesting that iMCD and AIHA share a common pathology caused by IL-6. [Conclusion] The possibility of AIHA should be considered in anemia with iMCD and tocilizumab should be effective.

P63-4

Successful treatment cases of Psoriatic arthritis with CKDG5D under maintenance hemodialysis treatment by guselkumab (an interleukin-23 blocker)

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Conflict of interest: None

[Objective] In Japan, PsA, a chronic inflammation, it’s like the arthropathy amalgamated by the frequency of the 3~10% in the psoriasis which is keratosis. A PsA patient is to a daily life function decline with progress of joint destruction. GUS is complete human-type monoclonal antibody medicine manufacturing to IL-23p19, and IL-23 is obstructed in peculiar way. There are no differences by MTX use and non-use to PsA, and the utility is expected of a haemodialysis patient. So far, there are almost no reports that GUS was thrown to the haemodialysis patient with PsA. [Case 1] Sixties and the female. A successful treatment case of PsA with frequent Vascular Access trouble repair. [Case 2] Fifties and male. A successful treatment case of PsA with uremic arthropathy and gout. [Consideration] Cross-linkage between natural immunity and acquired immunity participates in the clinical condition in Ps and PsA. In particular, IL-23/ -17 ancestry accomplishes a criterion. [Conclusions] Psoriasis was improved promptly by GUS, and frequent vascular access trouble also decreased sharply. A safe and useful possibility of IL-23/ -17 system control by GUS was suggested in a maintenance hemodialysis patient, too. Further, it’s necessary to be doing further long term observation.

P63-5

A case of neurosarcoidosis that could not be diagnosed by physical findings and CT scan but could be diagnosed by PET/CT

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Conflict of interest: None

[Case] 55 years old, male [Chief Complaint] Fever, headache [Present Illness] Brain tumor was removed and chemoradiotherapy was performed in X-3 years. In year X, a fever and a headache appeared. He visited our hospital on the 4th day after the onset of illness, and was admitted to our department for the purpose of treatment because the heat source could not be pointed out by physical findings, blood tests, and whole body CT scan. PET-CT showed accumulation in multiple lymph nodes, and right inguinal lymph node biopsy was performed. Cerebrospinal fluid examination showed increased cell count and head-enhanced MRI FLAIR images showed hyperintensity along the sulci, suggesting aseptic meningitis. On the 16th hospital day, lymph node biopsy revealed noncaseating epithelioid cell granulomas, and the patient was diagnosed with meningitis due to neurosarcoidosis. After mPSL 1000 mg for 3 days, remission was induced with PSL 55 mg (1 mg /kg/day), and fever and headache improved. [Clinical significance] Brain and meningeal biopsies are required for definitive diagnosis, but it is important to search for other biopsy-possible sites that are highly invasive. In this case, PET-CT showed that FDG had accumulated in small lymph nodes, which led to lymph node biopsy and could be diagnosed.

P63-6

Successful Use of Infliximab in a relapsing case of Ulcerative Sarcoidosis

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Conflict of interest: None

A 64-year-old woman presented with recalcitrant left lower leg ulcer. Pruritic and painful ulcer had gradually enlarged in two years without significant improvement with topical treatment. Physical examination revealed bilateral inguinal lymphadenopathy and pruritic erythema of lower legs and ulcerative lesion over the left shin. Chest Xray and ECG were unremarkable. Screenings for tuberculosis, syphilis, HIV, HBV, HCV and EBV were negative. Computed tomography scan with contrast revealed bilateral neck, hilar, paraaortic and bilateral inguinal lymphadenopathy. Inguinal lymph node and ulcer biopsy showed non-caseating granuloma, which confirmed the clinical diagnosis of sarcoidosis. Lymphadenopathy resolved with prednisolone 30 mg daily. Worsening of ulcer on methotrexate prompted initiation of Infliximab 5 mg/kg every 6 weeks, showing complete remission in 12 months. Ulcers as skin manifestation of sarcoidosis is rare. Although no definitive treatment for sarcoidosis is present, our case showed successful treatment of recalcitrant ulcer with infliximab.

P63-7

New-onset myasthenia gravis and sarcoidosis under tocilizumab treatment for rheumatoid arthritis

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Conflict of interest: Yes

A 72-years old woman was evaluated for a one-month history of generalized weakness. She was treated with tocilizumab for rheumatoid arthritis under good control. Six months before this presentation, the patient was diagnosed with ocular sarcoidosis. On admission, the neurological examination revealed proximal muscle weakness. Chest computed tomography showed patchy reticulation and bilateral hilar lymphadenopathy. The level of anti-acetylcholine receptor antibody was highly elevated, and repetitive nerve stimulation studies revealed a decremental response besides the significant improvement of muscle weakness by the edrophonium test. These results were consistent with the diagnosis of generalized myasthenia gravis. A high dose of methylprednisolone, intravenous immu-

noglobulin and tacrolimus were started, leading to the gradual improvement of her symptoms. Three months after this discharge, symptoms of myasthenia gravis relapsed, and abatacept was started subcutaneously. At one year of treatment, she has maintained clinical remission with prednisolone 5 mg/day and abatacept. We report our experience of new-onset myasthenia gravis and sarcoidosis under tocilizumab treatment for rheumatoid arthritis with some literature review.

P63-8

A case of Behcet's disease with MPO-ANCA positive autoimmune neutropenia

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Conflict of interest: None

A 36-year-old female was admitted to our hospital because of high fever and abdominal pain. She was diagnosed with Behcet's disease 14 years ago, and treatment with prednisolone and infliximab was started. Her blood test revealed high titer of CRP and liver enzyme. Her symptoms improved temporarily with antibiotics. But 4 days later, her symptoms worsened again, with significantly decreased neutrophil count (249 /μL). Bone marrow examination revealed that the granulocytic system was in a maturation arrest state. Immunological tests showed high levels of antinuclear antibodies (1:320) and MPO-ANCA (42.2 U/mL). G-CSF for febrile neutropenia was initially effective, but later became ineffective. Although not apparently complicated by systemic lupus erythematosus, she was diagnosed with autoimmune neutropenia. After increasing corticosteroid, we succeeded in improving her neutrophil count. After that, the dose of corticosteroid could be reduced by using mycophenolate mofetil in combination, and the neutrophil count became stable. The main pathological condition of Behcet's disease is considered as the autoimmune response of innate immune system. Therefore, it is rarely complicated by autoimmune neutropenia. It is considered that MPO-ANCA may help the diagnosis of autoimmune neutropenia.

P63-9

Eight cases of RS3PE (remitting seronegative symmetrical synovitis with pitting edema) syndrome in our hospital

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Conflict of interest: None

[Objective] To elucidate the backgrounds of RS3PE syndrome in our hospital [Methods] Eight cases for RS3PE syndrome patients were analyzed retrospectively from medical records. [Results] Sex ratio (Male 5: Female 3), average age 72.4 year-old, maximun predonisolone mean dosage 13.4 mg/day, maintenance predonisolone mean dosage 3.25 mg/day (One patient has been treated with methotrexate only throughout the treatment. Three patients have just started their treatments.) There were two cases of malignancies. One patient had a lung cancer (operated). The other had early stomach cancer (operated). There were two cases with diabetes mellitus patients who had been treated with dipeptidyl-peptidase IV (DPP-4) inhibitors throughout their courses of RS3PE syndrome without failures. Therefore, we could not assume that DPP-4 inhibitors were the cause of RS3PE sydrome in our cases. [Conclusions] It may be important to seek malignancies through their courses of RS3PE syndrome. Further accumulation and evaluation of RS3PE syndrome patients with diabetes mellitius, especially with DPP-4 inhibitors, might be necessary.

P63-10

Case experiences of multicentric reticulocytosis and a discussion focused on imagings

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Conflict of interest: None

[Case] A 74-year-old woman with a history of breast cancer was referred to our hospital because of polyarthralgia and skin eruptions. On examination, tenderness and swelling were noted at the distal interphalangeal (DIP), proximal interphalangeal (PIP), metacarpophalangeal (MCP), and hand joints. Multiple small papules were also observed on the fingers elbows, and face. X-rays revealed multiple erosions in the DIP joints, and FDG-PET showed no malignancy but accumulations in bilateral shoulder, elbow, hand, finger, and knee joints. A diagnosis of multicentric reticulocytosis (MRH) was made based on skin biopsy. Methotrexate and etanercept were started and remission was achieved. [Discussion and clinical significance] Radiographic features of MRH include the symmetric distribution, predilection for the DIP joints, "worm-eaten-like" sharp marginal erosions rapidly progress to involve the entire joint surface, and the lack of periosteal reaction such as periarticular osteopenia or new bone formation. While MRH progresses very rapidly and early diagnosis are desirable, it is still uncommon to encounter MRH in Japan. We will report on the clinical course of a case of MRH along with the case reported in JCR2019 WS12-3, with literature review focusing on imagings.

P63-11

A case of Hypocomplementemic urticarial vasculitis with airway stenosis caused by angioedema

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Conflict of interest: None

A 43-year-old woman with hypocomplementemic urticarial vasculitis (HUV) presented with acute attack of dyspnea and systemic urticaria without obvious trigger. Three years ago, she was diagnosed with systemic lupus erythematosus (SLE) and HUV. Her persistent rash remained stable with 5 mg predninsone and 25 mg diaphenylsulfone. In July of X year, she was taken by ambulance to the hospital. Because of the dyspnea, systemic urticarial rash and purpura, she was diagnosed with anaphylaxis. Intramuscular injection of adrenaline, intravenous administration of hydrocortisone and antihistamines temporarily improved symptoms without purpura. However pharyngeal discomfort and systemic urticarial rash were relapsed two days later. Her disease markers of SLE was stable. Then we considered her condition was HUV attack. After the dose of prednisone was increased to 15 mg/day, all symptoms reduced and disappeared. Conclusion: Here we presented a rare case of acute urticaria attack of HUV with airway stenosis caused by angioedema. In the case of HUV with systemic disorders, it may be difficult to distinguish it from type I allergic reactions. Because the complaints of HUV may be similar to those of SLE, we also discussed the differences of rash in SLE and HUV including literature reviews.

P64-1

An analysis of 26 cases of rheumatoid arthritis with lymphadenopathy that underwent lymph node biopsies in our hospital

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Conflict of interest: None

[Objective] We did this analysis to gain more insights about rheumatoid arthritis with lymphadenopathy. [Methods] We analyzed 26 cases of rheumatoid arthritis with lymphadenopathy that underwent lymph node biopsies in Kyushu University Beppu Hospital. We compared age, duration of rheumatoid arthritis, dosage of MTX, administration period of MTX, maximum diameter of lymph nodes, and three blood test items between the malignant lymphoma group and the other. In cases of malignant

lymphoma, we compared age, stage, and two blood test items between the group that underwent chemotherapy and the other. [Results] 18 cases were diagnosed as malignant lymphoma and 8 cases were diagnosed as reactive hyperplasia and so on. In a comparison of these groups, a significant difference was found in the administration period of MTX, the maximum diameter of lymph nodes, and serum LDH level. In 18 cases of malignant lymphoma, 11 cases underwent chemotherapy, and 7 cases did not need chemotherapy. In the comparison of these groups, no significant difference was found. [Conclusions] Lymph node biopsy is indispensable to make a diagnosis. Chemotherapy was given in the majority of cases of malignant lymphoma. We should carefully observe the progress after discontinuing the immunosuppressant.

P64-2

Clinical characteristics of Methotrexate-associated Lymphoproliferative Disorder (MTX-LPD) in Rheumatoid Arthritis (RA) patients

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Conflict of interest: None

[Objective] To summarize data of RA patients who developed MTX-LPD in our institution. [Methods] We retrospectively analyzed 11 RA patients who developed and were treated for MTX-LPD from April 2011 to Sep 2020. [Results] Mean age was 66.9 years, median duration of disease and MTX use were 11 and 5 years respectively. 4 cases among 11 (4/11) received biological DMARDs (bDMARDs) prior to diagnosis. Majority of cases (5/11) were diagnosed with Diffuse large B cell lymphoma. 4/11 presented lymphadenopathy alone, 4/11 presented extranodal lesions alone and both were seen in the remainder 3/11. Extranodal lesions included tonsil, thyroid, stomach, liver and pleura. EB virus encoded RNA (EBER) was positive in 4/11. After discontinuation of MTX, 3/11 regressed (regression group: RG) and 8/11 (persistent group: PG) required chemotherapy, all of which achieved complete response. After treatment of MTX-LPD, RA treatment did not include MTX or bDMARDs. Among the RG, 2/3 have moderate/high disease activity and additional bDMARDs is required. Among the PG, 2/8 are in remission untreated and 6/8 have low disease activity receiving conventional synthetic DMARDs (MTX excluded) or low dose glucocorticoid. [Conclusions] MTX-LPD is a rare condition, but with proper management we can expect favorable results.

P64-3

MTX-associated lymphoproliferative disorder (MTX-LPDs) in patients with rheumatoid arthritis: report of 6 cases

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Conflict of interest: None

[Objective] Methotrexate (MTX) is the first choice drug for rheumatoid arthritis (RA) and is refered to as an anchor drug. Its use has been increasing. MTX-related lymphoproliferative diseases (MTX-LPD) has emerged as important complications in the patients with RA. We report herein on six cases of patients with RA who diagnosed as MTX-LPD. [Methods] This was a retrospective study, 6 patients of MTX-LPD with RA who underwent MTX therapy between 2015 and 2019. [Results] The mean age of these patients was 67.2 years, the duration of illness was 18 years, the duration of MTX therapy was 8.1 years, and the mean MTX dose was 9.2 mg / week. Two of the patients had bDMARDs, infliximab in 1 and tocilizumab in 1. Histpathologically, diffuse large B cell lymphoma (DLBCL) in three, Hodgkin lymphoma in one and MALT lymphomain one. All patients discontinued MTX and the lesions disappeared in three cases. Another three had chemotherapy and good clinical courses are followed. [Conclusions] In the case of patients with RA who are taking MTX, tacrolimus or b DMARDs, MTX-LPD should be noted for early diagnosis.

P64-4

three cases of MTX-LPD in patients with psoriatic arthritis (PsA)

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Conflict of interest: None

Most cases of methotrexate-associated lymphoproliferative disorders (MTX-LPD) develop in patients with rheumatoid arthritis (RA). Only few of them develop in patients with psoriatic arthritis (PsA). We herein report three cases of PsA-LPD. Case 1: A 52-year old woman who had a 38-month history of PsA was diagnosed as atypical lymphoid proliferation with EBER-1 positive on inguinal lymph node biopsy. She had been receiving MTX for 35 months at 6 to 12 mg/w. Withdrawal of MTX induced tumor regression, which continued for 13 months. Case 2: An 88-year old man with PsA for 83 months developed Hodgkin lymphoma (HL), which was diagnosed using cervical lymph node biopsy. He had been receiving MTX for 74 months at 8 mg/w and tacrolimus for 78 months at 1 mg/day. After pathological diagnosis, the patients immediately received ABVD therapy and continued complete remission (CR) for 8 months. Case 3: A 61-year old male patient with PsA for 25 months was diagnosed as having HL by cervical lymph node biopsy. He received MTX for 12 months at 6 mg/w. Immediately after one course of ABVD therapy, C-MOPP therapy was administered and continued CR for 39 months. Considering the pathogenesis of MTX-LPD, it is useful to examine the features of PsA-LPD because they could exclude the effect of RA.

P64-5

A case of OIIA-LPD appearing on the dorsal side of the right ankle and proximal part of the right forearm during treatment for rheumatoid arthritis

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Conflict of interest: None

A 65-year-old woman with rheumatoid arthritis had been treated with MTX 12 mg, PSL 2.5 mg and GLM 100 mg. But she was discontinued from GLM because of suffering from cryptococcal pneumonia and organized pneumonia. Egg-size tumors appeared on the dorsal side of her right ankle and right forearm, so she visited our hospital. TJC 15 joints, SJC 5 joints, PGA 80 mm, CRP 1.58 mg/dL, DAS28CRP 5.89, HAQ-DI 0.93, sIL-2r 2540.4 U/mL. CT showed thickening of the soft tissue concentration structure around tendon group of right ankle and swelling of the proximal radial carpi radialis, brachioradialis and supinator muscles of right forearm. MRI showed an 8 cm-sized soft tissue mass surrounding the dorsal tendon group from the front of the right lower leg with T1WI low, T2WI intermediate intensity and uniform enhancement effect, and a tumor spreading inside and outside the joint from elbow to the forearm with T1WI low, T2WI non-uniform intensity and abnormal enhancement effect. Histopathological findings of right foot tumor is shown diffuse infiltration of large atypical lymphocytes with degenerative necrosis with CD20+, CS30+, CD3-, and numerous EBER (ISH)-positive cells. She was diagnosed with OIIA-LPD. Withdrawal of MTX led tumors regression. LPD rarely occur in these areas and should be noted.

P64-6

A case of the methotrexate-related lymphoproliferative disease with multiple bone lesions

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Conflict of interest: None

Case: 56 years old man. He presented with polyarthritis during treat-

ment of the pemphigus in X-14 year, and diagnosed as RA due to significant joint destruction of the both hands joint. He received MTX 8 mg/week and tacrolimus 3 mg/day and maintained clinical remission. Lumbago developed from March in X year and CRP (5.50 mg/dl) increased one month later. Both LDH 327 U/L and sIL-2R 1,051 U/ml were increased, but ALP 330 U/L was normal. Systemic CT showed multiple osteolytic lesions. The bone marrow biopsy showed euplasia marrow and bone biopsy showed the CD20-positive B-cell lymphoma. Complete remission may be obtained only by MTX cancellation, but we performed rituximab (375/m^2) monotherapy in treatment four cycles in total because the cortical bone of the right humerus cortex already became remarkably thin, and the significant bone pain appeared. The treatment succeeded, as the bone pain improved, the osteolytic lesion reduced and the cortical bone recovered. Clinical significance: The MTX-LPD case with the multiple bone lesion was able to prevent a pathologic fracture by early rituximab administration in addition to MTX cancellation. It was thought to be important to prognosis improvement that we should chose treatment depending on extent of the lesion.

P64-7

A case of elderly-onset adult-onset Still's disease complicated with testicular malignant lymphoma under treatment with tocilizumab and tacrolimus

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Conflict of interest: None

A 80-year-old man was presented with fever and macular salmon-pink eruption. Laboratory findings showed high levels of WBC count, aminotransferase, and ferritin. Bone marrow biopsy revealed hemophagocytosis. There was no evidence of infection, malignancy, and vasculitis. He was diagnosed with adult-onset Still's disease (AOSD). Since treatments of steroid pulse therapy and tacrolimus did not achieve enough improvement, tocilizumab was added and his symptoms ameliorated. Six months later, he was hospitalized for left abdominal pain and appetite loss. CT scan showed left testicular tumor and abdominal lymphadenopathies. Left high orchiectomy was performed and pathological findings revealed malignant lymphoma (DLBCL). Since we suspected ''Other iatrogenic immunodeficiency-associated lymphoproliferative disorders'' provoked by immunosuppressive therapies, tocilizumab and tacrolimus were discontinued. But his general condition was not ameliorated and he died. Even though lymphomas account for only 1% to 7% of all testicular malignancies, they represent the most common testicular tumor in men older than 50 years of age (*J Clin Oncol*, 2003). There has been no report of elderly onset AOSD complicated with testicular malignant lymphoma, and here we report the interesting case.

P64-8

A case of iatrogenic immunodeficiency-associated lymphoproliferative disorders (LPD) presented monoclonal gammopathy (MG)

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Conflict of interest: None

A 94-year-old female with rheumatoid arthritis (RA) has been treated with prednisolone (PSL), methotrexate (MTX) since May, 2010 and added Golimumab (GLM) since January, 2015. She was treated with PSL (5 mg/d), MTX (4 mg/w), GLM (50 mg/2 m) recently and has had anorexia after a fever, developed pneumonia, pleural effusion and mass shadow by CT subsequently, admitted to our hospital on November 15, 2019. Pneumonia was treated with antibiotics and oxygenation after discontinuation of MTX and GLM, but PSL continued. The respiratory function and anorexia were improved accordingly. Complication of LPD was assumed by elevated sIL-2R (2470 U/ml) and MG. CT shadows were improved on December 14 and MG disappeared at the same time, but the suspicion of IgG-λtypeMG continued. We guess that MG, pleural effusion and mass occurred in LPD disappeared by withdrawal of MTX and GLM. Clinical significance is that LPD presented MG is rare and disappeared by withdrawal of MTX and GLM, reported. Next MG is evidence of proliferation of monoclonal lymphocytes and plasma cells, hence a relapse of LPD requires attention, being not the relapse by October, 2020, because it is possible existence of IgG-λtypeMG. Finally we infer Lymphoplasmacytic lymphoma as LPD, however the pathology is unknown for spontaneous regression.

P65-1

Incidence rate of osteonecrosis in patients with systemic lupus erythematosus using Japanese health insurance database

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Conflict of interest: Yes

[Objective] To investigate the time-trend of incidence rate (IR) of osteonecrosis (ON) in patients with systemic lupus erythematosus (SLE). [Methods] Using claims data provided by Medical Data Vision Co., Ltd, we defined individuals as SLE cases if they had at least one ICD10 code of SLE, had at least one medication for SLE between January 2010 and January 2017, and were ≥18 years old (n=16,386). ON was defined by ICD10 code. Patients were followed from the next month of the first month in which cases met the above criteria until the earliest of the month of the first ICD-10 code of ON, the month of loss of follow-up, or December 2017. We calculated IR in each year and adjusted relative risk (RR [95% CI]) for ON using a Poisson regression model. [Results] The mean age was 53.7 years, 81.3% were female, and total observation term was 47,138 patient-years (PY). IR/1,000 PY of ON in each year from 2010 to 2017 was 13.2, 10.6, 11.0, 13.3, 13.1, 9.8, 8.5, and 7.3, respectively. Adjusted RR in each year from 2011 to 2017 compared to 2010 was 0.5 [0.2-1.4], 0.3 [0.1-0.9], 0.6 [0.3-1.4], 0.7 [0.3-1.6], 0.4 [0.2-0.8], 0.4 [0.2-0.8], and 0.3 [0.1-0.7], respectively. [Conclusions] Significant decrease of IR of ON after 2015 was observed in Japanese patients with SLE.

P65-2

Study of complications associated with prognosis of rheumatoid arthritis patients

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Conflict of interest: None

[Objective] In order to elucidate complications which affect prognosis of rheumatoid arthritis (RA) patients. [Methods] 522 cases of RA diagnosed between 2008 and 2019 were analyzed for complications resulted in hospitalization, death or serious aftereffects. [Results] Demographics of patients were as follows: 59.5±14.2 y/o; duration of RA 20.5±86.2 y; male 29.7%, female 64.3%. Infectious diseases were found in 16.8%, respiratory infections 60.2% (bacterial infections 36.4%, pneumocystis pneumonia 15.9%), and skin infections 30.7% (shingles 22.7%, cellulitis 8.0%). Malignancies were found in 22.8%; solid cancers 51.3%, hematopoietic tumors 48.7%, and other iatrogenic immunodeficiency-associated lymphoproliferative disorders (Oii-LPD) 26.9%. The mortality rate was 10.3%: age of death 74.9 ± 9.6 y/o; duration of RA 16.0 ± 15.5 y; male 42.1%, female 57.9%. Causes of death were as follows: infectious diseases 32.8%, malignant tumors 27.6%. [Conclusions] Infectious diseases and malignant tumors were the most common complications leading to death during treatment for RA. It is recommended that RA patients should be carefully followed-up for infectious diseases and malignant tumors.

P65-4

Clinical features of 22 patients with rheumatic disease who underwent transcatheter arterial embolization to control severe bleeding

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Conflict of interest: None

[Objective] To determine the clinical profile of rheumatic disease patients who underwent transcatheter arterial embolization (TAE) to control severe bleeding. [Methods] Data from 22 rheumatic disease patients treated by TAE for severe bleeding, between April 2010 and April 2020 in our hospital, were retrospectively analyzed. [Results] The underlying diseases were rheumatoid arthritis (n = 8 cases), systemic lupus erythematosus (SLE; n = 4), ANCA-related vasculitis (n = 5), polyarteritis nodosa (n = 1), Takayasu's arteritis (n = 1), and others (n = 3). Causes of bleeding included underlying disease (SLE and microscopic polyangiitis, n = 2) and complications/comorbidities (n = 16; 3 cases of bronchiectasis, 1 case of chronic respiratory tract infection, 1 case of lung cancer, 7 cases of gastrointestinal bleeding, 1 case of acquired hemophilia, 1 case of thrombotic microangiopathy, and 2 cases of segmental arterial mediolysis). The bleeding sites were the bronchial artery (n = 5), intraperitoneal/gastrointestinal organs (n = 15), retroperitoneal organs (n = 1), and the humeral artery (n = 1). [Conclusions] Both the causes of bleeding and the bleeding sites, in rheumatic disease patients who underwent TAE, are very versatile.

P65-5

Retrospective analysis of risk factors for insulin introduction in high-dose steroid therapy

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Conflict of interest: None

[Objective] Steroid diabetes can promote immunodeficiency and organ damage, cause various disadvantages to patients. Steroid induced hyperglycemia often requires enough treatment with insulin. The purpose of this study was to investigate the introduction of insulin in patients using high-dose steroids in our department, and to examine their risks and therapeutic effects. [Methods] Patients admitted to our department who required 0.8 mg/kg or more in terms of prednisolone for the treatment of autoimmune diseases were collected. They were divided into regular insulin introduced group and non-introduced group and their comparison was made between the groups. [Results] Of the steroid introduced patients, 34.3% needed insulin treatment at discharge. Univariate analysis revealed a significant difference in HbA1c, Hb, eGFR and age. The cutoff point shown by the ROC curve was HbA1c 6.1% (AUC 0.83) and age 68 years (AUC 0.75). During the 6 months after the start of treatment, HbA1c was suppressed to within 6.5% on average in both groups. [Conclusions] High dose steroid use resulted in frequent insulin introduction. High HbA1c levels and older people could be a risk of insulin induction. Even in those high-risk patients, insulin treatment provided proper glycemic control.

P65-6

Retrospective analysis on clinical features of pulmonary hypertension associated with connective tissue disease

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Conflict of interest: None

[Objective] To elucidate the clinical features and current therapeutic status of pulmonary hypertension associated with CTD-PH in our institute. [Methods] Medical records of 32 patients with CTD-PH who were treated in our hospital were reviewed and analyzed retrospectively. [Results] Baseline CTD include 12 SSc, 4 MCTD, 2 SLE, 3 PM, 1 SjS, 3 RA and 7 overlap syndrome. Average age at onset of PH was 59.1. Interstitial pneumonia (IP) was complicated in 21 cases. Simultaneous onset of PH and CTD was seen in 11 patients. Mean pulmonary arterial pressure was 33.4 mmHg and average pulmonary arterial wedge pressure was 12.4 mmHg. Five patients were treated only with immunosuppressive therapy including prednisolone. On the other hand, 6 patients were treated only with PAH-specific drugs. Twenty patients received both immunosuppressive agents and PAH-specific drugs. One patient was untreated. Eleven dead patients had IP more frequently compared to 17 alive patients. [Conclusions] Some CTD patients can be treated successfully only with immunosuppressive agents without PAH-specific drugs. On the other hand, most SSc patients with CTD-PH may need PAH-specific drugs irrespective of immunosuppressive therapy. Complication of IP was the only significant factor associated with mortality.

P66-1

A case of cutaneous mucormycosis complicated by microscopic polyangiitis and difficult to differentiate from pyoderma gangrenosum

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Conflict of interest: None

[Case] An 81-year-old man. He was diagnosed with microscopic polyangiitis due to fever, high inflammatory response, renal dysfunction, interstitial pneumonia, and skin rash. A skin biopsy was performed on December 17, and vasculitis including fibrinoid necrosis was observed in the capillaries and medium-sized blood vessels. For the diagnosis of pyoderma gangrenosum associated with microscopic polyangiitis, oral minocycline and topical tacrolimus were started, but there was a tendency to worsen the disease. PAS and Grocott staining of the skin pathology specimens revealed vascular occlusion due to fungal organisms. The diagnosis of cutaneous mucormycosis was made based on the fungal morphology and treatment with skin debridement and Liposomal Amphotericin B (L-AMB) 5 mg/kg/day was started on January 7. Skin findings improved, and L-AMB was discontinued from March 13 due to epithelialization completion. [Discussion] Mucormycosis has a strong vascular affinity and causes purpura and ulceration of the skin. In this case, it was difficult to distinguish cutaneous mucormycosis from pyoderma gangrenosum based on clinical symptoms alone. It is important to recall cutaneous mucormycosis in localized skin lesions that do not respond well to treatment.

P66-2

A case of infected rheumatoid vasculitis who had done lower limb amputation triggered by steroid dose reduction

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Conflict of interest: None

[Purpose] We report a case of rheumatoid arthritis sufferd from toe ulcers with infection and treated with anticoagulant therapy, steroid dose reduction, who had to be done an below kneee amputation. [Current medical history] 85 years old, female. Elderly onset of 73 years. Stage 4, class 3. Past History: multiple spinal compression fractures, proximal femur fracture, osteoporosis, lumbar spinal canal stenosis. Smoking history: 6 cigarettes / day. At the age of 83, MTX 6 mg and PSL 7.5 mg was initiated. At the age of 85, a contusion wound was formed on the right second toe. After 60 days, the ulcer didn't improve. She administrated due to foot pain. CRP 0.84 ESR 67 mm/H. RF 72. Treatmetnt with anticoagulants was started. One the 3rd day, Since local redness and heat were observed, the PSL dose was reduced to 5 mg. The ulcer worsened rapidly and ischemic necrosis occurred. She had to get below knee amputation. Postoperative wound healing was prolonged and improved with PSL dose increase. [Discussion] In the treatment of toe ulcers accompanied by infection, it may be difficult to judge whether to increase or decrease steroids. In this case, It was thought the complication of rheumatoid vasculitis, but the increase of steroids is troublesome with infection and ASO.

P66-3

Case report: Two cases of thrombotic microangiopathy (TMA) associated with dermatomyositis (DM), polymyositis (PM)

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Conflict of interest: None

(Case 1) A 86-year-old man with muscle weakness, Gottron's signs, elevated creatine kinase (CK), and anti TIF-1 antibody positive was diagnosed with DM. He was treated with prednisolone (PSL) 60 mg/day. As PSL was effective, we gradually tapered PSL dose. However, Hemolytic anemia and thrombocytopenia was present, and fragmented red cells were appeared in peripheral blood. It was considered with complication of TMA. As it was difficult to treat with plasma infusion because of old age and low general condition, we treated with supportive therapy. Unfortunately, he developed complication of aspiration pneumonia and died. (Case 2) A 77-year-old man with muscle weakness, elevated CK, and anti ARS antibody positive was diagnosed with PM. We started PSL 50 mg/day. As the therapy was effective, we tapered PSL with combination of tacrolimus (TAC). However, Hemolytic anemia and thrombocytopenia was present, and fragmented red cells were appeared in peripheral blood. We also diagnosis of complication of TMA. TMA was gradually improved after cessation of TAC. However, he developed complication of heart failure and died. TMA is occasionally associated with systemic erythematodes, sclerodema, and vasculitis. There are few reports of TMA with DM, PM and we had experience of two valuable cases.

P66-4

A case report: a patient with rheumatoid arthritis who developed rheumatoid meningitis during administration of golimumab

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Conflict of interest: None

Background: We report a case of the patient with rheumatoid arthritis (RA) who developed rheumatoid meningitis (RM) during administration of golimumab. *Case*: The patient with RA was a 74 year-old Japanese woman. Her affected duration of RA was two years. She received a monotherapy of golimumab 100 mg/month for RA. Because she felt lower-extremity weakness and top-heavy feeling and had a high fever, she was treated fluid therapy in the hospital. 10 days after admission, her symptoms were improved and left the hospital. Golimumab was resumed because of worsening disease activity. However, she felt top-heavy feeling and faintness on her left side again, she was hospitalized for intense scrutiny. She was diagnosed RM because the findings of MRI showed right temporo-parietal meningeal enhancement. Cell counts in cerebrospinal fluid (CSF) increased 70/μg, density of protein was 50.7 mg/dl and IL-6 was 361 pg/mL. All specific antibody for connective tissue disease, and viral, bacterial, mycobacterial and fungal testing of CSF were negative. Findings of MRI and CSF were improved after receiving steroid pulse therapy. *Conclusion*: Rheumatoid meningitis is a rare extra-articular manifestation of RA. The reports of RM in the patients who received biologics for RA is limited yet.

P66-5

A Case of rheumatoid arthritis noticed proteinuria, hematouria, renal function degeneracy after administration of sarilumab

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Conflict of interest: None

Case; A 71-year-old woman had RA 23 years ago, she had been treated with infliximab in addition to MTX for a long time. So her RA had been in remission. She had been on medications for hypertension and diabetes. Because she had MTX-LPD at the age of 69, the therapy with infliximab in addition to MTX were ceased. MTX-LPD disappeared two months later. But her disease activity of arthritis was exacerbated. Biologic therapy was resumed. She was treated with sarilumab. Her laboratory data showed that liver transaminase were slightly high, further her urine analysis showed proteinuria and microscopic hematuria 1 to 2 months later. Her disease activity of diabetes and hypertension were well-controlled. However proteinuria was sustained, the maximum amount of proteinuria was 2 g/day. Her renal function decreased gradually. Her urine sediment did not show any abnormal casts. Antinuclear antibody, PR3-ANCA and MPO-ANCA were negative. Drug-induced kidney injury caused by sarilumab was considered. The therapy with sarilumab was discontinued. Her amount of proteinuria was decreased, renal function was improving. The report of renal dysfunction caused by sarilumab could not find. This case suggests that we need to pay attention to renal function even when sarilumab is administrated.

P66-6

A case of segmental arterial mediolysis with multiple abdominal aneurysms diagnosed in a patient with rheumatoid arthritis

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Conflict of interest: None

[Case] 75-year-old woman with rheumatoid arthritis (RA) was admitted to our hospital due to fever and black vomit. Upper gastro-intestinal endoscopy did not reveal the source of bleeding. On the 5th day of hospitalization, she developed anemia and contrast-enhanced CT scan revealed retroperitoneal hematoma. Angiography demonstrated multiple aneurysms and dissections in the celiac artery and superior mesenteric artery branches. Embolization was performed for ruptured aneurysms. The next day, CT scan showed a new dilatation of the anterior superior pancreaticoduodenal artery. The typical fusiform aneurysms and dissections of arteries suggested segmental arterial mediolysis (SAM). The aneurysms had shrunk and did not rebleed after careful follow-up with CT scan. [Clinical significance] SAM is a rare disease causing multiple aneurysms and sudden intra-abdominal hemorrhage, and known to resolve spontaneously. Polyarteritis nodosa is a common cause of aneurysms, and rheumatoid vasculitis is often expected in patients with RA, both of which require remission induction therapy with immunosuppressive drugs. SAM is an important differential in cases of multiple aneurysms and hemorrhage in small to medium sized abdominal arteries because of the significant difference in treatment strategies.

P66-7

A case of cytomegalovirus ulcer following immunosuppressive therapy for pyoderma gangrenosum associated with systemic lupus erythematosus

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Conflict of interest: None

The patient is a 64-year-old woman treated with corticosteroid and hydroxychlorquine for systemic lupus erythematosus (SLE) and Sjögren's syndrome. She had suffered from left lower leg painful skin ulcer at 63 years old, and her skin ulcer did not resolve with conservative treatment. Skin biopsy from her leg ulceration was performed, this specimen showed extensive neutrophilic infiltration. She was diagnosed with pyoderma gangrenosum and got treatment with oral high dose corticosteroid and oral cyclosporin, however, her skin ulcer did not heal. After a month, we performed re-biopsy from her ulceration, the histology revealed typical cytomegalovirus (CMV) -infected cells with CMV inclusions confirmed by immunohistochemistry. Furthermore, there were many CMV-antigen-positive leukocytes, suggesting an active CMV infection, which is serious in compromised hosts. Valganciclovir was commenced and corticosteroid was decreased gradually, consequently, her left leg ulcer ameliorated and CMV-antigen-positive leukocytes became undetectable. We should require attention for CMV infection in patients who have immunosuppres-

sive therapy. Pyoderma gangrenosum has been rarely associated with SLE and little is known. We report a case of this association and review the current literature.

P66-8

A case of Behcet's disease that developed gastrointestinal bleeding when the drug was discontinued due to an increase in gastric polyps associated with the administration of a proton pump inhibitor (PPI)

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Conflict of interest: None

54 year old female. She is visiting our department because of Behcet's disease. Because of an increase in gastric polyps, she consulted with the prescribing doctor and the prescription was changed from omeprazole 20 mg / day to famotidine 20 mg / day. Nausea appeared 2-3 days later, black stools appeared 8 days later, and food intake became difficult 10 days later. Palpitations during body movement became noticeable, and 11 days later, she visited our hospital. She was admitted urgently because Hb, which was 11.1 g / dl at the time of the previous regular visit, was significantly reduced to 6.4 g / dl. Upper gastrointestinal endoscopy revealed bleeding from the upper body of the stomach. In recent years, the increase in gastric polyps associated with PPI administration has been pointed out by endoscopists, and prescribing doctors may be consulted by patients. It is desirable if PPI discontinuation is possible, but it is necessary to carefully consider other drugs used in combination, such as steroids and antiplatelet drugs, when determining this. If the risk of gastrointestinal bleeding due to PPI discontinuation is determined to be high, the option of continuing PPI with careful follow-up should be considered.

P66-9

A case of anti tif1 gamma antibody positive dermatomyositis complicated with type2 autoimmune hepatitis

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Conflict of interest: None

[Case] 63 year old man [Main complaint] skin eruptions [Progress] Since February X, skin eruptions have been observed on the face, neck, trunk, and limbs. In June of the same year, the patient visited our hospital because no improvement in symptoms was observed. Skin lesions such as Gottlon's rash and periungual erythema were observed, and anti-TIF1 antibody-positive dermatomyitis was diagnosed based on increased inflammatory response, muscle pain, interstitial pneumonia, and anti-TIF1 antibody positivity. Elevated AST and ALT were observed, an, anti-LKM1 antibody positive. Abdominal echo showed heterogeneous image of liver parenchyma, and liver image MRI showed changes in chronic hepatitis. A liver biopsy was performed, and as a result, infiltration of inflammatory cells, mainly plasma cells, was observed in the portal area, and the patient was diagnosed with type 2 autoimmune hepatitis. We started prednizolon and tacrolimus. The effect on interstitial pneumonia and myitis was good, but mild liver damage remained. [Discussion] In Japan, cases of anti-LKM1 antibody-positive autoimmune hepatitis are extremely rare, and since there are no reports of complications with dermatitis, we report this with some literature review.

P66-10

A case of hemophagocytic lymphohistiocytosis with a significant response to baricitinib

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Conflict of interest: None

A 51-year-old woman was admitted to the hospital with recurrent fever, lymphadenopathy and arthralgia. Based on the lymphadenopathy, high LDH level, and findings on PET-CT, she was considered to have malignant lymphoma. A right cervical lymph node biopsy was performed, but no malignant findings were found. Prednisolone 50 mg was started, but she did not improve. A rebiopsy of the supraclavicular fossa lymph nodes was performed, which also showed no malignant findings. Cyclosporine was started, which improved briefly, but relapsed again. Steroid pulse therapy was administered, but her leukopenia and thrombocytopenia progressed, and a bone marrow examination revealed a diagnosis of hemophagocytic syndrome (HPS). After treatment with etoposide, the fever and joint pain improved, but the neutropenia was prolonged, partly due to the effects of chemotherapy. Fungal infections were also complicated, and consolidation therapy with etoposide was not performed. However, the disease flared up. Chemotherapy in the presence of active infection was not advisable and baricitinib was started. Her fever and arthralgia quickly improved, and her blood cells also tended to increase. Since there have been no previous reports of HPS in which baricitinib has been effective, we report this.

P66-11

A case of acquired hemophilia A during with scleroderma

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Conflict of interest: None

Acquired hemophilia A (AHA) is a rare blood disorder caused by the production of antibodies against coagulation factor VIII. AHA is known to be associated with autoimmune diseases, but becouse AHA is a rare disease, it is rarely experienced to most rheumatoidologist. We report a case of AHA in a patient with scleroderma. 72 years old woman, developed scleroderma about 15 years ago. She also had pulmonary fibrosis. In October 2019, he had fever, nausea, and vomiting, She could not take all the drugs including steroids for several days. From the same period, swelling of the left and right feet and reticular purpura of the lower legs appeared (R < L). In November 2019, she visited our hospital and was given oral antibiotics, but not effective. She is hospitalized for treatment. Hematoma found in the left lower leg in the first hospital day. The hematoma has expanded. PT was normal even though APTT was highly extended. Blood coagulation level was normal at about 5 years ago. She was suspected AHA. Factor VIII activity was below sensitivity. Factor VIII Coagulation Inhibitor was 16 Bethesda. AHA was diagnosed because other coagulation factors were normal. She was improved byadministration of prednisolone 1 mg / kg (40 mg / body) for 3 weeks.

P66-12

A successfully treated case of hyperviscosity syndrome caused by non-malignant disease by prednisolone monotherapy

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Conflict of interest: None

[Case report] A 68-year old woman was admitted to our hospital because of three months history of hyperviscosity syndrome (HVS). Five years before admission, she had been diagnosed with rheumatoid arthritis, which remitted by abatacept and methotrexate (MTX). One year before, she developed mild pancytopenia persisting after discontinuation MTX. Although screening plasma cell dyscrasias revealed the existence of IgG-κ type monoclonal gammopathy, it was of undetermined significance. Three months before, HVS had appeared with fatigue, rouleaux formation in peripheral blood, microthrombus in palmoplantar, micro hemorrhage in eyeground. Further investigation also revealed heart failure but no evidence of malignant plasma cell dyscrasias. Thus, we diagnosed HVS as not caused by malignant disease and described prednisolone (PSL) solely to reduce M-protein. After the induction of monotherapy, M-protein reduced dramatically with the improvement of each symptom of HVS. [Discussion

and Conclusion] Although HVS is generally caused by plasma cell dyscrasias, it rarely occurs with mainly rheumatic diseases. Of those cases, clinical features and therapeutic strategies have never been clarified. Our successfully treated case with PSL monotherapy might be a clinical hint for a similar case.

P67-1

A case of IgA vasculitis complicated with recurrent cytomegalovirus infection with hypersensitivity to both valganciclovir and foscarnet, successfully treated with mizoribine

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Conflict of interest: None

[Case] A 85-year-old man was referred to our department because of purpura and acute renal failure. Since skin biopsy revealed small vessel vasculitis with IgA deposition, he was diagnosed with IgA vasculitis. With the start of 60 mg of PSL, IgA vasculitis improved. However, CMV hepatitis developed and valganciclovir (vGCV) was started. While hepatitis improved, he began having tongue tremor and ataxia. As stopping vGCV ameliorated both tremor and ataxia, they were likely to be adverse effects of vGCV. C7-HRP, being once negative, turned positive. And myelosuppression, also attributable to CMV, was occurred and foscarnet was introduced. Although C7-HRP improved, elevation of Cr level, presumably due to foscarnet, prevented its continuation. Simultaneously, abnormal shadows of the lung developed, which was later proved pulmonary tuberculosis. PSL, which had been tapered to 25 mg, increased to 50 mg with the start of rifampicin. Mizoribine (MZR) was added for its expected effect against CMV. Interestingly, no recurrence of CMV infection has occurred. [Clinical significance] The anti-CMV effect of MZR has been described, but it is not employed popularly in the field of rheumatology. The present case indicates that MZR has an anti-CMV activity for such an immunocompromised patient.

P67-2

A case of microscopic polyangiitis complicated with HTLV-1-associated neurological disorder

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Conflict of interest: None

A 79-year-old woman suffered from anorexia, back pain, gait impairment, recurrent orthostatic syncope and body weight loss for a month and was admitted to our hospital. Two years ago, she was diagnosed with microscopic polyangiitis (MPA) based on arthritis, interstitial pneumonia (IP) and positivity of MPO-ANCA. High dose prednisolone (PSL) was effective in remission induction therapy. She was taking of PSL and mycophenolate mofetil in the last 6 months, and she had been maintained in clinical and serological remission. These symptoms were unlikely associated with exacerbation of MPA, because physical findings did not revealed arthritis and sign of exacerbation of IP and MPO-ANCA titer remained negative. She revealed extremity weakness with decreased deep tendon reflexes and orthostatic hypotension. MRI revealed swelling of the thoracic spinal cord with dural thickening, and adenosine deaminase and protein level in CSF were elevated. Finally we found anti-HTLV-1 antibodies were positive in blood and CSF. After ruling out other spinal cord diseases, she was diagnosed with HTLV-1-associated neurological disorder. mPSL pulse therapy showed marked improvement in clinical and laboratory findings. We report a rare case of MPA complicated with HTLV-1-associated neurological disorder.

P67-3

A case of systemic lupus erythematosus patient with a fatal course due to herpes zoster virus encephalitis

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Conflict of interest: None

The patient was a 52-year-old woman with a history of rheumatoid arthritis, systemic lupus erythematosus and antiphospholipid syndrome. For the last 5 months, her treatment had not be changed from HCQ, SASP, MTX, and TAC without steroid. Eleven days before admission, she was diagnosed with herpes zoster and was prescribed amenamevir for seven days. The day before hospitalization, she could not be contacted, and the next day she was found lying down at home and was transported by ambulance. At the time of visit, in addition to the right upper limb rash, vesicles with detection of VZV antigen were found in the abdomen. Impaired consciousness was observed, and hyperintensity region on FLAIR MRI was observed in the multiple parts of the brain, and VZV PCR test was positive on cerebrospinal fluid. She was treated with acyclovir and steroids, but her consciousness disorder rapidly progressed and she died 5 days after admission. [Discussion] We experienced a case of herpes zoster encephalitis that had a fatal turning point. Now that the number of adult shingles patients is increasing, it is extremely important to take sufficient precautions and measures against herpes zoster for all immunosuppressed patients. Therefore, we presented this case with a review of the literature.

P67-4

A challenging case of polymyalgia rheumatica with interspinous bursitis resembling abscesses around lumber spinous process

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Conflict of interest: None

[Case presentation] A 73-year old woman was admitted to our hospital because of polymyalgia and fever. Half year before admission, proximal polymyalgia appeared and caused the difficulty of raising her upper limbs and walking. Three months before, persistent fever and night sweat developed, then she visited our hospital. Enhanced CT revealed ring enhanced lesions around lumber spinous process, indicating the lumbar site abscess as fever origin. However, microbiology test of punctured specimen from lumbar site showed conflicting results; (1) no growing bacteria in the cultivation test of it, (2) broad range PCR of it detected the DNA of Staphylococcus epidermidis. Because initiated antimicrobial treatment with adequate dose of vancomycin was not clinically effective, finally we administered prednisolone (PSL) based on the diagnosis of polymyalgia rheumatica (PMR) accompanying interspinous bursitis. After induction of PSL, all of her symptoms remitted rapidly. [Discussion] Interspinous bursitis of PMR may be indistinguishable from abscess. Understanding the limitation of microbial test and careful assessment of clinical course including response to antimicrobial treatment might be a clue to such a challenging case.

P67-5

A difficult case of acute ground-glass lung lesions in a rheumatoid arthritis patient, later diagnosed with methotrexate-related lymphoproliferative disorder

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Conflict of interest: None

[Case] A 70-year-old woman with rheumatoid arthritis (RA) who took oral methotrexate (MTX) and iguratimod, presented with recent history of lymphadenopathy and fever. Lab tests revealed hypoxia, pancytopenia and lymphoma-like cells in the peripheral blood. CT showed lymphadenopathy and diffuse ground-glass lung opacification. Respiratory failure acutely exacerbated and though lab data and lymphadenopathy strongly suggested MTX related lymphoproliferative disorders (MTX-LPD), *Pneumocystis* pneumonia and MTX related lung disease could not be ruled out, and steroid pulse therapy was started with sulfamethoxazole-trimethoprim. She underwent lymph node biopsy while intubated and was diagnosed with diffuse large B cell lymphoma. After stabilizing, she was transferred to the hematology department, underwent chemotherapy and was discharged. [Discussion] Diffuse ground-glass opacification in RA patients present with many differential diagnoses and its acute clinical course may

result in prioritizing treatment over diagnosis. In this case, MTX-LPD was diagnosed by biopsy but the lung lesions were unable to be analyzed. We prioritized the administration of treatment and the patient was successfully discharged. Further study is warranted on diffuse ground-glass lung lesions in RA patients.

P67-6

The association of the periodontal inflamed surface area with the serum levels of neutrophil extracellular traps and disease activity in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The present study aimed to test the hypothesis that the periodontal inflamed surface area (PISA) is correlated positively with the serum levels of neutrophil extracellular traps (NETs) and disease activity of rheumatoid arthritis (RA) in patients with RA. [Methods] The rheumatologic and periodontal data were collected from 88 patients with RA in a retrospective cohort study. The PISA was calculated from the periodontal data to quantify the total periodontal inflammation for each patient. The serum levels of NETs were determined using an enzyme-linked immunosorbent assay. [Results] The patients with a PISA > the median measurement in all patients showed a significantly higher serum levels of NETs (p=0.04) and higher disease activity score in 28 joints using C-reactive protein (DAS28-CRP) (p=0.02) than those with a PISA ≦ the median. Both univariate and multivariate analyses revealed that the PISA was significantly correlated positively with the serum levels of NETs (p=0.02 and p=0.002) and DAS28-CRP (p=0.002 and p=0.004). The serum levels of NETs were also significantly correlated positively with DAS28-CRP in the same analyses (p=0.01 and p=0.01). [Conclusions] The PISA is correlated positively with serum levels of NETs and disease activity in patients with RA.

P67-7

A case of purulent hip arthritis due to hematogenous infection, which was misdiagnosed purulent sternoclavicular joint arthritis as spondyloarthritis

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Conflict of interest: None

Anterior chest pain associated with sternoclavicular arthritis has been considered as one of symptom of spondyloarthritis. Differentiating aseptic arthritis of the spondyloarthritis from purulent sternoclavicular joint arthritis is often difficult. We reported a 55-year-old woman with left hip joint and right sternoclavicular joint pain. Diagnosis and treatment were delayed because she was misdiagnosed with spondyloarthritis, and hematogenous infection spread to the purulent hip arthritis. She was diagnosed promptly after presenting to our hospital and underwent early debridement, and her hip joint and sternoclavicular joint was found to have almost no dysfunction. Differentiation between sternoclavicular arthritis of the spondyloarthritis and purulent sternoclavicular joint arthritis is clinically important and requires careful attention.

P67-8

Characteristics of connective tissue disease patients who need hospitalizations due to infectious diseases

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Conflict of interest: None

[Objective] To clarify the characteristics of collagen disease patients who required inpatient treatment due to infection at our hospital. [Methods] We retrospectively analyzed data obtained from 170 hospitalizations between 2016 and 2019 required by 118 patients with collagen disease (30 males and 88 females). [Results] The primary diseases were rheumatoid arthritis in 45 cases, systemic lupus erythematosus in 28 cases. Average age was 68.3 ± 13.9 years, and the disease duration was 16.9 ± 13.0 years. During the observation period, 12 patients died and 38 patients were readmitted due to infection. Of the fatal cases, 11 (91.7%) had respiratory infections. We compared clinical findings of cases requiring readmission (38 patients) and cases not required readmission (55 patients). There were no significant differences in age, gender, steroid use. But the duration of illness was significantly longer (21.2 ± 13.0 vs. 14.7 ± 12.1 years, p = 0.017) and bone complications (fractures due to osteoporosis and femoral head necrosis) were more frequently observed in the group required readmission (81.6% vs. 18.2%, p <0.001). [Conclusion] When treating patients with longer disease duration or with bone complications, Rheumatologists need to consider the risk of repeated infections.

P67-9

Treatment of rheumatoid arthritis (RA) with pulmonary nontuberculous mycobacteriosis (NTM)

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Conflict of interest: Yes

[Objective] The aims of our study were to assess the safty of DMARDs in RA patients with pulmonary NTM disease. [Methods] Patients with RA who attended our department between April 2012 and September 2020 and were diagnosed with pulmonary NTM disease were studied for their background and clinical course using medical records. [Results] There were 11 RA patients with pulmonary NTM disease, 7 females/4 males, mean age of 73.8 years, and the drugs for RA were MTX (3 cases), TAC (1 case), PSL (5 cases), SASP (2 cases), and biological DMARDs (bDMARDs) (6 cases). Identified bacterial species were M. avium (4 cases), M. intracellulare (5 cases), and M. abscessus (2 cases). Antimicrobial treatment for pulmonary NTM disease was administered to 10 patients; 6 improved, 2 remained unchanged, and 2 died (1 pulmonary NTM disease and 1 lung cancer); 1 patient has survived without exacerbation without antimicrobial therapy. [Conclusions] As in previous reports, the use of bDMARDs for the treatment of RA can be considered feasible if the disease status of pulmonary NTM disease is stable. However, since there have been more than a few deaths due to NTM disease, each case needs to be carefully evaluated.

P67-10

Identification of a new biomarker for predicting herpes simplex and herpes zoster infection in rheumatoid arthritis using biologics

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Conflict of interest: None

[Objective] We reported in the 65th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology that rs10774580 on *OASL* (oligoadenylate synthetase like) may be involved in herpes simplex and herpes zoster infection. Therefore, we analyzed whether rs10774580 is useful as a biomarker for predicting herpes infection. [Methods] The subjects were 664 Japanese patients of rheumatoid arthritis (RA) using biologics. They were categorized into two groups: herpes group and non-herpes group. The genotype of rs10774580 was also categorized into two groups: major allele carrier and minor allele homozygous carrier. In order to analyze the effect of rs10774580 on the herpes infec-

tion, univariate logistic regression analysis and multivariate logistic regression analysis adjusted for sex and onset age of RA. [Results] The minor allele homozygous carrier was positively associated with herpes virus infection in the multivariate analysis. Unadjusted odds ratio (OR) and adjusted OR for the minor allele homozygous carrier was 4.4 (95% CI 2.1-9.0) and 3.7 (95% CI 1.7-7.9), respectively. [Conclusions] Our study has demonstrated that rs10774580 is one of the biomarkers for predicting herpes infection in RA using biologics.

P67-11

Two cases of connective tissue disease patients with false positive of EB virus anti-VCA IgM antibodies

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Conflict of interest: None

Fever, lymphadenopathy, and hepatotoxicity are the most common reasons for identification of viral infections such as EB virus (EBV) and cytomegalovirus (CMV). IgM antibody tests are used to diagnose acute viral infections, but false positives are also experienced in rare cases. We discuss the association between connective tissue disease and false positive of IgM antibodies. Case 1: 59-year-old woman was diagnosed with Sjogren's syndrome at a clinic more than five years ago, who developed a fever and a sore throat one week before. hepatotoxicity was observed. EBV anti-VCA IgM antibody was positive, but EBV nucleic acid quantification was negative and EBV infection was denied. Case 2: 55-year-old woman with rheumatoid arthritis who had been treated with methotrexate and adalimumab (ADA). She was found to have hepatotoxicity. Both drugs were discontinued and the patient was referred to our department. EBV anti-VCA IgM and CMV IgM antibodies were positive, but the patient was not infected with both viruses. Conclusion: There are various reports on the causes of false positive of viral anti-IgM antibodies, and interference by rheumatoid factor has been reported before. We have to take care in interpreting viral anti-IgM antibodies, in patients with connective tissue disease.

P67-12

A case of disseminated Mycobacterium absessus (M. absessus) infection in polyarteritis nodosa (PN) patient

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Conflict of interest: None

Case A 66 y. o woman admitted with multiple subcutaneous nodules, synovitis and arthritis. She was diagnosed with PN when she was 54 y.o. She had been treated with steroid and immunosupressants. but it recurred many times. 6 month before admission, she had to take PSL17.5 mg and immunosupressants, when her left arm was swollen and painful. 5 month before, her left hand and elbow joint was also swollen, and vaginal synovitis was detected. We thought RA or PN exacerbation, and we added MTX on. 3 month before, her right hip joint had pain. Many painful nodules also appeard in her legs, and she admitted. We performed a biopsy of the nodule, it appeard panniculitis and invation of neutrophils. MPSL pulse was performed, but nodules, pain and C-reactive protein got worse. She moved to another hospital. M. absessus was detected in her nodules and hip synovial fluid. She came back again, and we kept treating with Clarithromycin, sitafloxacin, imipenem, amikacin. We stopped immunosuppressant and, decreased steroid. She got quite well, though nodules still appeared and we kept treating with antibiotics. Conclusion We must think of nontuberculous mycobacterial (NTM) infection when we find synovitis. We should smear and culture not only for common bacteria but also for mycobacterium. We also can not rule out NTM by biopsy.

P67-13

Tuberculosis occurrence after a long term use of biologic DMARDs: two case reports

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Conflict of interest: None

Case 1. A 79-year-old woman with rheumatoid arthritis (RA) for 15 years was started on etanercept after being screened for tuberculosis (tb). No abnormality had been detected on the chest X-rays until she presented with worsening wet cough three years later, with her chest X-ray revealing a small cavity. Soon afterwards she was transferred as an emergency for pneumothorax and pus collection. Multiple cavities were identified in the lung after drainage while curettage specimen of the pleura grew *M. tuberculosis*. Case 2. A 68-year-old woman with RA, having an inadequate response to MTX, was started on abatacept in addition after being screened for tb. After four years wet cough gradually worsened, and bronchiolar inflammation became more marked on CT. Nontuberculous mycobacterium infection was suspected but repeated sputum cultures eventually grew *M. tuberculosis.* Clinical significance. Anti-TNF monoclonal antibodies (mAbs) are known to pose a higher risk of tb reactivation, typically early after initial dose. Conversely, tb development related to biologic DMARDs (bDMARDs) other than anti-TNF mAbs is often seen long after introduction and presumably in part due to new infection; therefore, regular checkup should be continued as long as bDAMRDs are in use.

P67-14

A case of laryngeal tuberculosis with rheumatoid arthritis

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Conflict of interest: None

She is an 83-year-old female with a history of rheumatoid arthritis diagnosed 23 years ago, her disease activity has been controlled with methotrexate and prednisolone. Although type 2 diabetes was also present, control was good with oral hypoglycemic agents. One day she developed a fever and a sore throat. Although withdrawal of MTX and administration of antibiotics, there was little amelioration in her sore throat, she visited our otolaryngology department, but no notable abnormalities were found. After the withdrawal of MTX, the sore throat was ameliorated for a while, but when MTX was restarted, the sore throat appeared, so MTX was stopped on October 7 in 2017. In 2018, when hoarseness appeared, she underwent laryngeal microsurgery, biopsy specimen was positive for the tuberculosis bacillus LAMP method. The next day, she had a sputum test positive for LAMP and Gaffky No. 8. We diagnosed laryngeal tuberculosis, she was admitted to the isolation ward and prescribed standard therapy. The clinical course was good. [Discussion] Laryngeal tuberculosis is rare at 0.24% of newly registered tuberculosis patients. Immunosuppressive therapy is important as a risk of tuberculosis infection, so it is important to distinguish laryngeal tuberculosis when hoarseness occurs in RA patients.

P67-15

Disseminated nocardiosis during the treatment for amyopathic dermatomyositis: A Case Report

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Conflict of interest: None

[Case] A 68-year-old male was diagnosed with amyopathic dermatomyositis (CADM) and interstitial pneumonia (IP) in October 2018. Steroid pulse therapy, intravenous cyclophosphamide therapy (IVCY), and tacrolimus (TAC) were used in combination to induce remission. In December 2018, exacerbation of lung shadow was noted, and the patient started taking cyclophosphamide (100 mg/day) (POCY). In mid-January 2019, an exacerbation of the pulmonary involvement was noted. And he was readmitted in late January. [Clinical Course] After the admission, antibiotic treatment was started. On the 7th day of admission, headache, incontinence, and disorientation were noted. The examination of cerebrospinal

fluid led to a diagnosis of bacterial meningitis. Brain MRI showed multiple brain abscesses. After that, abscesses were found in the right anterior chest and the left kidney. The blood culture at the admission detected *Nocardia farcinica*, and the patient was diagnosed with disseminated nocardiosis (DN). Antibiotics were changed according to drug sensitivity, and general condition improved without flare of CADM. Finally, he was discharged. [Discussion] Although it is a rare complication, we should consider the possibility of disseminated nocardiosis during the immunosuppressive treatment.

P67-16

A case of pulmonary actinomycosis (PA) in a young adult female with high tacrolimus trough level

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Conflict of interest: None

A 22-year-old Japanese woman with proximal muscle weakness and Gottron's sign was diagnosed with anti-MDA5 positive dermatomyositis 4 months ago. She was treated with high-dose corticosteroids and tacrolimus. The trough level of tacrolimus was 14.6 ng/mL. Remission induction therapy was successful. A month and a half ago, chest CT scan showed consolidation with a cavity in the lingular segment of the left lung. Despite oral antifungal treatment, chest x ray findings gradually worsened. Gram-positive rods were found in her sputum smears, suggesting pulmonary nocardiosis. MEPM and TMP-SMX were administered. Because *Actinomyces graevenitzii* was identified in her sputum culture by mass spectrometry, the treatment was changed to oral AMPC. After 10-week AMPC therapy, the lung lesion had almost disappeared. PA has been reported to be more common in male in their 50s in Japan. *Actinomyces* species are anaerobic gram-positive bacilli, difficult to identify in culture. PA is frequently confused with malignancy. Surgery often provides the approach to definite diagnosis. This case is rare in that it occurred in a young woman and the organism could be identified from sputum culture. PA might be one of the important complications to be aware of during high-dose tacrolimus treatment.

P67-17

Clinical features of patients with infectious endocarditis mimicking connective tissue disorders

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Conflict of interest: None

[Objective] We investigated the clinical features of patients with infectious endocarditis (IE) mimicking connective tissue disorders in our hospital. [Methods] Data from 99 patients diagnosed as having IE according to the modified Duke criteria in our department over 10 years (between July 2010 and June 2020) were analyzed retrospectively. [Results] Arthritis was noted in 12 (12%) patients, and the affected joints were small joints (3 patients) and large joints (9 patients). Seventeen patients (17%) experienced cutaneous manifestations, including palpable purpura in 14 patients. The cutaneous manifestations were found on the limbs (15 patients) and on the trunk (2 patients). Myalgia occurred in 4 patients (4%), and all of these patients had muscle pain in the thigh. Thrombosis occurred in 10 patients (10%). Cerebral infarction was observed in 9 patients, renal infarction in 3 patients, and splenic infarction in 4 patients. Of 31 patients, 10 (32.2%) tested positive for rheumatic factor. Of 25 patients, 1 (4%) tested positive for ANA. Of 19 patients, 1 (5%) tested positive for ANCA. Four patients (4%) were referred to the Division of Rheumatology and Allergy. [Conclusions] Clinical manifestations mimicking connective tissue disorders, in patients with IE, were frequently present.

P67-18

Coinfection with ESBL producing Escherichia coli, Pneumocystis jirovecii and Mycobacterium tuberculosis in a patient with rheumatoid arthritis

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Conflict of interest: None

A 79 years old female was diagnosed with RA, and commenced on MTX, but arthritis were not improved. In addition to ADL decline, the gangrene of the finger appeared, and nodular polyarteritis was suspected. She was admitted to our department and prescribed a methylprednisolone pulse therapy, followed by mPSL 20 mg and TCZ. She was discharged with MTX 12 mg/wk + TCZ 162 mg/wk + mPSL 8 mg. One month after hospital discharge, she had increased coughing and malaise, and had a fever of 39°C. At the visit, chest CT revealed multiple GGO in all segments of the lungs and pleural effusion. Septic shock and septic pulmonary edema were considered, we started to administer MEPM. The next day, ESBL-producing E. coli was detected in urine and blood, and we diagnosed it as urosepsis. After that, P. jirovecii and M. tuberculosis were found in the sputum specimen at the time of admission. Although antituberculous drug was started, she died of respiratory failure on the 7th hospital day. Autopsy revealed the formation of caseous granulomas and Zn stain-positive microorganisms in multiple organs including the lung. Furthermore organisms staining positive with Grocott were confirmed in the lungs. We report a rare case of PCP, Tb, and bacterial septicemia occurring at the same time.

P67-19

A case of sigmoid colon diverticulitis with abscess that developed during treatment for polymyositis with interstitial pneumonia and that was difficult to diagnose from diverticular colitis

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Conflict of interest: None

[Case] 4x-year-old female. At 4 years after the treatment of polymyositis with interstitial pneumonia, left lower abdominal colic began and sigmoid diverticulitis were diagnosed. Endoscopy denied ulcerative colitis and malignant tumors. The pain was relieved by treatment and relapsed repeatedly. After 2 years, an increase of immunosuppression for interstitial pneumonia coincidentally released the pain. Becasuse the pain worsened by reduction of immunosuppression and repeatedly released by enhancement of immunosuppression, diverticular colitis was suspected. A trial laparotomy performed, and she was diagnosed with sigmoid diverticulitis with intramural abscess which was surgically resected. [Discussion] The chronic abdominal pain that was relieved by immunosuppression in a woman being treated for polymyositis with interstitial pneumonia had the same characters as diverticular colitis. Diverticular colitis was active inflammation of the intestinal mucosa between diverticula, which is common in the elderly, is relieved by immunosuppression, and is considered to be a subgroup of inflammatory bowel disease (Kucejiko JR, 2018). We report that the final selected trial laparotomy helps the diagnosis of sigmoid diverticulitis with abscess from diverticular colitis in this patient.

P67-20

Two cases of nocardiosis deaths while being treated for rheumatoid arthritis

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Conflict of interest: None

[Case 1] A 71-year-old woman was diagnosed with SLE in 1981 and RA in 2008. Due to high disease activity, from April 2019, she took PSL12.5 mg+MTX8 mg+BAR4 mg+HCQ. Since November, she has been experiencing generalized malaise and cough. On December 27th, she was admitted to the hospital with GGO in both lungs. She was treated with steroidal pulse therapy and discontinued MTX, and then tapered PSL. CT

scan showed cavitary lesions and crazy-paving appearance in the lung field, and bronchial lavage showed nocardia. Her general condition worsened and she died despite the use of various antibiotics and a tapered BAR. [Case 2] A 60-year-old man developed mantle cell lymphoma in 2008, which was in remission with chemotherapy. He developed RA in August 2018. In October 2018, he developed interstitial pneumonia and stopped TCZ and MTX and improved with PSL increase. On January 7, 2020, he had reduced his PSL to PSL22.5 mg+TAC2 mg. After that, general malaise appeared, and he went to the hospital on January 28. He was diagnosed with multiple organ failure due to infection. CT scan showed cavitary lesions in the lung field. Nocardia was identified by sputum culture, and various antibiotics and steroidal pulse therapy were administered, but he died.

P67-21

Examination of 8 patients with rheumatoid arthritis who developed active tuberculosis

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the clinical course of patients who develop active tuberculosis while receiving rheumatoid arthritis (RA) treatment. [Methods] Subjects were 8 RA patients who have developed active tuberculosis at Higashi Nagoya Hospital since 2010. We retrospectively investigated changes in patient background, clinical course, and disease activity [Results] The patient background at the onset of tuberculosis was an average age of 65.2 years, 3 females (37.5%), and average disease duration was 2.1 years. In 3 cases, IGRA was confirmed as a screening for latent tuberculosis (LTBI) before RA treatment. MTX and biologics were used 7 patients and 2 patients respectively. There were 5 cases of pulmonary tuberculosis and 3 cases of extrapulmonary tuberculosis (2 cases of pleural membrane and 1 case of skin). After treatment for tuberculosis, one MTX and one ABT were used, respectively. The average DAS28-CRP transition was (0 week / 24 weeks / 1 year / 2 years: 3.1 / 2.8 / 2.7 / 2.4 / 2.9). [Conclusions] The importance of comprehensive evaluation for LTBI should be recognized and thoroughly implemented. In many cases, disease activity was relatively stable without MTX or biologics after tuberculosis treatment, so tapering may have been possible.

P67-22

A case of syphilis between marital infection had been suspected of connective tissue diseases because of positive antinuclear antibody

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Conflict of interest: None

[Case] 29-year-old woman [Main complaint] Low-grade fever, fatigue, low back pain [Current medical history] She had a low-grade fever, fatigue, and low back pain, so she visited a nearby doctor and was prescribed clarithromycin. But there was no improvement and the antinuclear antibody was 320 times higher, therefore connective tissue diseases suspected. She visited our department 20 days later. RPR and TPLA were strongly positive, with a slight increase in the inflammatory response. No symptoms such as rash or chancre were observed, but the patient was diagnosed with untreated syphilis infection. Her husband also had a fever and fatigue. Because he was also positive for RPR and TPLA, he was diagnosed with syphilis infection and this couple was treated with amoxicillin. Symptoms disappeared after treatment. [Clinical significance] We experienced the case of a young woman who was positive for the antinuclear antibody and suspected of having connective tissue diseases and was diagnosed with syphilis infection. In recent years, the number of syphilis patients is increasing especially among young people in Japan. Since syphilis presents with various symptoms, it is thought we require consideration of this disease when distinguishing autoimmune diseases.

P67-23

A case of disseminated nontuberculous infections with Mycobacterium avium during sarcoidosis

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Conflict of interest: None

[Case] A 75-year-old man was diagnosed with sarcoidosis on the basis of noncaseating granulomas proven by lymph node biopsy eight years ago. He was also diagnosed with sick sinus syndrome due to cardiac sarcoidosis. Upon initiation of oral steroid therapy, his symptoms were improved. He arrived at the hospital due to his buttock pain that had been going on for two months. The laboratory data showed high serum CRP. The pelvis MRI showed multiple osteolytic lesions in the ilium. We performed a bone biopsy from the ilium and found that there were the granulomatous lesions with multinucleated giant cells. We added acid-fast bacillus cultures and Mycobacterium avium was detected. Finally, we diagnosed disseminated nontuberculous infections. There are some reports that anti-IFNγ antibody is involved in the development of disseminated nontuberculous infections. We measured anti-IFNγ antibody and confirmed that it was positive. Clarithromycin, rifampicin, and ethambutol was started, and the patient was improved. To the best of our knowledge, this is the first report of anti-IFNγ antibody-positive disseminated nontuberculous infections during sarcoidosis.

P67-24

A case of extraperitoneal abscess during treatment for rheumatoid arthritis

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Conflict of interest: None

[Case] A 68-year-old woman. In January X, she was diagnosed with rheumatoid arthritis accompanied with adult onset Still's disease-like symptoms, fever, pericarditis, and hyperferritinemia. With high dose prednisolone and methotrexate (MTX), the condition had gradually improved. In July, after the transfer for rehabilitaion, she moved to an outpatient and as of September, she was admitted again because of appetite loss and dysuria. In addition to urinary tract infection (UTI), imaging showed an abscess in the peritoneal lumen, thus insertion of urethral catheter, discontinuation of MTX, antibiotic and drainage of abcess was conducted. A close examination revealed bladder perforation, but no traffic with the abscess and bladder and intestinal tract had already been observed. The treatment improved the abscess, and the palliative removal of urethral catheter was scheduled. [Clinical significance] We experienced a case of extraperitoneal abscess accompanied with UTI during immunosuppressive treatment. Pressure on the lower abdomen and fragility of the tissue may involve in the cause of bladder perforation. The case required early diagnosis and close examination based on other departments, we report it with a review of the literature.

P67-25

Antibiotic-associated hemorrhagic colitis caused by Klebsiella oxytoca after taking low-dose trimethoprim-sulfamethoxazole to prevent Pneumocystis pneumonia

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Conflict of interest: None

Trimethoprim-sulfamethoxazole (TMP-SMX) occasionally induces Clostridium difficile infection (CDI) but during prophylaxis therapy of low-dose TMP-SMX for Pneumocystis pneumonia (PCP), there are few gastrointestinal problems. Antibiotic-associated hemorrhagic colitis (AAHC) is observed during therapy with penicillins, cephalosporins and quinolones. We describe here AAHC caused by Klebsiella oxytoca after taking low-dose TMP-SMX to prevent PCP. A 74-year-old woman was admitted to our hospital with relapse of ANCA-associated vasculitis with hypertrophic pachymeningitis. Prednisone was increased to 30 mg/day and low-dose TMP-SMX was also started on admission. On the 1st hospital day, rituximab was administered as 500 mg. On the 5th hospital day, she had fever, bloody diarrhea, vomiting. Her inflammatory markers were raised and abdominal CT scan with contrast showed bowel wall thickness. C. difficile antigen and toxin in stool were not detected. Cytomegalovirus pp65 antigenemia was negative. Gram's staining of stool revealed K. oxytoca. Her symptoms were promptly improved after discontinuation of TMP-SMX, so she was diagnosed as AAHC caused by K. oxytoca after taking low-dose TMP-SMX. Thus, our case indicated that prophylaxis of low-dose TMP-SMX for PCP induced AAHC caused by K. oxytoca.

P67-26

A case of Atypical Ramsay-Hunt syndrome in a patient with Rheumatoid arthritis after treatment with MTX

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Conflict of interest: None

[Objective] An 86-year-old woman, diagnosed as RA in 2011, had been treated with MTX, and remission. She felt tongue pain and visited otolaryngologist in private clinic, diagonised as Herpes simplex, firstly, there after as Ramsay-hunt sydrome caused facial nerve palsy and vertigo. Herpetic vesicles in or around the ear, facial nerve paralysis, and vestibulo-cochlear nerve paralysis manifesting hearing loss and vertigo characterize Ramsay-Hunt syndrome. Early intervention is important for complete recovery of the paralysis, but if not, it is more likely to remain permanent damage Although several reports about VZV reactivation in RA patients are very few. Here we report a cese of Ramsay Hunt syndrome recognized in a patient with RA after treatment with MTX. Ramsay-Hunt syndrome is a rare condition which is caused by reactivation of latent or persistent infection of VZV in the geniculate ganglion of facial nerve, occurring mostly in the host's immunosuppression. Its major [Conclusions] When this condition is suspected, immediate treatment should be introducing after the proper diagnosis by an otolaryngology specialist.

P67-27

The situation of outpatient clinic against COVID-19 and rheumatoid arthritis patients

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Conflict of interest: None

[Objective] The numbers of patients with fever gradually increase in 2020 so we started the Returnees and Contacts Outpatients Clinic. One patient with COVID-19 appeared in hospital in April and we opened fever outpatient clinic. We investigate those situation and rheumatoid arthritis (RA) patients. [Methods] Patients with 37.5 degree go to fever outpatient clinic through other rote. If we suspect respiratory infection, they accept CT scan or COVID-19 PCR tests. If they are positive, public health center correspond. If they are negative, we treat with normal ways. [Results] From April to October in 2020, the numbers of patients who came to fever outpatient clinic were 993, the numbers who accepted COVID-19 PCR test were 361 and the numbers with COVID-19 PCR test positive were 40. 12 RA patients came but there were no patients with COVID-19. 4 patients were pharyngitis, 2 patients were upper respiratory inflammation and RA fever. Others were periodontitis, oral candida, rhinitis and infective endocarditis. [Conclusions] There were no RA patients with COVID-19 but we must always think about infection. Our purpose are that distinguishing with COVID-19 and other diseases, providing safety to patients and protecting our stuff from any infection. We must continue our medical support.

P67-28

COVID-19 in a Patient with Rheumatoid Arthritis Receiving Conventional Disease-Modifying Antirheumatic Drugs

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Conflict of interest: None

[Case] A woman in her 70s had been suffered from anti-CCP-positive rheumatoid arthritis (RA) for 27 years. She was in low disease activity with 10 mg/week of methotrexate, 1000 mg/day of salazosulfapyridine, and 1 mg/day of prednisolone. She had chronic kidney disease and hypertension, but no lung disease, diabetes mellitus, cardiovascular disease, obesity, or smoking history. Due to the persistent fever over 39.0°C, fatigue and appetite loss for 2 weeks, she visited our clinic. Because a CT scan revealed multiple non-segmental ground-glass opacities in both lungs, she was admitted to our hospital. The SARS-CoV-2 PCR tested positive, and she was diagnosed as COVID-19. In spite of the risk factors for severe COVID-19, her condition was judged as moderate base on the slight hypoxemia. Her lab exams showed CRP 11 mg/dL, D-dimer 0.5 μg/mL, ferritin 625 ng/mL, and KL-6 428 U/mL. She was treated with favipiravir without increasing the dose of corticosteroids. Her symptoms, such as fever, resolved in 4 days. She was discharged home on day 11. [Clinical significance] This was the first COVID-19 case in our 4000 RA patients cohort. Considering that some 92000 cases had been reported in Japan, the risk of COVID-19 infection does not seem to be higher in RA patients than in normal population.

P67-29

A case of bilateral flexor tendonitis after COVID-19 showing a remarked response to glucocorticoid therapy

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Conflict of interest: None

(Case) A 45-year-old man with medical history of hypertension, dyslipidemia, hyperuricemia visited a hospital because of fever and cough in March 2020. The chest CT revealed ground-glass opacities, and the nucleic acid testing for SARS-COV-2 RNA of his nasopharyngeal swab was positive. He was admitted to our hospital due to dyspnea in April and took favipiravir treatment. His was discharged in June. From the discharge, he noticed morning stiffness in his fingers, and then edema and tenderness gradually occurred around proximal interphalangeal joints in his both middle fingers in July. CRP was slightly positive (0.22 mg/dL). RF, anti-CCP antibody, ANA. MMP-3, TSH, fT4 was within normal limit. Reactive arthritis was suspected, but salazosulfapyridine and celecoxib did not improve his symptoms. Hand MRI with contrast revealed bilateral flexor tendonitis around PIP joints of his both middle fingers whereas synovitis was unclear. Glucocoriticoid therapy (PSL 15 mg/day) began in August, and had remarked improvement. Findings of tendonitis disappeared in the second MRI in September. (Discussion) There are several reports about associated symptoms of COVID-19, but limited about musculoskeletal symptoms. We would herein discuss about rheumatic manifestations about COVID-19.

P68-1

A case of prolonged fever suggesting the involvement of NOD2 mutation

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Conflict of interest: None

[Case presentation] 51-year-old male. Chief complaint: fever. in January X. He presented with polyarthritis and a fever of 39°C. An antigen test

diagnosed influenza B, and oseltamivir and antipyretics were prescribed. However, the fever persisted and the patient was referred to our hospital two weeks later with a rash on his trunk. There was no obvious bacterial or fungal infection, rheumatoid collagen disease, or malignancy, and the fever in the 38s persisted for more than 2 months, with CRP around 10 mg/dl. Based on the fact that he had had several similar episodes in the past, exacerbation of symptoms due to cold weather, and a rash, we suspected an auto-inflammatory syndrome and prescribed colchicine. The patient was discharged from the hospital with a decrease in CRP. A rare variant of NOD2 was identified in the genetic examination. Since this mutation had not been functionally analyzed before, we performed NF-κB reporter assay using HEK293 cells, and showed a prolonged NF-κB activation compared to the wild type. [clinical significance] Our case showed a rare variant of NOD2, suggesting that this was resulting in a prolonged inflammatory response as a phenotype.

P68-2

A case of palmoplantar pustulosis osteoarthritis in which 16S rRNA analysis was performed on the radicular cyst

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Conflict of interest: Yes

Case 45 year old female At the age of 32, he developed palmoplantar pustulosis and anterior chest wall pain, and he was treated by a nearby doctor with biotin/ointment for palmoplantar pustulosis and NSAIDs for pain. Present illness at the first visit Palmoplantar pustulosis with stronger symptoms was observed. Tenderness in both sternoclavicular joints, costal joints, and Achilles tendon enthesitis. ASDAS 3.0 (3-3-10-4-0.99) was highly disease-activity. Blood biochemical tests were negative ACPA / RF / HLA B27. Medical history, etc. Right maxillary first premolar chronic apical periodontitis: root canal treatment discontinued Based on the above, we diagnosed palmoplantar pustulosis osteitis. The upper right 4 teeth judged to be the lesion infected part were extracted in 2019. Treatment findings: A radicular cyst with a diameter of 3 mm was attached to the root of the extracted tooth. A blood culture test was performed immediately after tooth extraction, and Fusobacterium nucleatum was found in both sets. Furthermore, 16S rRNA analysis of radicular cyst was performed at the Department of Immunology, Osaka University, and Actinomyces (42.9%), Rothia (19.6%), Porphyromonas (7.2%), and Fusobacterium (4.4%) were detected. Currently under follow-up.

P68-3

Examination of the significance of E148Q variant in Japanese patients with recurrent fever

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Conflict of interest: None

[Objective] The *MEFV* variants in familial Mediterranean fever (FMF) patients in Japan have few exon 10 variants with established diagnostic value compared to the Mediterranean region, and *MEFV* polymorphisms are frequently present in healthy individuals. In this study, we investigated the importance of variant in the *MEFV* gene E148Q (Glu148Gln) in patients with recurrent fever. [Methods] The clinical phenotype and genomic variants of systemic autoinflammatory diseases (SAIDs) including *MEFV* were analyzed in211 Japanese patients with recurrent fever in this study. Genetic analysis was performed via next-generation sequencing. [Results] Twelve patients met the diagnostic criteria for SAIDs other than FMF. Considering 199 patients with recurrent fever, 137 cases (68.8%) were clinically diagnosed with FMF. The compound heterozygous group containing E148Q was found to have a significantly higher risk of developing the FMF phenotype ($P = 0.036$) than the heterozygous group containing E148Q. [Conclusions] Patients with compound heterozygous E148Q with other *MEFV* alleles exhibited higher expression of FMF phenotype than those with heterozygous E148Q, and thus, E148Q may act as a modifier for other risk alleles.

P68-4

Splicing mechanism of ASC variant found in Japanese patients with palindromic rheumatism (PR)

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Conflict of interest: None

[Objectives] We previously investigated the inflammasome molecule ASC, and found the ASC splicing variant lacking exon2 (Δexon2 ASC) which increases IL-1β production as compared to wild type in Japanese patients with palindromic rheumatism (PR) (Asian Pac J Allergy Immunol, 2019). We also found that rs8056505 (A→G) SNP contribute to the production of Δexon2 ASC using HEK 293 cells, and reported in JCR 2018 meeting. Here we investigated the effects of IL-1β and its downstream signaling molecule, C6-Ceramide, on Δexon2 ASC production by using monocyte derived THP-1 cells. [Methods] Δexon2 ASC production *via* rs8056505 wild type A or mutant G allele was examined under IL-1β 0-200 pg/mL or C6-Ceramide 0-20 μM condition by using exon trapping method in THP-1 cells. [Results] Δexon2 ASC expression which dominantly expressed in the case with G allele as compared to A allele without stimulation was suppressed under 100 pg/mL IL-1β or 20 μM C6-Ceramide conditions. [Conclusion] Our results suggest that IL-1β and C6-Ceramide, which are increased *via* Δexon2 ASC, interfere with the splicing of ASC cooperatively with rs8056505 G allele and causes periodic expression of Δexon2 ASC.

P68-5

Familial Mediterranean fever (FMF) phenotype progression into anti-cyclic citrullinated peptide antibody positive rheumatoid arthritis: A case report

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Conflict of interest: None

FMF is caused by dysfunction of the *MEFV* gene product, pyrin. Here we report a case of FMF phenotype which developed into RA. A 42-year-old woman presented with polyarthralgia associated with menstruation lasting for over 6 months. No fever was reported. Laboratory tests revealed elevated CRP and RF. Autoantibodies including anti-CCP Ab and ANA were all negative. Genetic analysis identified an R304R homozygous mutation in *MEFV*; however, the pathological significance is unclear because this mutation does not cause amino acid substitution. We diagnosed incomplete FMF phenotype despite the lack of fever due to periodic arthritis, lack of autoantibodies, and complete resolution of arthritis following colchicine treatment within a day. Several months later, increased arthralgia persistently occurred. US revealed typical synovitis. Anti-CCP Ab turned into positive. Therefore, we finally diagnosed RA. Arthritis diminished following administration of MTX and SASP. We consider the possibility that pyrin dysfunction may have affected the acquired immunity, contributing to the onset of RA as an autoimmune disease. This is an interesting case of equivalent FMF progressing into RA and will be valuable to raise awareness of continuum from autoinflammatory to autoimmune disease.

P68-6

A case of familial Mediterranean fever with longitudinal ulcerative lesions localized to the distal end of the ileum during treatment with canakinumab

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Conflict of interest: None

[Case] A 24-year-old woman had been suffering from fever in the range of 38°C for about 3 days with chest pain and oligoarthralgia for 10 months. She was suspected to have familial Mediterranean fever (FMF) and introduced daily colchicine (COL). Since she did not respond to treatment with COL, she was referred to our hospital for further evaluation. She did not present findings suggestive of infection or autoimmune disease. Afterwards genetic analysis revealed a heterozygous variant in exon 5 of the *Mediterranean fever (MEFV)* gene (S503C), and we diagnosed her as a typical case of FMF with COL-resistance. We treated her with canakinumab (CAN), and the frequency of her fever attack was decreased. However, as of 4 months after treatment with CAN, she had a persistent fever with prolonged abdominal pain. These symptoms were different from those of her FMF attacks and she admitted to our hospital. Colonoscopy showed longitudinal ulceration localized to the distal end of the ileum. Crohn's disease was suspected, but the biopsy results showed only nonspecific inflammation without granulomas. Her fever and abdominal pain were in spontaneous remission. [Clinical significance] This is a valuable case that may contribute to the understanding of the pathogenesis of enteritis in FMF patients.

P69-1

A case of COVID-19 induced hemophagocytic syndrome

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Conflict of interest: None

A 62-year-old Japanese man was admitted for COVID-19 complicated with pneumonia. His past medical history was type 2 diabetes mellitus. He had fever for a week and positive for SARS-CoV-2 PCR, had pulmonary infiltrates on CT scan. After the initial therapy with dexamethasone, nafamostat mesylate, and favipiravir, his symptoms subsided. However, on 17 of hospitalization, he experienced a recurrence of fever without evidence of bacterial infection and referred to our department. Laboratory findings included platelets 70,000/μL, LDH 428 IU/L, FDP 14.7 μg/mL, and ferritin 2390 ng/μL, which suggested hemophagocytic syndrome (HPS). After bone marrow examination, he received 80 mg/day of methylprednisolone. His fever subsided again with the improvement of the laboratory findings. He was diagnosed as HPS based on hemophagocytosis in bone marrow and immunologic testing including low NK cell activity and elevated soluble IL-2 receptor. His HPS was attributed to COVID-19 due to absence of laboratory evidence indicating other viral infections. In COVID-19, there are reports of conditions associated with hyperinflammatory syndrome, such as HPS. Rheumatologists can play a role in the treatment of HPS provoked by COVID-19 with the experience of similar conditions related to rheumatic diseases.

P69-2

Utility of the new system in the home care of the autoimmune disease

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Conflict of interest: None

[purpose] It performs as a national measure to shift from treatment in hospital to home care. However, from the deficiency of the physician performing home care for the refractory autoimmune disease, The construction of the home care system of this rheumatology field is necessary. We sent weekly a rheumatologist to the home care clinic and reviewed the effect this system. [method] It applies to patients with refractory autoimmune disease admitted to this hospital from January, 2010 to April, 2020. We reviewed our difficulty indicator for transfer to hospital based on difficult indicator from the Japanese institutional society. Furthermore, we compared the number of days in hospital of the patients with positive indicator in clinic with rheumatologist and without rheumatologist. [results] Our difficulty indicator included use expensive drug, immunosuppressive drug, biological drug except the common difficulty index. It was the tendency that clinic with rheumatologist had a shorter in the number of days. [conclusions] The construction of the treatment at home system is difficult in our university hospital. Using the present system, the utility of this home care system with rheumatologist was shown.

P69-3

The study of Prednisolone oral pulse therapy efficacy for polymyalgia rheumatica

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Conflict of interest: None

Objective To examine effectiveness of pulsed oral steroid (oral-P) for polymyalgia rheumatica (PMR). ***Methods*** The patients who visited our hospital from Apr. 2015 to Jul. 2017, were diagnosed with PMR based on ACR/EULAR criteria, and were treated with oral-P were examined for its effectiveness. One course of oral-P comprised 0.4 or 0.8 mg/kg/day prednisolone (PSL) for 3 days, followed by 0.1 or 0.2 mg/kg/day for 11 days (0.4P, or 0.8P). Three to five courses were administered; then the dose was gradually tapered off. Serum CRP level and ESR at the first visit, at the start and the end of each course were followed. ***Results*** Thirty-four patients (0.4P, 15; 0.8P, 19) were included. 7 patients with 0.4P and 5 with 0.8P had already withdrawn from steroid. CRP level and ESR were significantly higher in 0.8P group of patients than that in 0.4P group. In both groups, after the first course, CRP level and ESR significantly decreased from that prior to oral-P, and maintained throughout follow-up. During after the first course, both CRP level and ESR showed no difference between 0.4P and 0.8P groups. ***Conclusion*** Oral-P brought a prompt and good therapeutic response in PMR patients. Oral-P would be beneficial, as dosing duration and total dose are saved for elderly patients being affected with PMR.

P69-4

Seropositive inflammatory arthritis after immune checkpoint inhibitor therapy

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Conflict of interest: None

[Background] In treating cancers, the use of immune checkpoint inhibitor therapy (ICI) is growing. There is a scarcity of reports about seropositive inflammatory arthritis after ICI treatment. [Methods] This was a retrospective study of 9 patients who received an ICI in whom symptoms of arthritis between April 2017 and April 2020. [Results] The median age was 65.4 years. 55.6% were female. Type of malignancy (n); Melanoma (2), non-small cell lung carcinoma (5), Urothelial carcinoma (1), malignant pleural mesothelioma (1). ICI therapy (n); Nivolumab (4), Pembrolizumab (2), Atezolizumab (3). Rheumatoid factor or anti-CCP antibody-positive was found in 6 patients. 4 patients fulfilled the 2010 ACR/EULAR criteria. A modified diagnostic algorithm for inflammatory arthritis by the Society for Immunotherapy of Cancer Toxicity Management Work-

ing Group; 4 patients were grade 1, 5 patients were grade 2. 2 patients were treated with NSAIDs. PSL was used in 7 patients. All cases had clinical improvement. [Conclusions] In short-term outcome after ICI administration, all inflammatory arthritis patients who met 2010 ACR/EULAR criteria showed improvement with NSAIDs or PSL.

P69-5

Two cases presented rapidly developing flexion contractures of hands

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Conflict of interest: None

[Case 1] A 67 year-old-woman presented with 8-months history of progressive contractures of the hands. Though the orthopedist diagnosed with Dupuytren's contraction and underwent dissection of right palmar fascia, her symptoms got worse. The CT scan showed swollen right ovary, but tumor markers were normal level. She is followed by gynecologist, and flexion contractures of hands is unchanged. [Case 2] A 52 year-old-woman with breast cancer showed contractures of the hands which proceeded within 6 months. Further examination revealed lymph node metastasis of the cancer and chemotherapy was started. She tried low dose corticosteroids but flexion contractures did not improved. [Clinical significance] Palmar fasciitis and polyarthritis is a rare paraneoplastic rheumatic disease originally associated with ovarian cancer. This syndrome is clinically characterized by rapidly developing bilateral flexion contractures of hands and often precede the diagnosis of malignancy. The characteristic finger contracture may provide a clue to diagnose latent malignancy.

P69-6

Three cases with Sjögren syndrome with peripheral neuropathy successfully treated with intravenous immunoglobulin

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Conflict of interest: None

Sjögren syndrome associated peripheral neuropathy are rare, but refractory. We present three cases with Sjögren syndrome-associated peripheral neuropathy, who were successfully treated with intravenous immunoglobulin (IVIG). A 77-year-old woman was diagnosed Sjögren syndrome and peripheral neuropathy. Predonisolone (PSL) was administered with 20 mg per day, but not effective for her sensory disturbance. An addition of IVIG therapy improved her symptom. A 58-year-old woman with Sjögren syndrome had an episode of fever and her limbs became numb. Nerve conduction study showed peripheral neuropathy. Although 50 mg per day of PSL and 50 mg per day of cyclophosphamide did not improve peripheral neuropathy, the following IVIG therapy brought into decrease of numbness of her legs and the findings of nerve conduction abnormality. A 51-year-old man had numbness of his feet, decrease of sensation of his legs and swelling of his feet. He was diagnosed Sjögren syndrome. The findings of nerve conduction study showed peripheral neuropathy. PSL and IVIG therapy was successful for improvement the condition of numbness of his legs and the findings of nerve conduction study.

P69-7

A case of infective endocarditis that was difficult to distinguish from rheumatoid arthritis

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Conflict of interest: None

An 84-year-old woman developed single arthritis in left wrist in August 2019. Blood examination showed CRP 4.3 mg/dL, RF negative, and anti CCP antibody negative. ultrasonography showed moderate tendon sheath synovitis, and MRI showed bone erosion. There were no signs of infection or tumor, and the left wrist joint fluid culture was negative. We diagnosed as rheumatoid arthritis and administered golimumab in March 2020. However, 3 weeks later, fever and fatigue appeared, and blood examination showed CRP 22 mg/dL. No significant findings were found on whole body contrast enhanced CT, echocardiography, or various culture tests, but empirical administration of cefozopran improved the general condition and CRP. After discharge, left wrist arthritis persisted and fever with elevated CRP appeared intermittently. In July 2020, she developed acute congestive heart failure and was diagnosed with infective endocarditis (IE) because echocardiography revealed aortic valve vegetation and aortic regurgitation with valve destruction. Left wrist arthritis disappeared after treatment with IE, and it was considered that bloodstream was the cause from the beginning of the onset.

P69-8

A case of pseudohyper-CRP due to a non-specific reaction to IgM-type rheumatoid factor

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Conflict of interest: None

The case is a 53-year-old woman, who was diagnosed with a high rheumatoid factor (RF) of 2544 in her physical examination in X-2 years. The patient was referred to our hospital for systemic search and antibody screening. After repeated questioning, detailed physical examination and various imaging studies, the cause of the elevated CRP level was unclear. Blood tests were repeated, but similarly high levels persisted. Since there was a significant discrepancy between the clinical findings and other test results, dilution quantification was confirmed. As a result, the CRP quantification of undiluted sample was as high as 11.46 mg/dl, but the CRP value was significantly lowered to 0.08 mg/dl by 2-fold dilution, and quantification was not obtained. When analyzed by gel filtration chromatography, an abnormal CRP peak was found around Fraction 13, which is the same as IgM and RF, instead of Fraction 24, which is a normal site. It was confirmed that a non-specific reaction of CRP by IgM-type RF was occurring. It is difficult to completely avoid non-specific reactions with immune reagents. If an unacceptable hyper-CRPemia was observed, a comprehensive judgment should be made after confirming the dilution quantification of the reagent.

P69-9

A case of systemic lupus erythematosus complicated by neuromyelitis optica spectrum disorders successfully treated with a combination of immunosuppressive therapy

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Conflict of interest: None

[Case] 50 year-old, female. The patient developed polyarthritis and facial rash at the age of 34 years (X-16 year). She was diagnosed as SLE based on positive anti-nuclear antibody (Ab), anti-DNA Ab, anti-Sm and anti-U1-RNP Ab tests. Glucocorticoid therapy was started, and SLE reached remission. She had been stable with prednisolone 6 mg daily. X-6 year, loss of visual acuity of the right eye appeared, and the diagnosis of neuromyelitis optica spectrum disorders (NMOSD) was made with positive anti-aquaporin (AQP) -4 Ab test. After methylprednisolone pulse therapy, high dose glucocorticoid and mycophenolate mofetil were given, and her symptoms were partly recovered. X-2 year, lower leg numbness, bladder and rectal disorder appeared due to myelitis. After immunoadsorption therapy, belimumab and high dose intravenous immunoglobulin therapy were administered. Neurological symptoms persisted, however, clinical

remission of NMOSD was attained with the decrease of anti-AQP-4 Ab titers. Treatment of NMOSD will be discussed.

P69-10

A case of acute lymphocytic leukemia differentially diagnosed from polymyalgia rheumatica (PMR) by MRI

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Conflict of interest: None

[Case] A 40-year-old woman was admitted to our hospital due to several months history of severe pain in the left axilla, shoulders and arms. On admission, laboratory data showed elevated levels of CRP: 4.24 mg/dL while titers of serum rheumatoid factor, anti-CCP antibody and antinuclear antibody were normal. Based on her symptom and the high inflammatory condition, polymyalgia rheumatica (PMR) was suspected. MRI showed high signal intensity on short-TI inversion recovery (STIR) T2-weighted imaging in the bilateral femurs and pelvis. 0.5% of metamyelocytes, 1% of myelocytes, and 3% of erythroblasts were found in peripheral blood. To differentially diagnose from hematological disorders, bone marrow aspiration was performed, and the patient was finally diagnosed as acute lymphocytic leukemia. After the commencement of chemotherapy, her systemic pain disappeared. [Discussion] MRI is useful for differential diagnosis of systemic pain that may be caused by rheumatic diseases or acute leukemia. Our case demonstrates that hematological disorders should be diagnosed in case of high signal intensity of bones by MRI in patients with systemic pain.

P69-11

A case diagnosed with myelodysplastic syndrome, mimicking Systemic Lupus Erythematosus

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Conflict of interest: None

[Case] A 24-year-old female presented to our hospital with Raynaud's phenomenon, repeated oral and pharyngeal ulcers, pancytopenia (WBC 2400 /μl, Hb 8.0 g/dl, MCV 109.6 fl, PLT 90000/μl), and positive anti-nuclear antibody. she experienced headache, nausea, anorexia, and weight loss. There was no abnormal finding by physical examination and ultrasonography. Laboratory examination showed that anti-DNA antibodies, anti-Sm antibody, antiphospholipid antibody, and Coombs were negative. Although anti-SS-A antibody was positive, pathological examination of lip biopsy didn't fulfill the classification criteria of Sjögren syndrome. Ophthalmologic examination revealed papilledema. CT and MRI showed no abnormality findings. Finally, pathological examination of bone marrow showed myelodysplastic syndrome. [Clinical Significance] In case young women with pancytopenia, Raynaud's phenomenon, and anti-SS-A antibody positivity, we usually suspect of Systemic Lupus Erythematosus. When we encounter anemia without hemolysis, we should consider hematological disorder as differential diagnosis.

P69-12

Untypical cases of MTX-associated lymphoproliferative disorder that we had hard time to diagnose

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Conflict of interest: None

Methotrexate (MTX) lymphoproliferative disorder is a serious adverse event that should be noted when treating with MTX. We report cases that developed with untypical symptoms and was difficult to diagnose. Case 1 male 85y. o C. C dyspnea P. H 70y. o He developed rheumatoid arthritis (RA) and was started to treat with MTX. P. I He visited clinic and complained Dyspnea on light effort In April 202x. BT36.3°C BP 106/66 mmHg PR 90 / min regular SpO2 95% Chest CT scan No abnormality in the lung field No swelling of hilar lymph nodes A large amount of pericardial fluid was accumulated. We had pericardial drainage. Histological examination revealed B-cell lineage atypical lymphocytes. Case 2 male 53y. o C. C disturbance of consciousness P. H 38y. o developed *Behçet disease* (BD). 41y. o was started to treat with MTX. P. I He was discovered half-naked and falling in the bathroom in January 202x. He was awake but could not answer pertinently questions.

P69-13

A case of interstitial pneumonia in systemic sclerosis treated with mycophenolate mofetil

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Conflict of interest: None

[Case] A 70s man was admitted on our hospital with skin edematous on limbs at August 20XX-2. He was diagnosed as systemic sclerosis (SSc), showing positive anti-topoisomerase 1 antibodies and Raynaud phenomenon and skin thickening on limbs, face and chest (mRSS30). His chest CT scan showed interstitial lung disease (ILD) characterized by progressive ground-glass opacities of the lungs. Pulmonary function tests showed evidence of restrictive ventilatory impairment (September 20XX-2: FVC 67.9%, FEV1.0 77.3, %DLCO 75.3). We started treatment with prednisolone (PSL) 0.5 mg/kg/day and added mycophenolate mofetil (MMF) 1000 mg/day at October. But his lung FVC and %DLCO declined to 66.7% and 67.3 at November. Therefore PSL and MMF were increased to 1.0 mg/kg/day and 3000 mg/day. He had thrombotic thrombocytopenic purpura (TTP) during high-dose PSL. We performed plasmapheresis and TTP improved. Since then, we gradually reduced the dose of PSL and he continued to take MMF3000 mg/day. His lung function improved (April 20XX: FVC 84.0%, FEV1.0 64.5, %DLCO 78.6). [Discussion] At interstitial lung disease in SSc (SSc-ILD), lung function declines during the first 5 years after disease onset. We thinked that administration of treatment by MMF early in the course of SSc-ILD may lead to suppressed the deterioration of lung function.

P70-1

Satisfaction with golimumab auto-injector in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate patient satisfaction with the Simponi Auto Injector (GOLAI). [Methods] Patients were asked to use the GOLAI in the abdomen using a demo machine as described in the brochure and to rate their satisfaction with a VAS on a 10-point scale. Patient satisfaction was divided into two groups: those who scored less than 6 points and those who scored more than 6 points, to see if there was any difference in patient background. [Results] 95% of patients were able to complete the self-injection movement on the demonstration machine. Overall patient background (mean or percentage) was 60.5 ± 15.6 years of age, 89% female, disease duration 17.8 ± 13.2 years, BMI 21.4 ± 3.7, grip strength 15.3 ± 8.3 kg, pinch strength 2.4 ± 2 kg, intra-gyration 80 ± 21.1 degrees, extra-gyration 81 ± 17 degrees, DAS28 2.1 ± 0.9, H and 20. 31.3±27.9 points, 51% of the respondents had experience with self-injection. The mean satisfaction score was 6.6 ± 2.3. Twenty-seven patients scored less than 6 points and 75 patients scored more than 6 points. Patients scoring less than 6 points were older and had a longer duration of disease [Conclusion] The G O LA I demonstrator could be used in 95% of R A patients. Older and longer-duration patients were less satisfied.

P70-2

Examination of factors affecting self-injectable consciousness of patients with golimumab autoinjector (GLM-AI) - From the perspective of treatment responsiveness, physical and psychological status, social background -

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Conflict of interest: None

[Objective] We investigated psychological factors during patient's treatment course to identify patient background factors differentiating between patients who may be feasible for self-injection (SI) and patients who may be unsuitable for SI. [Methods] 70 RA patients treated with subcutaneous injections of GLM syringe preparation at our institution are included. We switched the patients' treatment to AI, and asked about the change. [Results] There were significant differences in the degree of fear for SI drug use ($p = 0.0028$), the degree of pain ($p = 0.0065$), and the ease of the procedure ($p = 0.003$). For GLM-AI device, the data showed significant difference in injection pain ($p = 0.0211$), easy procedure ($p = 0.0196$), outpatient problems ($p = 0.0127$), physical pain ($p = 0.002$), in the image of injection, and the others including home environment, and physical condition / mood factors. There was a discrepancy between the patient's assessment of SI and the nurse's assessment of SI. [Conclusions] From the comprehensive evaluation of AI devices, patients have more options for SI. The relationship between patients and healthcare professionals and the benefits of hospital visit may have a major impact on patients view, such as patient's psychological, social background and physical situation.

P70-3

Survey on nurses' experiences and necessity on rehabilitation-related education for patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] This study aimed to investigate the current state and the necessity of rehabilitation-related education for patients with RA by nurses. [Methods] Registered nurses engaged in rheumatic care were enrolled in national-scale nursing workshops and at the participants' facilities. The survey contents were: nurses' experiences on educating patients and being asked by patients, the necessity of education with 0-10 rating scale (0=none, 10=full), the reason of disagreement. They were assessed regarding 6 items about rehabilitation. [Results] 274 nurses completed the questionnaire (the average age: 40.9 years old). The percentages of experiences being asked and experiences on educating were: a) exercise at home (62.3%/52.3%), b) orthosis (70.1%/42.4%), c) self-help equipment (48.5%/41.3%), d) evaluation of joint movement (9.8%/5.2%), e) precautions in daily life (71.1%/77.3%), f) review of living environment (33.3%/41.9%). The average on necessity were: a) 8.02, b) 7.79, c) 7.97, d) 7.25, e) 9.20, f) 8.55. The reasons were mainly lack of time and knowledge. [Conclusion] There was a difference between the experiences being asked and experiences on educating for each item. This study elucidated the nurses' needs for rehabilitation-related education and challenges of knowledge and time.

P70-4

Survey of joint conditions in patients with rheumatoid arthritis having sport and exercise habits

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Conflict of interest: None

[Objective] To clarify the existence of at-risk patients with joint misuse and/or overuse in rheumatoid arthritis (RA) patients who play sports. [Methods] A cross-sectional survey of 85 RA patients with sport habits (molecular targeted drug use: 52%, prednisolone use: 14%). We performed descriptive statistics according to the severity of the findings. [Results] Patients practiced underwater exercise (n=16), yoga or taijiquan (n=10), walking or jogging (n=13), croquet (n=9), golf (n=8), muscle training (n=6), and hula or ballroom (n=3), and others played ball games such as soccer. The clinical findings (%) for the parameters assessed were as follows: disease activity score 28 remission: 68, low: 19, middle: 13, high: 0; Steinbrocker's stage I: 31, II: 41, III: 10, IV: 18; serum CRP <0.2 mg/dL: 77, 0.2 to <1.0: 16, >1.0: 7; and health assessment questionnaire >0.5: 20. Of the 28 joints, the percentage of patients without tender and swollen joints was 73% and 81%, respectively, and 55% of all had pain in the lower extremities. [Conclusions] RA patients with inflamed joints and advanced joint destruction also play sports. Strengthening self-care management so that RA patients can enjoy playing sports without deteriorating the condition of joints is necessary as a new perspective of nursing.

P70-5

Questionnaire survey on the actual situation of support for patients with rheumatoid arthritis by medical staff-toward the creation of a support guide for patients with rheumatoid arthritis according to their life stage-

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Conflict of interest: None

[Objective] To clarify the current status and needs of medical staff to

support patients with rheumatoid arthritis (RA). [Methods] A questionnaire survey was conducted by mail to medical staff involved in RA medical care. The subjects are the certified nurses (n=1268), pharmacists (n=526), and physical and occupational therapists (n=147) by Japan Rheumatism Foundation, and the members of Japanese Association for Rheumatism Rehabilitation (n=143), 2084 persons in total. This study was approved by the ethics review board of National Hospital Organization Sagamihara National Hospital, and supported by a grant from the Ministry of Health, Labor, and Welfare of Japan. [Results] Valid responses were 769 (36.9%). There were differences among occupations in age and work history. However, it was common opinions that there are not enough time and staff to support, no support manual, and no guidance fee for support, and that it is difficult to be required for support in other specialized fields. [Conclusions] In order to enhance RA patient support by medical staff, it was considered important to improve the environment, acquire a wide range of knowledge, and collaborate with other occupations. We would like to utilize these results in the "Patient Support Guide" that we plan to create.

P70-6

Questionnaire survey on the actual situation of support for patients with rheumatoid arthritis by medical staff - Comparison of the current situation of 3 medical professions -

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Conflict of interest: Yes

[Objectives] To compare the current status and needs of 3 medical professions toward a better rheumatic care. [Methods] A self-administered questionnaire was mailed to medical staffs certified by Japan Rheumatism Foundation. This survey was supported with a grant from the Ministry of Health, Labor, and Welfare of Japan. [Results] Valid responses were 426 (Nurse; Ns), 205 (Pharmacist; Ph) and 100 (rehabilitation staff; Rh). Fewer Rh can explain "basic knowledge of RA" while needs of patients were high. Regarding concerns, the percentage of Ns and Ph is high for "time and staff shortage" and "consultation fee" while "lack of manual" and "cooperation between occupations" are high in all occupations. "Disaster", "medical welfare service" and "costs" were concerns for all. Regarding pregnancy support, Ns and Ph had a high percentage of response in "drugs" and "RA and mutual effects of pregnancy" while Rh had a high response in "daily life", "rehabilitation" and "joint protection". Concerning elderly, all professionals paid attention to "osteoporosis and compression fracture". Ns and Ph have more experiences in consultations and explanations regarding malignancy and anti-rheumatic drugs. [Conclusion] These results will be helpful to develop a better needs-based "Patient Support Guide".

P70-7

Questionnaire survey on how medical staff support patients with rheumatoid arthritis-Current Status of Support for Rheumatoid Arthritis Patients by Rehabilitation Professionals-

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Conflict of interest: None

[Purpose] To determine the current status and needs of rehabilitation-related professionals in supporting patients with rheumatoid arthritis (RA). [Methods] A self-administered questionnaire survey was conducted by the Japan Rheumatism Foundation and the Japan College of Rheumatology and Rehabilitation Research under the auspices of a grant-in-aid from the Ministry of Health, Labour and Welfare for "Research on Support for Rheumatoid Arthritis Patients According to Life Stage". [Results] Of the 290 subjects, 100 (34.5%) gave valid responses. Problems in patient support included lack of a specific rehabilitation manual (34.0%), lack of interprofessional cooperation (32.0%), and few staff members who could actually provide support (26.0%). On the other hand, the importance of support for RA patients in childhood and pregnancy was not fully implemented, although the importance of support was understood. [Conclusion] The results show that there are interprofessional-specific problems in the field of RA patient support, and the creation of a patient support guide for the acquisition of knowledge and skills necessary for solving problems at each stage of life and for the practice of support is needed. We have found that interprofessional collaboration is important for its utilization.

P70-8

Questionnaire survey on the actual situation of support for patients with rheumatoid arthritis by medical staff - The current situation and issues from rheumatology nurses' perspective -

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Conflict of interest: Yes

[Objectives] To clarify the current status and needs of rheumatology nurses to support patients with rheumatoid arthritis (RA). [Methods] A self-administered questionnaire was mailed to nurses certified by Japan Rheumatism Foundation. This survey was supported with a grant from the Ministry of Health, Labor, and Welfare of Japan. [Results] There were 426 valid responses (33.6%), with a median age of 46 y. o, and RA care experience of 10 years. More than half of the nurses were asked by patients about "RA in general", "effects and side effects of drugs", "medical expenses", "daily life" etc. The areas that nurses struggle with are: "the medical system", "medical expenses", "in time of disasters". Only 20% of nurses could explain the "RA guidelines". 62% of nurses experienced pregnancy-related support, and the guidance such as "effects of drugs" and "influence of RA on pregnancy" was the most common. For the elderly, nurses were careful about "infection risk," "steroids and methotrexate," and "osteoporosis and compression fractures." The reasons for trouble with support were due to "insufficient time and staff," "no consultation fee," and "lack of manuals." [conclusions] This result elucidated the current situation of nurse support, leading to a needs-based "Patient Support Guide".

P70-9

Questionnaire survey on the actual situation of support for patients with rheumatoid arthritis by medical staff -the current situation and problem of the patients with rheumatoid arthritis by the pharmacist-

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Conflict of interest: None

[Objective] To clarify the current status and needs of pharmacists' support for rheumatoid arthritis (RA) patients. [Methods] We conducted a writing by oneself questionnaire investigation in the Certified Pharmacist by Japan Rheumatism Foundation by Japan Rheumatism Foundation, by a grant from the Ministry of Health, Labor, and Welfare of Japan. [Results] Of 526 subjects, 205 (39.0%) validated responses, 41y. of age, 18y. of work history, and 7y. of RA care (median) were provided. The half supported the less than 5 patients a week. The answer in trouble had much "no instruction charges". By the rehabilitation, activities of daily living, joint

protection law was supported. 18% have cared for JIA, as a school and an office, a trouble on living a life. The other than the drug, explained RA and pregnant relations. In the elderly patients, there were few information and cooperation with other courses. As for the cancer prevention, half or more replied, “no explain”, but most explained a therapeutic drug and a cancer, malignant lymphoma. [Conclusions] For a pharmacist, wide knowledge were demanded, but it was originally the contents, other types of job. We will utilize these results in the “Patient Support Guide” of the plans to create for the patients support and pharmacist education.

P71-1

Pregnancy Outcome of Patients with Connective Tissue Disease in our Hospital

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Conflict of interest: None

[Objective] To investigate outcome of pregnancy and childbirth in patients with connective tissue disease (CTD) in our hospital. [Methods] We examined medical records of patients who became pregnant and gave birth between 2011 and 2020. [Results] There were 45 pregnancies, in 28 women. There were 15 cases of rheumatoid arthritis (RA), 12 cases of systemic lupus erythematosus, 5 cases of Sjogren’s syndrome, 4 cases of mixed connective tissue disease, 2 cases of adult-onset Still’s disease, 2 cases of idiopathic thrombocytopenic purpura, 2 cases of Bechet’s disease, 1 case of Takayasu’s arthritis, 1 case of familial Mediterranean fever, and 1 case of protein S deficiency. The outcomes were spontaneous abortion in 1 case (2.2%), abortion in 2 cases (4.4%), stillbirth in 1 case (2.2%), childbirth in 37 cases (82.2%), and preterm birth in 5 cases (11.1%). HELLP syndrome was found in 1 case (2.2%). In RA patients, etanercept (ETN) was used in 8 cases and certolizumab pegol was used in 3 cases. All biologics were withdrawn during pregnancy. In one case, it worsened immediately after the ETN withdrawal, so it resumed and continued at the time of delivery. [Conclusions] Pregnancy with CTD in our hospital did not have a higher frequency of obstetric complications than previously reported.

P71-2

Pregnancy outcomes in women with rheumatoid arthritis

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Conflict of interest: None

[Objective] Pregnancy with rheumatoid arthritis (RA) has been reported to have a poor prognosis, especially when disease activity is high. Our hospital established a outpatient clinic in 2014 to start to support the planned pregnancy of RA patients. The purpose of this study is to clarify the pregnancy outcomes of RA patients. [Methods] Among patients who wished to have children who visited our clinic between 2014 and 2020, the patients who have gotten pregnancy were included. we investigated the pregnancy outcomes, obstetric complications and disease flare during Postpartum. Disease flare was defined as a case where additional or changed drugs were required due to arthritis within 1 year after delivery. [Results] The average age of pregnancy was 35.6 years. Miscarriage was 5 pregnancies (14.3%), preterm birth was 1 pregnancy (2.9%). FGR and HDP were 1 case (2.9%) each. Postpartum disease flare was observed in 13 patients (44.8%). This result was close to the general prognosis of pregnancy. [Conclusions] The prognosis of RA patients who became pregnant intentionally was considered to be almost the same as that of the general population. Furthermore, it was revealed that relapse of arthritis within 1 year after delivery was observed in about half of the patients.

P71-3

Outcome of pregnancy in patients with rheumatoid arthritis after methotrexate discontinuation for family planning

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Conflict of interest: None

[Objective] We investigated the outcome of pregnancy in patients with rheumatoid arthritis (RA) with methotrexate (MTX) withdrawal to desire for childbearing. [Methods] In RA patients with MTX withdrawal for pregnancy, the infertility factors were examined. [Results] Fourteen gave birth and 12 had infertility. The average time from MTX withdrawal to birth was 32.5 months. The age at the MTX withdrawal was significantly different between the birth group 31.0 years and the infertility group 35.6 years ($p = 0.002$). Non-steroidal anti-inflammatory drugs (NSAIDs) and salazosulfapyridine (SASP) were not used in the birth group, and 4 cases and 3 cases in the infertile group ($p=0.033$, $p=0.048$). There was no difference in the use of steroids and biologics after MTX withdrawal. The both groups had low disease activity of RA at MTX withdrawal. In the infertile group, 36.3% after MTX withdrawal showed deterioration of RA disease activity. In the childbirth group, 41.6% showed worsening of RA disease activity during pregnancy. [Conclusions] The infertile group was relatively older at MTX withdrawal, and used NSAIDs and SASP after MTX withdrawal. There was no difference in RA disease activity between the both groups. It is necessary to increase the number of cases and analyze further factors.

P71-4

Does DMARDs discontinuation effect on disease activity and pregnancy outcome in pregnancies complicated with rheumatoid arthritis?

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Conflict of interest: None

[Objective] Some DMRARDs such as biologics and anti-rheumatic drugs could be continued during pregnancy, and it has become possible to control disease activity. There are few evidences whether these drugs continue or not and when they were discontinued. We investigated the effects of DMARDs discontinuation on disease activity and pregnancy outcomes. [Methods] We retrospectively investigated 24 pregnancies in which DMARDs was administered at the time of conception. We analyzed the association between timings of DMARDs discontinuation and disease activities or pregnancy outcomes. [Results] In 15 cases (62.5%) of all, DMARDs was discontinued at first trimester, and they were continued after second trimester in 9 cases (37.5%). There were no significant differences on simplified disease activity index of first and third trimester and rate of exacerbation during pregnancy. However, timing of exacerbation was 14.3±3.8 weeks v.s. 28.5±6.4 weeks, which tended to be worsened after discontinued DMARDs. There was no significant differences on gestational age at delivery, birth weight of newborns, and rate of preterm birth or LFD. [Conclusions] Continuing DMARDs have no effect on adverse pregnancy outcomes, which suggesting that it may be an effective RA treatment option during pregnancy.

P71-5

5 cases of rheumatoid arthritis (RA) using tocilizumab (TCZ) during pregnancy and lactation

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Conflict of interest: None

Case 1: 27 years old. She had been treated with two kinds of TNF inhibitors and abatacept. After changing to TCZ monotherapy, She became pregnant. She delivered a 2494 g girl at 40 weeks of gestation. Case 2: 29 years old. Second child pregnancy in case 1. She became pregnant under continuation of TCZ. TCZ was discontinued at 30 weeks of gestation. She delivered a 3032 g boy at 40 weeks of gestation. TCZ was restarted one

month after the delivery. Case 3: 33 years old. She had been treated with methotrexate (MTX) and three kinds of TNF inhibitors. After changing to treatment with TCZ and tacrolimus (TAC), She became pregnant. She delivered a 2814 g boy at 40 weeks of gestation. Case 4: 33 years old. She had been started treatment with MTX and TCZ. After changing to TCZ monotherapy, She became pregnant and delivered a 3256 g girl at 40 weeks of gestation by emergency cesarean section. Case 5: 41 years old. She had been treated with two kinds of TNF inhibitors. After changing to TCZ, TAC, and SASP, She became pregnant. TCZ was discontinued at 30 weeks of gestation. She delivered a 3474 g girl at 39 weeks of gestation. TCZ was restarted on the 5th day after delivery. [Conclusion] No adverse events such as malformations or infections were observed in any of the children.

P71-6

Consideration of the safety of rheumatoid arthritis biological agent treatment during pregnancy using a large-scale claims database

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Conflict of interest: None

[Background] Although using of biological agent during pregnancy with rheumatoid arthritis (RA) is accepted in treatment guidelines, there are few evidences in Japan. [Objective] We considered the relationship between biological agents and pregnancy outcomes (normal birth, congenital malformation / stillbirth) and also pregnancy related events. [Methods] Using claims database owned by JMDC Inc., identify patients who were prescribed therapeutic agents for RA during pregnancy, and whether biological agents were prescribed. We evaluate the frequency of congenital malformations / stillbirths and pregnancy related events separately. [Results] Congenital malformations and stillbirths were occurred in 13 of 68 patients in the biological agents prescribed group and 53 of 190 in the non-prescribed group, and the odds ratio for association with the use of biologics was 0.61 (95% confidence interval: 0.31-1.21). Similarly, there was no significant difference in the frequency of pregnancy related events between the two groups. [Conclusions] No significant association was found between using of biological agents during pregnancy and pregnancy outcomes or pregnancy related events, which is the same as the treatment guidelines and overseas research results.

P71-7

Effects of anticoagulant therapies on adverse pregnancy outcomes (APOs) and analysis of risk factors for APOs in patients positive for antiphospholipid antibodies

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Conflict of interest: None

[Objective] Antiphospholipid antibodies (aPL) induce obstetric complications, and anticoagulant therapies with low dose aspirin (LDA) or low weight molecule heparin (LWMH) are needed. We investigated the effects of anticoagulant therapies on adverse pregnancy outcomes (APOs) and their risk factors. [Methods] We examined 54 aPL-positive pregnancies who were managed from 2007 March to 2020 September. We retrospectively analyzed the effects on APOs with or without anticoagulant therapies and their risk factors. [Results] 29 cases (53.7%) were treated with anticoagulant therapies, and 11 cases (37.9%) was treated with both LDA and LWMH. In the group of anticoagulant therapies, the rate of histories of obstetric complications was higher (P<0.01). Additionally, the rate of preterm birth and low birth weight was higher in that group (P=0.03, 0.02). The rate of lupus anticoagulant (LAC) positivity, glucocorticoid (GC) use and mean GC dose during pregnancy was higher in APOs (P<0.01, 0.01, <0.01). However, there was no significant differences in the group of non-anticoagulant therapies. [Conclusions] In aPL-positive patients, rate of preterm birth and low birth weight was high even with anticoagulant therapies, and LAC positivity and GC administration should be noted as risk factors for APOs.

P72-1

A case of antiphospholipid antibody syndrome (APS) preceded by thrombosis and treated with low molecular weight heparin during pregnancy

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Conflict of interest: None

[Background] Despite low molecular weight heparin (LMWH) is used worldwide in pregnancies with APS preceded by thrombosis, there is no report in Japan. [Case] A 27-year-old woman with a history of Hashimoto's disease was referred to our department because of thrombocytopenia, aPTT prolongation and the positivity of lupus anticoagulant. Due to pregnancy induced hypertension and fetal growth restriction, cesarean section was performed at 36 weeks. After delivery, she developed arteriovenous thrombosis. A Libman-Sacks lesion and the positivity of phosphatidylserine dependent anti prothrombin IgG antibody were also revealed. We diagnosed her as primary APS and introduced warfarin (WFN). For raising a second child, WFN was changed to LDA and hydroxychloroquine. After confirming the pregnancy (31 years old), unfractionated heparin (UFH) was started. After 14 weeks, she was admitted due to rash and eosinophilia, which made UFH difficult to continue. Of UFH and LMWH, the intradermal test was positive only for UFH. After starting LMWH, she was able to give birth to a second child without complications. [Clinical significance] There are not little cases where UFH treatment is difficult. LMWH should be a treatment option in Japan, especially in pregnancies with APS preceded by thrombosis.

P72-2

Survey of pre- and post-pregnancy changes in bone mineral density in women with systemic lupus erythematosus (SLE)

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Conflict of interest: None

We investigated changes in bone mineral density during perinatal period in SLE women taking long-term steroids, along with their background. [Method] The cases were 31 SLE women who gave birth during steroid treatment from 2013 to 2020. We measured the bone mineral density (BMD) and YAM values of the lumbar spine and femur before pregnancy and within 1 and 2 years after delivery. [Results] The age was 34 years old. Breastfeeding period is 11 months. The PSL dose was 10 mg/day. Pre-pregnancy and post-partum BP administration was in 19/29 cases, respectively. There were 2 compression fractures during the perinatal period. The BMD and YAM values before pregnancy (n=13) were lumbar spine: 1.19 g/cm3, 106% and femur: 0.89 g/cm3, 95.5%, respectively. The rate of change in BMD value from pre-pregnancy to 1 year after childbirth (n=12) decreased by 1% for the lumbar spine and 2% for the femur, respectively. The rate of change in BMD value from pre-pregnancy to 2 year after childbirth (n=8) decreased by 2% for the lumbar spine and 4% for the femur, respectively. [Conclusion] The risk of osteoporosis in young SLE women is diverse. Prophylactic treatment for osteoporosis needs to be fully considered even in the pre-pregnancy stage.

P72-3

Examination of postnatal immunity of infants exposed to immunosuppressive drugs in utero

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Conflict of interest: None

[Purpose] To clarify the effect of intrauterine immunosuppressive drugs exposure on neonatal immunological development whose mothers have used immunosuppressive drugs during pregnancy. [Method] We conducted single center prospective cohort study. Patients with autoimmune diseases who were treated with immunosuppressive drugs (IS) during pregnancy were assigned to IS group. Women treated with steroids alone and those not prescribed steroid nor IS were assigned to PSL group and control group, respectively. Pregnancy outcomes, neonatal complications such as severe infection and immunological parameters among three groups. [Results] 25 patients has taken IS during pregnancy. 20 were treated with tacrolimus (TAC), 3 with azathioprine (AZA) and 2 with TAC and AZA. There was no difference in the gestational age and birth weight of the infants in each group. One neonate in IS group developed sepsis due to urinary tract infection at 2 months after birth. However it was associated with congenital urinary tract abnormalities. There was no difference in the number of subsets of lymphocytes, the results of the lymphocyte blastogenesis test and the level of serum IgG. [Conclusions] Our data suggest that intrauterine IS exposure during pregnancy might not lead to neonatal immunocompromised status.

P72-4

Investigation of transitional medicine in rheumatic diseases

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Conflict of interest: None

[Objective] We aimed to investigate trends in treatment and disease activity in patients with rheumatic diseases when referred from pediatrician to internist. [Methods] Patients with rheumatic diseases referred from Saitama Children's Medical Center to our hospital from April 2015 to October 2020 were included. We retrospectively reviewed the medical records and collected data about the treatment and disease activity. [Results] Thirty-three patients of whom 27 were females were included. Median age of onset was 12 years, at the transition was 22.5 years. The diagnosis of the patients were 14 juvenile idiopathic arthritis, 8 systemic lupus erythematosus, 4 Takayasu's arteritis, 3 mixed connective tissue disease, 2 Behcet's disease, 1 granulomatosis with polyangiitis, and 1 juvenile dermatitis. PSL doses was reduced from 4.76 ± 1.01 mg at the time of transition to 2.86 ± 1.04 mg (p=0.005) at the last visit. Dose increase, addition or change of drug were required to intensify treatment in 8 cases. MTX, MMF were changed in 3 patients because they wanted to have children. [Conclusions] In patients referred to our hospital, their treatment dose was reduced. Adjusting drugs which are contraindicated during pregnancy is one of the important roles for internist.

P72-5

Pregnancy outcomes of eight cases complicated with myositis in our institution

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Conflict of interest: None

[Objective] In pregnancies complicated with myositis, it was not revealed whether disease was exacerbated and risk factors for pregnancy outcomes. We analyzed pregnancies with myositis, and clarified disease activities and pregnancy outcomes. [Methods] We examined the association between disease activity, treatment agents, and pregnancy outcomes in eight pregnancies. [Results] Mean age at delivery was 28.3±3.8 years old, and mean disease duration was 5.1±3.6 years. Glucocorticoid (GC) was administered in seven cases, and mean dose of GC was 7.1±4.4 mg/day. We needed to increase GC dose because disease was worsened in three cases, and myositis occurred in one case. Immunosuppressants were continued in two cases. As for pregnancy outcomes, one case was spontaneous abortion, and the other was ongoing pregnancy, and the least were live births. There were two preterm births and three low birth weight, with mean gestational age at delivery of 34.5±5.2 weeks and mean birth weight of 2315.3±1139.7 gram. In these cases, disease activity was elevated and needed to increase GC dose. [Conclusions] Pregnancies with myositis tended to have more adverse pregnancy outcomes. In these cases, disease activity increased, which suggests it leads to improve pregnancy outcomes to control disease activities.

P72-6

Pregnancy and delivery in the patients with juvenile idiopathic arthritis (JIA) of our hospital in the last decade

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Conflict of interest: None

[Objectives] We retrospectively investigated pregnancy and delivery in patients with juvenile idiopathic arthritis (JIA) in our hospitals in the last decade. [Methods] The study included 4 women, with 8 pregnancies, 8 childbirths, from 2009 to 2018. We analyzed age at pregnancy, disease duration, DAS28CRP (4), medication, adverse event during pregnancy period. We divided 4 women into biologics (BIO) group (biologics used before pregnancy) and non-BIO group (not using biologics). We analyzed by Student t-test. [Results] Mean age at pregnancy was 28.9 years-old (25-32), mean disease duration was 14.6 years (9-20). DAS28CRP (4) at pre-pregnancy and after delivery were 1.9±0.4 and 3.6±1.2 in total (p<0.01), 1.9±0.4 and 4.1±1.1 in BIO (p<0.01), 1.9±0.5 and 2.3±0.3 in non-BIO. There were 5 births at BIO group and 3 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 2 of them in BIO group, csDMARDs had been stopped in all cases and they not used any drugs in pregnancy. There were no premature births and low birth weight infants. [Conclusions] During pregnancy period in the patients with JIA, their disease activity had been worse in BIO group and non-BIO group.

AUTHORS' INDEX

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RS .... **Representative Session**

SS .... **Special Symposium**

S .... **Symposium**

EL .... **Educational Lecture**

MTE .... **Meet the Expert**

MS .... **Morning Seminar**

LS .... **Luncheon Seminar**

AS .... **Afternoon Seminar**

ES .... **Evening Seminar**

W .... **Workshop**

ICW .... **International Concurrent Workshop**

P .... **Poster Session**

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