MODERN RHEUMATOLOGY

Volume 30 Supplement 2020

ABSTRACT SUPPLEMENT

The 64th Annual Scientific Meeting of the Japan College of Rheumatology

August 17 - September 15, 2020
A web-based online meeting

Japan College of Rheumatology

JAPAN COLLEGE OF RHEUMATOLOGY ABSTRACT SUPPLEMENT

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Presidential Lecture

PL

Creating tomorrow's rheumatoid arthritis treatment–Development of next-generation in rheumatoid arthritis research–

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Conflict of interest: Yes

The significance of academia, especially university hospitals, is the implementation of research and education in addition to medical care. We believe that the establishment of a research system centered on doctors with research minds is essential for the development of medicine. The training of Physician Scientists (research physicians) is an indispensable item, especially when considering future medical development. It is clear that knowledge of basic medicine is required to understand the mechanism of action of advanced medicines. Educational opportunities for nurturing researchers are provided through two directions of study: basic research and clinical research. Clinical medicine without basic medical understanding may be savage in a sense. We are studying cartilage metabolism as basic research. Cartilage destruction is an important part of joint destruction in rheumatoid arthritis. Cartilage destruction is completely different from bone destruction. In rheumatoid arthritis, it occurs simultaneously, but in osteoarthritis, cartilage destruction is dominant. The research on cartilage destruction has progressed dramatically thanks to advances in molecular biological techniques in recent years. Proteolytic enzymes have been shown to play a central role. However, the mechanism by which these enzymes are produced remains a major research theme. Chondrocytes work with the extracellular matrix to maintain cartilage tissue. Among them, research themes centering on sugar chains, especially hyaluronic acid, will also help resolve clinical issues. It is a beauty of our country that a clinician conducts basic research. It gives you the opportunity to learn basic medicine techniques and gain basic knowledge of biology. On the other hand, in reality, the experience of clinical research is equally important, considering the reality that most people are active as clinicians. For clinicians, solving clinical problems in front of them leads to satisfaction. Therefore, it is important to provide opportunities to experience clinical research. We believe that multicenter research with related hospitals not only helps to solve clinical problems, but also helps to exchange information, and leads to knowledge leveling and improvement as a whole. I believe all these activities will lead to the development of Physician Scientists. And I think that the activities of next-generation human resources will bring "new happiness" to people who still suffer from diseases.

Representative Session

RS

Innovation and Future Society

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Conflict of interest: None

In February 2011, IBM Watson won against two most successful human contestants on "Jeopardy!". Since then, all the sudden, the word of "AI" appeared more often in so many places. During my several decades of career in IT business and technology field, it seems the boom was not just a one-time hype, but came out of the absolute necessity of the current world. As the word "Artificial Intelligence" or "AI" adopted to more and more places or occasions, it is still a questionable how many people actually understand what they are, and how to use them properly. There are a lot of academic papers and books out there, and many news articles talking about AI in the context of business or speculation of it future opportunities and threats. But it is hard to find the articles or document for broader audience, who are looking for the advice and guidance to actually adopt this technology and apply to their own business or daily life. In my talk, I am going to introduce the overview of overall technology trends of AI from present to the future, with few examples of the most advanced research topics in IBM. I will also discuss how we can better apply this new technology to improve our workplace, society and ultimately our life. There are also some risk that we need to be aware of, when adopt AI to the real-world application, particularly for the mission critical tasks. And finally, I would like to spend some time to discuss the role of human, and the required skill and capabilities in the AI era.

Special Symposium

SS1-1

The problems at issue and the future direction of training systems of the Japanese Medical Specialty Board (JMSB)

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Japanese Medical Specialty Board

Conflict of interest: None

JMSB has been established to certify specialist physicians in 2014 based on the report of the committee on Japanese medical specialties set by Ministry of Health, Labour and Welfare (MHLW). The primary operation concepts of JMSB are as follows, 1, to be independent certification organization, 2, to adopt two-step system, primary specialty training first then subspecialty training, 3, to establish the General Practitioner Specialty as a primary specialty, 4, to operate according to the concept of Professional Autonomy. JMSB made great efforts to establish the training system according to the guidelines set by JMSB during first 2 years. However, apprehension about mal-distribution of physicians was pointed out by the subcommittee of Medical Ethics Council (MEC) set in MHLW. To resolve the problems, number limit, so-called ceiling system, was introduced in 5 large prefectures. Since the ceiling system was not satisfied by both the subcommittee and JMSB, it is now under repeated discussions. It is an urgent problem to establish the alternative system not to worsen the mal-distribution of physicians. Another problem at issue is subspecialty training. Training in some subspecialty areas can exceptionally be started in coordination with that in primary specialties, Internal Medicine, Surgery and Radiology. So far, JMSB approves 19 primary specialty and 23 subspecialty areas coordinated to Internal Medicine, Surgery and Radiology as primary specialties. Since the Medical Practitioners Law and Healthcare Law of Japan were revised in 2018, MHLW has been able to interfere in JMSB-certified medical specialty systems. The start of 19 primary specialty areas were approved in 2018, however that of 23 subspecialty areas were suspended in 2019 according to the concerns raised by the subcommittee of MEC. JMSB is now blushing up our subspecialty training systems for better understandings by the subcommittee members, related specialty organizations and public.

Symposium

S1-1

The role of semaphorins in immune diseases and their potential as clinical markers and therapeutic targets

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Conflict of interest: None

Following their initial discovery, semaphorins were characterized as molecules involved in repulsive axon guidance during development. However, it is becoming clear that they play key roles in immune regulation and inflammatory diseases (Nishide and Kumanogoh, ***Nat Rev Rheumatol.*** 2018). We previously reported an inhibitory function of semaphorin 4D (SEMA4D) in neutrophil activation and its pathological involvement in ANCA-associated vasculitis (AAV) (Nishide et al. ***Ann Rheum Dis.*** 2017). Serum levels of soluble SEMA4D are elevated in AAV patients and correlated with clinical disease scores. Membrane-bound SEMA4D functions as a regulator of neutrophil activation, raising the possibility that SEMA4D could serve as a disease activity marker and a target for therapies for vasculitis. Based on this work, we are trying to validate the clinical significance of elevated levels of serum SEMA4D in vasculitis patients. In addition, we are developing mice model of AAV to investigate its therapeutic potential. Recently, we found another semaphorin-mediated signaling in the disease with eosinophilic inflammation such as Eosinophilic chronic rhinosinusitis (ECRS). Soluble SEMA4D enabled eosinophil trans-endothelial migration, and treatment with anti-SEMA4D antibody ameliorated eosinophilic infiltration in sinus tissues in the ECRS animal model. I would like to introduce our current works and have a chance to discuss possibility of semaphorins as clinical markers and therapeutic targets for autoimmune and allergic diseases.

S1-2

Functional genomics approach to diverse immune-mediated diseases

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Conflict of interest: Yes

Immune-mediated diseases (IMDs) show a variety of clinical symptoms. The responsible cells and molecular pathogenesis of IMDs are largely unknown, limiting our chance to discover the disease-specific treatment targets. Genome wide association studies (GWAS) have achieved a great success in identification of genetic polymorphisms associated with IMDs. As most of the associated polymorphisms lie in non-coding regions of the genome, GWAS results itself do not often indicate the causal molecules or conditions where they play roles. In order to take full advantage of GWAS results and understand the function of genetic variants, analyzing the association of genetic variants and gene expression (expression quantitative trait locus analysis, eQTL) in a variety of cell types is one of the straightforward strategies. When we focus on IMDs, eQTL data of immune cells might be a clue to unravel disease pathogenesis. For this purpose, we constructed a gene expression and eQTL database which consist of >10000 RNA-seq samples from 28 immune cell subsets of >400 donors with 10

IMDs and healthy individuals. Characteristic gene expression signatures across immune cells and IMDs were observed, which largely distinguished autoimmune diseases from autoinflammatory diseases. Our eQTL analysis revealed genetic variants which are associated with gene expressions for more than 60% of expressed genes in each cell subset, part of which show cell type specific patterns. Further, some of the eQTL effects had heterogeneity across patients in their effect sizes in an inflammatory gene expression dependent manner. A number of IMD GWAS associated variants co-localized with eQTL variants of immune cells, which can help our understanding of function of GWAS variants. In this session, we'd like to introduce our dataset and obtained results so far, and discuss about the utility of multi-omics, patient-derived dataset for understanding complicated and diversified pathogenesis of IMDs.

S1-3

Multi-omics research towards personalized medicine in rheumatoid arthritis

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Conflict of interest: Yes

Sustained remission without drug treatment has not yet been accomplished, implying that disease-modifying antirheumatic drugs (DMARDs) treat symptoms of rheumatoid arthritis (RA) but may not fully address molecular mechanisms that characterize patients with RA. Indeed, it is unclear whether the achievement of clinical remission (CR) reflects the state in which molecular profiles are closer to those of healthy individuals (healthy controls; HCs) than to those of RA patients, which we refer to as molecular remission (MR). We conducted a longitudinal multi-omics study of HCs and patients with RA treated with widely used DMARDs to understand the extent to whichdrug treatments return the molecular phenotypes in RA to thehealthy state. Sixty-seven patients with RA and 35 HCs were used for analysis of the whole-blood transcriptome, serum proteome, and immunophenotyping and 45 drug-naive patients with RA were used for the training models. We first elucidated the molecular features that characterize drug-naive RA based on multi-omics profiling. We then revealed that drug treatments alter the molecular profile closer to that of HCs at the transcriptome, serum proteome, and immunophenotype level and a greater effect of infliximab and tocilizumab than methotrexate on molecular profiles and that molecular profiles after treatment define stable CR. Patient follow-up suggested that the molecularprofile after drug treatments was associated with long-term stable CR. This high-dimensional phenotyping provided a quantitative measure of molecular remission. We propose a concept of molecular remission in RA. The concept will help us to understand the pathogenesis and to conduct personalizedmedicine in RA.

S1-4

Crosstalk between immune cells and fibroblasts in rheumatoid arthritis

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Conflict of interest: Yes

Bone destruction in rheumatoid arthritis is attributed to the abnormal activation of osteoclasts, in which we have long proposed synovial fibroblasts play a critical role. RANKL was identified as a membrane-bound factor expressed by mesenchymal cells that support osteoclastogenesis in bone marrow, but also found as a T cell cytokine of the TNF family. RANKL is essential for osteoclastogenesis, lymph node organogenesis, mammary gland development, thymic medullary epithelial cell differentiation and gut M cell differentiation. In rheumatoid arthritis, RANKL is the critical factor that induces osteoclasts and bone damage. We have explored the interaction of synovial fibroblasts and the immune cells in the context of RANKL regulation. Th1 and Th2 cells inhibit osteoclastogenesis because they produce anti-osteoclastogenic cytokines such as IFN-ϒ and IL-4, respectively. Th17 cells secrete IL-17 to stimulate the RANKL expression on synovial fibroblasts as well as the local inflammation. Inflammatory cytokines including TNF and IL-6 further enhance RANKL expression on synovial fibroblasts. Using the mesenchymal cell specific Cre lines, we have shown that synovial fibroblasts, rather than T cells, are the major source of RANKL in arthritis. Thus, T cells are not the cells that directly induce osteoclasts through their own RANKL but the cells that help fibroblasts express RANKL. Here I summarize our recent study on osteoimmunology emphasizing the importance of immune-mesenchymal interaction.

S2-1

Rheumatoid arthritis related interstitial lung disease - clinical problems and its new approach to their management

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Conflict of interest: None

The advent of biologic agents and potent csDMARDs have substantially improved the management of rheumatoid arthritis, including its extra-articular manifestations. The only exception is lung complications, especially interstitial lung disease (ILD). RA-ILD is increasing in incidence and prevalence worldwide and now was reported to be the third most common cause of mortality of RA patients in Japan. RA-ILD is commonly classified to subtypes such as UIP pattern, or NSIP pattern. It has been postulated that patients with UIP pattern have poorer prognosis compared to those with other types. However recent studies of large scale reported that pulmonary function and its deterioration rate are the true prognostic factors. As for the pathogenesis of UIP type, we have reported that the honey-combing is formed via the destruction of the peripheral airway through persistent inflammation. Affirmative studies are emerging in recent days. It is widely accepted that RA-ILD is associated with high titer of RF and ACPA. Especially ACPA is reported to be related to the development, expansion, and severity of ILD, although its precise mechanism has not been elucidated. Also, it is said that activity of B cell immunity participates to the formation and progression of RA-ILD. Based on these knowledges, treatment strategy has been focused to proper suppression of excess immunity. Rituximab and abatacept, which are effective to suppress B cell immunity, are reported to be effective to control the progression of ILD. The efficacy of Tacrolimus is also reported in Japan. Aside from this, it is supposed that the injury of airway and alveolar epithelium are the initial step of inflammation of ILD. Various possible treatment is proposed to reduce the inflammation, such as modifying the microbiomes of the airway or control of GERD, the latter of which are regarded as one of the aggravation factors of RA-ILD. Also inhaled corticosteroid is suggested to regulate the airway inflammation.

S2-2

Recent advances in pathological aspects of RA-ILD

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Conflict of interest: None

Among rheumatoid arthritis-associated interstitial lung disease (RA-ILD), UIP is most prevalent. The histological features and prognosis of RA-UIP and RA-NSIP have been reported, in comparison with those of idiopathic interstitial pneumonias. However, the pathological details and development of lung architectural change due to the peripheral airway disease of RA lung has not been enough examined. In this symposium, the details of the peripheral airway disease in RA-ILD will be discussed in relation to the architectural distortion of RA lung. We will further demonstrate the pathological features obtained by transbronchial lung cryobiopsy (TBLC) as a new diagnostic tool. 1) RA-ILD Among the RA-ILD, RA-UIP has been reported as more frequent and poor prognosis, compared with those of RA-NSIP. However, the details of preceding ILD in RA has not been studied. We present here 10 cases (7 females, 3 males) who had undergone surgical lung biopsy and had been diagnosed as idiopathic interstitial pneumonia by multidisciplinary discussion. Pathologically, 7 cases showed UIP dominant and 3 cases NSIP. The average time of overt RA was 50 months. Histologically, distinct infiltration of plasma cells and intra-lobular cellular and destructive bronchiolitis were observed, remark-

ably in the lower lobes. 2) Bronchiolar disease and alveolar remodeling of RA-ILD Hyperplasia of BALT can be observed in RA-ILD, not only in the broncho-vascular bundle, but also in the alveoli. In the areas of BALT and cellular/destructive bronchiolitis revealed loss of elastic fibers belonging to the bronchiolar and alveolar walls. The area involved by cellular/destructive bronchiolitis infiltrated by lympho-plasma cells, and developed to cystic change of the lobule. Chronic inflammation with destruction of intra-lobular bronchioles is considered to be an important lesion of cystic alteration of a lobule in RA-ILD. This pathological findings suggest that cystic lesion of RA-ILD is different from honeycomb lesion of IPF/UIP. 3) Application of TBLC in RA-ILD As the bronchus and bronchioles can be easily obtained by the use of TBLC. cellular /destructive bronchiolitis, and inflammatory cell infiltration can be evaluated, and further NSIP, OP, DIP, UIP can be diagnosed from the lung parenchyma. By the use of TBLC, appropriate treatment can be achieved.

S2-3

A novel strategy for RA-ILD

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Conflict of interest: None

A large percentage of patients with rheumatoid arthritis (RA) develop pulmonary complications as an extra-articular manifestation of the disease. Interstitial lung disease (ILD) is a common and potentially severe RA-associated pulmonary complication. The treatment for RA-ILD is empirical because no randomized placebo-controlled trials have discussed this issue. We recently performed a retrospective study of a series of 26 patients with connective tissue disease-associated ILD, which included 11 patients with RA. The study showed that two courses of pulse dose methylprednisolone therapy followed by the administration of low-dose prednisone and oral tacrolimus was associated with multidimensional efficacy and was well tolerated. Notably, patients with UIP also showed clinically significant multidimensional improvement. There is growing interest among researchers investigating the development of RA-ILD. Bronchus-associated lymphoid tissue (BALT) identified in patients with RA is associated with an inflammatory cytokine response and the production of anti-cyclic citrullinated peptide antibodies. Compared with patients with IPF, patients with RA-ILD reveal a more distinct formation of peribronchiolar B cell follicles and an increased number of B cells, plasma cells, and CD4+ T cells. Takemura reported that intralobular chronic inflammatory bronchiolar damages promoting the destruction of not only the intralobular bronchioles, but also the alveoli can result in unexpected cystic lesions in a considerable number of cases with long-standing RA-ILD. These findings suggest that appropriate therapy for bronchiolar and alveolar inflammation is essential to prevent the destruction of the alveolar structure. In this session, we discuss the practical and mechanical approach to treat patients with RA-ILD.

S2-4

Immunological approach to the pathophysiology of lung diseases associated with connective tissue diseases

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Conflict of interest: None

Interstitial lung disease (ILD) associated with connective tissue diseases (CTDs) has characteristic chest high-resolution CT and bronchoalveolar lavage (BAL) findings for each underlying disease. The individual inflammatory and immunological pathophysiology of CTD-ILD, however, are not well known. Lung lesions associated with rheumatoid arthritis (RA) are roughly classified into two groups: ILD and airway lesion group. An examination of 120 patients with RA with pulmonary disorders revealed 78 cases (65%) in the ILD group and 30 (25%) in the airway lesion group. BAL findings in RA showed an increased neutrophil ratio compared to other CTDs. We compared the cell fraction in BAL fluid between the ILD and the airway lesion group but found no difference between the two groups. Finally, when we performed immunohistochemical staining on lymphocytes in lung tissue, we found $CD8^+$ cells predominantly in the interstitium. These results suggest that both groups in RA may have the same inflammatory and immunological pathophysiology. About 40% of the patients with polymyositis or dermatomyositis (PM/DM) are accompanied by ILD, some of who result in fatal respiratory failure. In the disease, the anti-MDA-5 antibody is regarded as an indicator of poor prognosis. The antibody titer, however, decreases during the treatment in both survivors and death cases. We performed cytokine panel analysis on 26 anti-MDA-5 antibody-positive DM-ILD patients (17 survivors). Serum IL-15 levels before treatment in the death group were significantly higher than those in the survival group. We compared the daily change rates (slope) of cytokine concentrations in 17 subjects (11 survivors) and found the slopes of IL-10 and IL-15 were significantly increased in the death group. These results suggested that IL-15 and IL-10 may be prognostic factors for the disease. Immunosuppressive therapy with corticosteroids has been used for CTDs-ILD. There are several fatal cases, however, despite the treatment of a combination of immunosuppressive agents. Clarification of inflammatory and immunological pathophysiology of CTDs-ILD could lead to more appropriate treatment.

S2-5

Cutting edge of organizing pneumonia in rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is one of the autoimmune diseases, characterized by inflamed synovium. Organizing pneumonia (OP) occasionally precedes arthritis in patients with RA. The name of OP is derived from the pathohistological findings. The initiation of the development of OP with RA (RA-OP) is associated with injuries of alveolar epithelial cells caused by some factors such as disease activity of synovitis in RA itself, infections and drugs. In the histopathogenesis of OP, four processes are organized as below: (1) leakage of plasma proteins and inflammatory cells into the alveolar airspace, (2) activation of coagulation cascade, (3) organization of the alveolar airspace foamed with myofibroblasts and connective tissue matrix, and (4) resorption of fibrotic lesions. The characteristic pathohistological finding is principally no disruption of the lung architecture. The clinical features of OP are as follows: acute/subacute clinical course with fever, malaise and/or nonproductive cough, solitary or multiple consolidations with air bronchogram demonstrated in the lung imaging, no response to antibiotics, no detection of any organisms and tumor cells in the bronchial or lung specimens, and good response to intermediate dose of prednisolone (PSL). The diagnostic gold standard is the histopathological confirmation of intra-alveolar buds of granulations and fibrosis with mild interstitial inflammation. If the pathohistologcal evaluation is unavailable, RA-OP is clinically diagnosed based on the pathognomic clinical features mentioned above. The administration of 0.5-1.0 mg/kg BW/day dose of PSL is usually responsive to RA-OP. Otherwise, differential diagnosis, in particular, diffuse alveolar damage and malignancy, need to be reconsidered with pathohistological evaluation such as CT-guided or surgical lung biopsy. In this session, I would like to review pathophysiology, diagnosis and treatment of RA-OP, and introduce clinical management of RA-OP.

S3-1

Rheumatoid hand surgery today (finger and wrist)

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Conflict of interest: None

With the advent of biological therapy, an early diagnosis and early treatment with tight control have become increasingly important for the treatment of rheumatoid arthritis (RA). Many patients with RA can live a normal life without joint deformity. With the widespread use of various biological agents and Janus kinase inhibitors, the number of large joint surgeries has decreased, while the number of small joint surgeries, such as those for the fingers and wrists, has increased in our hospital. In fact, we cannot see the club-shaped sticky, swollen synovium, or bones that can be

crushed by the finger in the surgical site. Otherwise, scars, white fibrous tissue, osteophytes and hard bone tissue are often seen. Indications for joint surgery include not only dysfunction due to pain or deformation but also, increasingly frequently, cosmetic reasons, such as concerns about hand deformation. Surgical treatment should be performed with the goal of true remission and remission of the mind.

S3-2

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.

S3-3

Treatment strategy of shoulder joint in rheumatoid arthritis

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Conflict of interest: None

Recent advances in the treatment of rheumatoid arthritis (RA) using methotrexate, biologics, and Janus kinase (JAK) inhibitors have remarkably changed the goal of treatment from care to tight control of the disease. Nevertheless, there are still patients who suffer from joint destruction. In terms of treatment of rheumatic shoulder joints, oral administration of steroid is effective on synovitis in the rotator interval. Arthroscopic rotator cuff repair is recently getting to be performed among RA patients if they have got good disease control. Kanbe et al reported that arthroscopic capsulotomy and mobilization are useful for contracture rheumatic shoulder. Anatomical total shoulder arthroplasty has been an option for patients with RA in the destructive shoulders and reportedly has good outcomes if patients' rotator cuff is intact. On the other hand, patients with RA often have a rotator cuff deficiency or dysfunction. That's why treatment of rheumatic shoulder which have joint destruction and rotator cuff tears is a great rheumatic surgeon's problem for ages. The reverse shoulder arthroplasty (RSA) enable 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. Recently, several reports showed RSA for rheumatic shoulder has same results as well as RSA for CTA in the Western countries. We have performed 25 cases of RSA for Japanese elderly patients in RA since 2014 and investigated these data from a variety of angles and will report the results in this symposium. Rheumatic surgeon regard shoulder as forgotten joint for a long time. However, recent advances in the treatment of RA have remarkably increase treatment option for rheumatic shoulder and that will make improvement of ADL and QOL in these patients if that kind of option was gradually recognized among rheumatologist and orthopaedic surgeon.

S3-4

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.

S3-5

Evolution of osteoporosis treatment associated with rheumatic diseases: From the past to the future

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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, we would like to review the past evidences and discuss about the future treatment strategy of osteoporosis associated with rheumatic diseases.

S4-1

Current status and challenges of transitional medicine for pediatric rheumatic diseases emerged from a nationwide survey

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Conflict of interest: Yes

Background: It is not difficult to imagine that children with illnesses eventually enter the “adult transition period” and face various new hardships. Objective: In order to overcome the above situation, we aim to clarify the actual medical treatment of pediatric rheumatic diseases, and grasp the current situation and issues of transitional medicine from the information gathered. Method: We have targeted pediatric associations certified by the Japan Pediatric Society as the main pediatric rheumatic diseases such as JIA, SLE, JDM, SS, we conducted a questionnaire survey of the actual number of patients who were followed up at each facility. Medical issues for each region were extracted from the information collected at that time. Results: The response rate was as high as 91.3%. Further examination revealed that 57 institutions nationwide are treating more than 10 patients with JIA with a large number of patients, and one facility in each prefecture generally functions as “pediatric rheumatic core hospital ‘’in a unique pediatric rheumatic medical care network. On the other hand, enlightenment about transitional medicine is inadequate and about 80% are worried about transition and transfer. The transition period was examined according to the patient’s condition regardless of age, and information on the progress / prognosis of the disease itself, marriage / pregnancy / childbirth, and the medical system after adults were required in the medical field. Conclusions: Even in adolescence and adulthood, there are many pediatric rheumatic patients who need medical care. In the future, we hope that the transition group will raise awareness and dissemination of the “Transition support guide for the spread of transitional medicine,” so that the rheumatologists in the adulthood can dispel the habits of examining children and adult transitional patients. Acknowledgement: We would like to express my deep appreciation to the clinicians who cooperated in the nationwide questionnaire.

S4-2

Promotion and future of the transitional medical care of adult patients with childhood-onset pediatric rheumatic disorders in Japan

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Conflict of interest: None

Transition is a process involving purposeful, planned efforts to prepare pediatric patients to move from caregiver-directed care to disease self-management as adults. The transition of adult patients with childhood-onset chronic diseases from pediatric to adult health-care systems have recently received worldwide attention. The Japan Pediatric Society convened a committee of healthcare transition, summarized their statements, and the working group launched its activities in 2013. The course of childhood-onset rheumatic disorders often continues into adulthood. Regarding Rheumatology in Japan, the committees to support transitional medical care were established in the Pediatric Rheumatology Association of Japan and Japan College of Rheumatology in 2014 and 2018, respectively. So far, a checklist to evaluate patients’ independence, clinical practice guidance offering statements and recommendations addressing key clinical questions regarding transitional care proposed by leading pediatric and non-pediatric rheumatology medical experts and consisted of general core and disease-specific guidance, and an essential medical record notebook “Miraitalk” filled by patients were developed. In the West, the guidelines from EULAR and the Paediatric Rheumatology European Society recommend a set of quality standards for the care of young adults with childhood-onset rheumatic diseases during their transfer from pediatric to adult rheumatology care providers. Key components of a successful plan for health-care transition include encouragement of patient self-advocacy, tailoring of the process to each individuals’ needs, family adaptation, and readiness and training of relevant health-care providers. It is still in process of coordinated systematical transfer from pediatric to adult health care for the majority of the patients, however, taking an interest in non-pediatric rheumatologists to childhood-onset patients should be the first step to successful transitional medical care and research.

S4-3

Transitional care for childhood-onset adult rheumatic patients with complications

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Conflict of interest: Yes

Recent advances in medical science have improved the prognosis of pediatric patients with rheumatic diseases. As increasing numbers of patients survive into adulthood, understanding the adult outcomes of pediatric conditions has become more important. For example, cardiovascular events are reported to be so high in childhood-onset adult lupus patients, compared with adult-onset patients. Therefore, identifying modifiable risk factors for poor outcomes is vital to improving care for these patients. Like this, attention needs to be paid to complications in childhood-onset adult rheumatic patients.

S4-4

Life events and Drug Change

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Conflict of interest: None

With recent advances in treatment for young men and women suffering from childhood rheumatic disease, QOL is dramatically improved and they could have a chance to get job and marriage, become pregnanct and deliver their baies. Pregnancy, childbirth, and child-rearing are a major process of life that involves a tremendous amount of effort to nurture new lives in their body, send them to the world, and nurture the next generation while confronting our born children. This is an irreplaceable experience for many women to grow themselves mentally and physically. In men, the spiritual joy and growth gained by having a child with a partner and becoming a father is great. Now that treatment has progressed and QOL is required in addition to the cure of the disease, employment, pregnancy and childbirth in children with rheumatic diseases are important topics that cannot be avoided. For the men and women of child-baring age, thepreconception care is important. This concept is considered as “risk assecmet of diseaseactivity on pregnancy outcome and drug changes to which is affordable during pregnancy”. However, this is not limited to care based on pregnancy, but can be considered as “health management that should be widely supplied to young men and women”. For example, teenagers who are independent yet economically and phycologicaly must have the appropriate sexial and contraception education, so that contraceptive counseling is one of the important points for preconception care. In this lecture, I would like to consider the management for gwoun up patiets with pediatric rheumatic disease after finding employment, becoming pregnany and delivery.

S5-1

Importance of diagnostic imaging for pain discrimination in rheumatic diseases

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Conflict of interest: None

It is one of the basic skills required for rheumatologists to clarify the cause of joint pain and to be able to cope with it effectively in the treatment of collagen disease and osteoarticular diseases represented by rheumatoid arthritis. Various imaging tests such as X-ray which are often used in particular, ultrasound, MRI, and PET-CT sometimes provide decisive information and contribute to diagnosis. In addition to careful interviews and

examinations, in addition to making full use of the necessary imaging tests, it is a great advantage in the discrimination scene that the presence or absence of structural changes and inflammation can be captured with higher sensitivity than other clinical information. Familiarity with the interpretation and interpretation of various imaging tests is essential, and conversely, non-organic pain can be identified, and accurate treatment and orientation will be possible. In this lecture, we will introduce and discuss the positioning and importance of diagnostic imaging in joint pain diagnosis, including past interesting reports.

S5-2

The advantages of musculoskeletal ultrasound in the differential diagnosis of polyarthritis

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Conflict of interest: Yes

Musculoskeletal ultrasound (MSUS) has the advantages of high resolution, capability of inflammation assessment by Doppler mode and feasibility of multi-site scanning. MSUS can make a large contribution to the diagnosis of seronegative polyarthritis. The outline of usefulness of MSUS in the differential diagnosis of seronegative rheumatoid arthritis (SNRA), polymyalgia rheumatica (PMR), spondyloarthritis (SpA) and calcium pyrophosphate crystal deposition (CPPD) disease are discussed below. The patients with SNRA cannot fulfill the 2010 ACR/EULAR RA criteria unless they present with more than eleven swollen joints. MSUS can contribute to the detection of subclinical synovitis. Even when there are insufficient numbers of synovitis, the proliferating and/or bone-erosive feature of the synovitis can support the diagnosis of SNRA. In PMR patients, synovitis around both shoulders and hip joints strongly support the diagnosis. However, the positive rate of hip synovitis is low because hip joints are located in deep. Shoulder synovitis are frequently detected as subacromial/subdeltoid/subcoracoid bursitis as well as tenosynovitis of the long head of biceps. The synovitis has an exudative feature rather than proliferative feature that suggests SNRA. The diagnosis of SpA including psoriatic arthritis is dificult in the patients lacking symptoms of spine or skin. Tender enthesis should be examined with MSUS to determine enthesitis, although it is not clear whether the sensitivity for enthesitis is fully reliable. On the other hand, MSUS screening of major enthesis may be beneficial because subclinical enthesitis can be detected. MSUS can also disclose the typical feature of the dactylitis. The diagnosis of chronic CPP crystal inflammatory arthritis, so-called pseudo-RA, is especially difficult. X-ray can reveal the CPP deposition but cannot confirm its involvement in the on-going inflammation. Detection of CPP crystal by MSUS in the site of inflammation can support the diagnosis.

S5-3

Differential Diagnosis of Rheumatic Disorders

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Conflict of interest: None

Recent research indicates that the therapeutic management, including medication and therapy monitoring, has to be adapted for each type of arthritis. Hence, differential diagnosis of rheumatic disorders is important issue in daily practice. Clinically, it may be difficult to distinguish polyarticular psoriatic arthritis from rheumatoid arthritis, at least in cases where distal interphalangeal joints are not affected. In these cases, laboratory examinations may be helpful, but 30% of rheumatoid arthritis cases are seronegative (without rheumatoid factors or cyclic citrullinated peptide antibodies). Several studies have shown that MRI is more sensitive than conventional radiography in detecting early inflammatory changes in rheumatoid arthritis and psoriatic arthritis. In addition to synovitis and tenosynovitis, bone edema, periostitis, and erosions and their distribution play an important role in the differential diagnosis. Axial spondyloarthritis is a chronic rheumatic disease characterized by inflammatory back pain and several other disease manifestations and comorbidities. First published in 2009 with a revised consensus in 2016, the Assessment in SpondyloArthritis International Society (ASAS) classification system utilizes imaging features of the sacroiliac joints on MR imaging to assist in characterizing the presence of sacroiliitis: Required MRI features include bone marrow edema or bone marrow contrast enhancement. Importantly, back pain in patients with axial spondyloarthritis may well have reasons other than axial inflammation or new bone formation. There are several important differential diagnoses such as diffuse idiopathic skeletal hyperostosis and osteitis condensans. This review summarizes recent publications concerning the performance of imaging modalities in the field, such as conventional radiography, magnetic resonance imaging, computed tomography and dual energy x-ray absorptiometry including the trabecular bone score. In this talk, we will review the role of MRI in differentiating pain in rheumatic diseases.

S5-4

Utility of FDG-PET/CT in differentiating pain associated with rheumatic diseases

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Conflict of interest: None

Rheumatic diseases mainly cause joint, periarticular tissue, and entheses nociceptive pain due to local inflammation. FDG-PET/CT may aid in diagnosing collagen diseases without specific serum markers hard to assess by other modalities, finding lesions and biopsy sites, and assessing treatment response. Cytokine and activated inflammatory cell FDG uptake at inflammatory sites was high due to high glycolytic activity, with degree reflecting local inflammation status. Rheumatoid arthritis (RA) aids in arthritis distribution and degree evaluation and risks of later joint destruction correlate with baseline joint FDG uptake, aiding treatment decisions. Polymyalgia rheumatica (PMR) signs are sparse, causing issues with differential diagnoses. Ischial tuberosity (IT) and lumbar spinous process (LSP) uptake was high in PET comparisons of PMR vs. elderly-onset RA (EORA). Specific uptake patterns were seen in shoulders and hips per group, with PMR showing synovitis and EORA bursitis. Focal uptake before hip joints, showing iliopectineal bursitis, was also limited to the PMR group. For pain, interspinous bursitis findings, e.g. in lumbar regions, did not necessarily correlate with symptoms, e.g. back pain, thus PET also helped identify asymptomatic interspinous bursitis. Discerning elderly-onset seronegative spondyloarthritis (SpA) from PMR is hard. No significant differences in IT, greater trochanter, or LSP uptake were noted in PET comparisons of SpA vs. PMR, with uptake at these sites proving enthesitis in SpA and bursitis in PMR. Yet, sacroiliac joint uptake was significantly higher in SpA than PMR, distinguishing SpA from PMR. PET also aided in finding sacroiliac arthritis unidentifiable by MRI, very early stage pre-SpA. Thus, PET aided differential diagnoses and activity evaluation of varied painpresenting diseases and finding very early stage and asymptomatic lesions, leading to clarifying disease states. Thus, PET aided differential diagnoses and activity evaluation of varied painpresenting diseases and finding very early stage and asymptomatic lesions, leading to clarifying disease states.

S6-1

Treatment strategy of systemic lupus erythematosus - lessons from clinical trials

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Conflict of interest: Yes

Systemic lupus erythematosus (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 based on one kinetic molecular theory difficult, innovative approaches using biologics targeting molecules involved in the pathogenesis of SLE have been emerging. 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. IFN-stimulated genes, IFN signatures, are upregulated notably

in SLE and one phase III clinical trial of anifrolumab, an anti-IFN-alpha receptor antibody, met the primary endpoint in SLE patients. The phase IIB trial using anifrolumab showed that it was more efficacious in patients with high IFN gene signatures than those with low ones. Also, an anti-IL-12/IL-23 (p40) antibody ustekinumab was significantly effective in treatment of SLE, compared to placebo in a phase IIb trial. Furthermore, baricitinib, an orally available inhibitor of JAK1/2, which is involved in signaling via IFN and IL-12, significantly improved the signs and symptoms of active SLE despite standard of care with a safety profile. It is well known that an anti-BAFF antibody belimumab was the first approved biologic for SLE because of moderate efficacy and good tolerability. Soluble BAFF, type-I IFN and IL-12 are secreted by dendritic cells and regulate class switch and differentiation of B cells and T cells. Thus, targeting interaction between innate immunity and acquired auto-immunity may be more beneficial that targeting T and B cells directly. 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.

S6-2

Treatment strategy of idiopathic inflammatory myopathy – Lessons from clinical trials

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Conflict of interest: Yes

It is generally agreed that glucocorticoid (GC) is the anchor drug of initial treatment for polymyositis/ dermatomyositis (PM/DM) and additional immunosuppressants are sometimes used in severe or intractable cases, despite the lack of sufficient evidence by randomized controlled clinical trials (RCT). However, evidences from controlled study has been accumulated over the last several decades. In order to fully understand the results of clinical trials, it is important to know subjects and endpoints of the research because PM/DM encompasses a variety of phenotype with different affected organs, pathophysiology and reactivity to immunosuppressive treatment. Moreover, evaluation methods for endpoints should also be paid attention to. According to the treatment for myositis, azathioprine (AZP), methotrexate (MTX), cyclosporine (CyA), tacrolimus (TAC), mycophenolate mofetil and cyclophosphamide have been reported to have some possible beneficial effects on improvement of functional status, reducing GC, early achievement of remission or disease control in intractable cases with various evidence levels of clinical trials. Intravenous immunoglobulin has also been proven to have improving effect on myositis resistant to GC therapy by 3 RCTs. The latest RCT evidences on biologics for intractable myositis, such as Rituximab, Infliximab, Etanercept and Abatacept, have been accumulated. According to the treatment for interstitial lung disease (ILD), retrospective studies has been suggested that calcineurin inhibitors and cyclophosphamide provide better life prognosis and regression free survival or more improvement of respiratory function than GC monotherapy. Most recently, several prospective controlled trials have shown evidences for anti-MDA5-positive DM-ILD which often rapidly exacerbates and associates with poor prognosis. In this symposium, recent evidences from clinical trials for myositis treatment will be focused on.

S6-3

Treatment strategy of systemic sclerosis – Lessons from clinical trials

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Conflict of interest: Yes

Systemic sclerosis (SSc) is the most difficult-to-treat rheumatic disease today. There is only a few disease-modifying therapies helpful in improving the natural course of SSc; cyclophosphamide and mycophenolate mofetil for the skin and interstitial lung disease (ILD), methotrexate for skin, and nintedanib for ILD. Two trials reported autologous stem cell transplantation superior to intravenous cyclophosphamide, albeit at the price of significant procedure-associated early mortality. To overcome current dilemma, the world SSc community has worked together to find ways to solve problems by improving clinical trial protocols. First, it was difficult to identify "active and progressive" patients eligible for clinical trials, due to highly heterogenous clinical course. Nevertheless, patients who experience subsequent progression of skin thickness as measured by modified Rodnan total skin thickness score (mRSS) and/or ILD can be now identifiable by combination of risk predictors. Second, mRSS (for early dcSSc) or forced vital capacity (for ILD) was used as a primary endpoint, but we have learned that a single measure was not appropriate for a surrogate of future outcomes. ACR Provisional Composite Response Index for Clinical Trials in Early Diffuse Cutaneous Systemic Sclerosis (CRISS) has been proposed as a new composite measure, and is used as a primary endpoint in many ongoing clinical trials. Finally, a much greater understanding of SSc pathophysiology has developed by tremendous efforts of basic researches, leading to clinically testable hypotheses. Accordingly, novel therapies towards specific molecular and cellular targets have been tested in clinical trials. These include molecular targeting therapies to B cells, IL-6, JAK, TGF-beta, lipid mediators such as autotaxin and cannabinoid receptor signaling. This lecture summarizes ongoing SSc clinical trials and how to implement lessons leaned from trials in our daily clinical practice.

S6-4

New development of therapeutic strategy in sondyloarthritides: from results of the clinical trials

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Conflict of interest: Yes

Spondyloarthritis (SpA) is a group of rheumatic diseases characterized by axial and peripheral arthritis, enthesitis, extraarticular manifestations, such as anterior uveitis, and association of HLA-B27. Ankylosing spondylitis (AS) and "non-radiographic axial SpA (nr-axSpA)" are main diseases of axial SpA. For treatment of AS, conventional DMARDs are not effective while TNF inhibitors and, recently, IL-17 inhibitors show high clinical efficiency in patients inadequate response to NSAIDs. Furthermore, these are also effective and approved for nr-axSpA in Europe and the US. On the other hand, although IL-23 has been believed to the pathogenesis of AS, IL-23 inhibitor did not improve the clinical symptom. In sacroiliac joints and vertebrae of AS, bone erosion and subsequent new bone formation that causes formation of syndesmophytes are observed. TNF inhibitors, especially in early use, may prevent the long-term disease progression. IL-17 inhibitors may possibly be more effective for the bone disease since IL-17 induces both osteoclastogenesis and osteoblastogenesis. For treatment of peripheral disease of psoriatic arthritis, TNF inhibitors, IL-17 inhibitors, and also IL-23 inhibitors are used in cases of inadequate response to NSAISs and conventional DMARDs, and high clinical efficacy has been reported. In head-to-head comparison between a TNF inhibitor and a IL-17 inhibitor, it had been reported the efficacy for peripheral arthritis was equivalent, however, the IL-17 inhibitor was more effective for the skin disease. In addition, IL-17 causes new onset and exaggeration of inflammatory bowel diseases, even though the frequency is likely to be low. Furthermore, it has been reported that a IL-17 inhibitor did not increase a risk of uveitis in patients with AS. In this symposium, I would like to discuss the new therapies and its relation to the pathogenesis in SpA.

S6-5

Translational research to clinical trial in FMF

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Conflict of interest: Yes

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, and inflammasome by cell-free reconstructruction systems trying to develop new therapeutics for FMF. These projects have been supported by AMED. 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 SNP (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. Thus, we have focused on the screening of substances to inhibit activation of mutated inflammasome reconstituted by M694I pyrin. For cytokines/chemokines profiling in sera of FMF patients, our previous study identified that IL-6 had the best performance for distinguishing FMF in attack from healthy controls or FMF in remission. In addition, we also identified that microRNA-204-3p, expression of which correlated with disease activity of FMF, inhibits lipopolysaccharide-induced cytokines 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 closed and the results will be open in 2020. Regarding to cytokines/chemokines profiling, we have established the new detection assay system specific for caspase-cleaved, active form of IL-1β and IL-18 that was not revealed until now and been trying to examine their role in autoinflammatory diseases, especially focusing on IL-18. Regarding to screening of low molecular drug candidates through cell-free reconstituted pyrin inflammasome system, we have already chosen several substances inhibiting pyrin inflammasome. These substances are considered to be candidate low molecular drugs toward autoinflammatory diseases including FMF. In this symposium, we are going to discuss the ongoing roadmap of translational research of FMF and related autoinflammatory diseases.

S7-1

2020 update of Giant cell arteritis

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Conflict of interest: Yes

Giant cell arteritis (GCA) is characterized by vasculitis due to lesions in the superficial temporal artery, the maxillary artery, the ophthalmic artery, and the aorta or its branches. Large-vessel lesions (LVL) are detected in about 50-60% of the patients with GCA by imaging findings. ACR GCA classification criteria and temporal artery biopsy were common tool of diagnosis, but recently, imaging diagnosis has become important. Diagnostic and Classification Criteria for Vasculitis (DCVAS) cohort showed differentiation of GCA and TAK by using imaging data, and the draft of new diagnostic classification criteria is under consideration. Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS) has two cohorts of GCA and TAK, and we will validate the results of DCVAS. Disease activity was evaluated with cranial signs and symptoms, polymyalgia rheumatic (PMR), and constitutional symptoms, and LVL have been included in the criteria. However, clinical signs and symptoms of LVL are often not observed in the patients with relapse. 2018 Update of the EULAR recommendations defined clinical remission of LVL as structural non-progression by imaging data. Vessel wall inflammation is a candidate of items of disease activity, but algorithm of the evaluation has not been established. Study group of large-vessel vasculitis in JPVAS will establish agreement of expert opinions on the algorithm. We will discuss disease activity and remission criteria in this symposium. A paradigm shift is expected to occur since tocilizumab was approved. Increasing cumulative dose of glucocorticoids (GCs) is associated with adverse events, and reducing cumulative dose of GCs is a main target of the therapeutic strategy of GCA. Therefore, prognostic factors of GCA patients receiving GCs therapy are important to establish the treatment algorithm. We will review the data of JPVAS cohort, RCTs, and previous observational cohorts.

S7-2

Updates in the treatment of Takayasu arteritis

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Conflict of interest: Yes

Takayasu arteritis (TAK) is an idiopathic inflammatory disease that affects elastic arteries. It occurs frequently in young women, and when advanced, it can lead to aortic regurgitation, ischemic heart diseases, and visual impairments. In histopathology, inflammatory erosion of the arterial media and vascular remodeling (aneurysmal formation and luminal stenosis) are characteristic. It has been reported that both TNF inhibitors and IL-6 inhibitors are effective for TAK. In this lecture, the effects of TNF inhibitors and IL-6 inhibitors will be discussed in terms of 1) histopathology, 2) treatment response, 3) genetics, and 4) case reports. We have performed GWAS for TAK, and reported the association of IL-12/23 (Terao, AJHG, 2013). From the results, both TNF-α and IL-6 were considered important (Yoshifuji, MR, 2019). However, in the 2nd GWAS report, genes related to NK cells and innate immunity have been found (Terao, PNAS, 2018). Therefore, Th1, IL-12, and IFN-γ should be particularly important in its pathophysiology. On the other hand, the axis of IL-6, IL-23, and Th17 might be also important for the establishment of chronic inflammation. In 2019, anti-endothelial protein C receptor antibody and anti-scavenger receptor B-I antibody have been discovered in TAK, and their pathogenicity has been shown (Shirai, EULAR2019; Mutoh, ACR2019). The various evidences for the pathophysiological interpretation of TAK are currently confusing. There have been several reports from Europe and the US, in which aneurysmal formation and/or arterial stenosis progressed while using tocilizumab (TCZ), and the point has been disputed. In the last part of the lecture, the treatment guidelines for TAK will be compared among EULAR, ACR and Japan. Notably, TNF inhibitors are recommended over TCZ in the draft of ACR treatment guidelines for TAK, presented in November 2019. In this lecture, the backgrounds that lead to the political differences among the nations will be discussed.

S7-3

Updates on the pathogenesis of AAV

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Conflict of interest: None

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a vasculitis that affects systemic small vessels especially in the kidneys and lungs, accompanied by the presence of ANCAs in the serum. Similar to other autoimmune diseases, AAV develops in patients with a predisposing genetic background who have been exposed to causative environmental factors. Several genes such as HLA have been listed as susceptible or resistant genes, and it has been shown that environmental factors, including infectious agents and drugs, are involved in the development of this disease. The pathogenic mechanisms includes 1) priming of neutrophils, 2) ANCA binding to the primed neutrophils and an excessive activation of neutrophils with neutrophil extracellular trap (NET) release, 3) vascular endothelial cell injury due to NETs, and 4) disordered NET regulation and ANCA production. Recent studies have suggested the contribution of pro-inflammatory cytokines and the complements to the priming of neutrophils. Although NETs are essential elements in the innate immunity, decrease in serum activity of DNase I (physiological NET degradation enzyme), disorder of the semaphorin 4D and plexin B2 system (physiological NET regulation system), and acquired resistance to DNase 1 have been demonstrated in AAV patients. Therefore, a vicious cycle of NET formation and ANCA production is considered to be involved in the pathogenesis of AAV. In addition to this role of NETs in AAV, some other important discoveries have been made in the last few years. Incorporating these new insights into our understanding of the pathogenesis of AAV is needed to fully understand and ultimately overcome this disease.

S7-4

Update of treatment for MPA/GPA

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Conflict of interest: None

Diagnosis and treatment of MPA/GPA is progressing at a great speed in recent years. As for diagnosis, diagnostic criteria of MPA and GPA by HLWM of Japan has been used in our country for a long time, and EMEA classification criteria by Watts et al. has also been used for clinical trials. In Asian countries, characteristics of AAV are different from Western countries, such as great number of patients of MPO-ANCA positive GPA and high frequency of IP. Then, worldwide criteria for AAV was needed and the project of making worldwide criteria for AAV (DCVAS), in which clinical data from 6000 patients from 32 countries were analyzed including Japan, has progressed and the draft of that was released 2 years ago. As for treatment, in addition to steroid and immune-suppressant, anti-CD20 antibody, Rituximab (RTX), has been widely spread in the world after major two international trials. In Japan, RTX was permitted to use in 2013 and the guideline of AAV treatment made by research committee of HLWM of Japan revised in 2017 complying with the GRADE included RTX in the treatment recommendation. In this recommendation, treatment by CY had higher priority than that by RTX, meanwhile the guideline published by British society of Rheumatology in 2014 treated CY the same as RTX. The Japanese guideline aims to be revised in 2023. Several trials of French Vasculitis Groups regarding remission maintenance therapy by RTX are being in process and the results has been published gradually. On the other hand, avacopan, C5a receptor antagonist, has been applied for treatment of AAV and very effective. It is possible that avacopan replaced RTX as a major treatment for AAV.

S7-5

Update of the management of EGPA

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Conflict of interest: Yes

Eosinophilic granulomatosis with polyangiitis (EGPA) was first reported by Jacob Churg & Lotte Strauss in 1951, as unique systemic vasculitis with asthma, hypereosinophilia and necrotizing granulomatous angiitis. Since EGPA had been called as Churg Strauss syndrome for a long time, its name was changed to EGPA and the definition was brushed up in Chapel Hill Consensus Conference in 2012. For the diagnosis of EGPA, Japanese diagnostic criteria for EGPA was developed in 1998. However, classification algorithm reported in 2007 is widely used for the classification of EGPA internationally, which is based on the Lanham criteria and 1990-ACR classification criteria. Frequency of ANCA positivity in EGPA is reported to be low as 30 to 50%. As there are significant differences in clinical features between ANCA-positive and ANCA-negative patients, differential diagnosis between ANCA-negative EGPA and hypereosinophilic syndrome is a clinical problem. So more sophisticated, globally-accepted, classification criteria for EGPA is awaited. Glucocorticoid (GC) is still a mainstay in the remission induction therapy for EGPA and some refractory cases have been treated with combination with immunosuppressive agents such as cyclophosphamide. For the remission maintenance, several immunosuppressive agents such as azathioprine, methotrexate, etc. have been used. However, there are only a few evidences for the dosage and administration of these immunosuppressive agents. Recently, anti-IL-5 monoclonal antibody, mepolizumab was reported to be effective for EGPA and has been approved in Japan in May 2018. The new guideline for EGPA was submitted in the 2019-ACR annual meeting and treatment guide for EGPA is in preparation in Japan. I will talk about above issues and future problems on the management of EGPA.

S8-1

An introduction of Artificial Intelligence, and perspectives for its application to medical domain

Jun Sese
Humanome Lab., Inc.

Conflict of interest: Yes

The word “artificial intelligence” appears in newspapers everyday, which means that its application is spreading not only in basic research but also in various fields. One of the most promising fields is medical / preventive medicine. This is not a plan to take away the doctor’s work, but supports routine work for the doctor and checks if there is no oversight. And for patients, even outside the hospital, they can check their health status and be able to create alerts whenever something happens. So doctors can do their job and prevent patients before they get sick. We think that we can make new medicine with the airtificial intelligence. In particular, in the case of diseases such as rheumatism that are widely related from inheritance to lifestyle habits, the use of artificial intelligence may lead to a reduction in medical costs. In this talk, we introduce the current state of artificial intelligence technology, introduce our research, and what kind of artificial intelligence technology brings happiness to doctors and patients.

S8-2

Application of Deep Learning for Drug Discovery

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Preferred Networks, Inc.

Conflict of interest: None

Deep learning has dramatically improved in recent years, and achieved breakthrough results in many fields, including image recognition, speech recognition, machine control, and anomaly detection. Deep learning is also a promising technology in the field of biotechnology and life sciences, since it can automatically extract useful features in its process of learning, achieve multi-modal and multi-task learning naturally, and successfully handle data on genomic sequence, small-molecule compounds, and proteins, which are of varying size. In this presentation, we will introduce the latest applications of deep learning and explain how deep learning can be used in the process of drug discovery.

S8-3

Utilization of artificial intelligence in human genome data analysis

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Conflict of interest: None

Artificial intelligence (AI) is a computational simulation to build smart machines capable of performing tasks the typically require human intelligence. Machine learning (ML) is one of the computing technique in AI, which leans patterns of the target data to extract the features representing the entire dataset. Deep learning belongs to machine learning, which is characterized by multi-layer data mining architecture mimicking brain neuron network. Development of the GPU technology utilized in deep learning and construction of large-scale big data expanded the possibility of AI, even in the field of human genetics. Human genome data in the population is represented as a matrix consisting of the samples and the genetic variants. Thus, application of the classical machine learning methods to human genome matrix has been conducted (e.g., elucidation of cryptic structure of the Japanese populations consisting of the two major subclusters of “Hondo” and “Ryukyu”). Recently, application of non-linear machine learning methods (tSNE and UMAP) to obtain finer resolution of the population structure, and genome-based sample clustering focusing on the specific genome region such as the human leukocyte antigen (HLA) genes and mitochondrial genomes are reported (e.g., classification of white blood cell types of Japanese into combinations of the 11 patterns). Utilization of the whole human reference sequences as an input data, deep learning can computationally predict effects of any potential genetic variants on epigenome and gene expression profiles. Integration of diverse clinical information and selection of the tuned parameters is a promising approachd for implementation of personalized medicine. As a next step, further application of AI to a wide range of human omics data (e.g., genome, epigenome, metagenome, and phenome) is warranted.

S8-4

Rheumatology research using AI/machine learning

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Conflict of interest: Yes

Recent technological advances have enabled detailed analysis of the human genome and transcriptome information of immunocompetent cells. Since various immunocompetent cells are involved in rheumatic diseases, the information that can be evaluated in the immune system is becoming enormous. Information on these immune systems is thought to be useful for disease classification and prognosis prediction, however, because the amount of information is too large, intuitive recognition is very difficult. Artificial intelligence (AI)/machine learning, which allows a computer program to execute intelligent tasks and learning that humans perform, is expected to be useful for analyzing such enormous amounts of data. We collected various immunocompetent cell subsets in peripheral blood of patients with immune-mediated diseases by flow cytometry. We then analyzed transcriptome using machine learning techniques, identified subset-specific genes, constructed disease classifiers, and detected disease-specific gene expression and splicing events. The top 100 genes important for characterizing each subset were calculated by the random forest method. Also, in order to extract the elements that characterize each disease, gene expression and splicing events that are important for discrimination from HC and other diseases were selected for three types of autoimmune diseases (SLE, SSc, Myo) by the random forest method. The classifier was able to discriminate SLE vs. HC and SLE vs. others with a high accuracy rate of over 90%. Splicing event analysis showed that there are specific splicing events in SLE and Myo. Detected Myo-specific splicing events include known hereditary muscular dystrophy-causing isoforms. Using AI/machine learning in this way can be expected to contribute to understanding the pathophysiology of autoimmune diseases, identifying diagnostic markers, and developing disease-specific therapeutics.

S8-5

Advances in diagnostic imaging using artificial intelligence (AI)

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Conflict of interest: Yes

In image recognition using deep learning, which is the core technology in the current Artificial Intelligence (AI) boom, it is possible to extract features from images without human intervention. Due to its high discrimination ability and generalization performance, research and development of AI has been promoted in various fields, and there is high expectation in the field of diagnostic imaging in medicine especially. Deep learning was the focus of attention because of the high performance of natural image classification in the 2012 ImageNet Large Scale Visual Recognition Challenge (ILSVRC). The team of Hinton et al. at the University of Toronto won an overwhelming 10% difference over the second-ranked team using an 8-layer convolutional neural network (CNN). Furthermore, at the 2015 ILSVRC, the team of Microsoft Research Asia was reported to have fallen below the human error rate using 152 layers of CNN. Thus, CNN has already exceeded human recognition ability in terms of natural image classification, and its high discrimination ability is expected for lesion discrimination in radiological image diagnosis. Currently, not only such image classification but also methods related to lesion detection and organ region extraction have been proposed, and the range of application has expanded. In 2016, Hinton, the leading expert in deep learning research, said that it is no longer necessary to train radiologists because deep learning exceeds the capabilities of radiologists within five years, and he gave a big upset to radiologists. However, to date, there are no signs that AI will replace radiologists. Rather, as a trend in the past few years, AI is the center of topic in radiology-related societies, and there is an interest in how to apply the results clinically. Langlotz said, "AI will not replace radiologists, but radiologists who use AI will replace radiologists who do not use AI." He pointed out that it is important as radiologists in the future. From now on, it is considered that the disparity between radiologists who use AI and radiologists who do not use AI will become a major problem, rather than a diagram of AI versus radiologist.

S8-6

Utilization of ICT and AI in the clinical practice of rheumatic diseases

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Conflict of interest: None

In recent years, attempts have been actively made to utilize advanced ICT (Information and Communication Technology) such as AI (Artificial Intelligence) and IoT (Internet of Things) in the medical field. In the field of rheumatology, attempts have been made to utilize these latest technologies for imaging diagnosis support, prediction of patient outcomes, patient education, and the like. The medical ICT network is one of the familiar items in daily clinical practice. In Nagasaki Prefecture, where there are many remote islands and remote areas where there are no specialists, Nagasaki regional medical cooperation network system (AJISAI Net) has been used. The primary doctor can use medical chart information including image information of the basic hospital via the internet with the consent of the patient. This system not only strengthens cooperation between medical institutions, but also provides benefits such as the use of advanced medical equipment and the suppression of medical delays. Next, we will introduce the management of rheumatoid arthritis using ICT that we are working on. 1) Establishment of ultrasound imaging diagnosis support system using AI / IoT: Although ultrasound has weaknesses such as variations between evaluators and long time required, AI can be used to standardize grading and automatically create finding tables. This system not only contributes to medical care but also helps educate medical professionals who learn joint ultrasound. 2) Telemedicine for patients with rheumatoid arthritis using AI / IoT: A mixed reality (MR) will be created in a remote examination room as a base for remote RA specialized practice in areas where specialists are depopulated. 3) Big data management of Goto City resident screening cohort by ICT: By constructing a cohort database in which multiple departments intervene, multi-disciplinary research becomes possible. This symposium outlines the current status and future prospects of rheumatic practice using ICT.

S9-1

Cancer immunotherapy by immune checkpoint inhibitors

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Conflict of interest: Yes

Immune-checkpoint blockade and T-cell based adoptive cell therapy have shown durable clinical response in patients with various advanced cancers. However, there are many partial and non-responders. Thus, identification of biomarkers to select appropriate patients and immunotherapies as well as improvement of immunotherapy efficacy possibly through combination treatment are needed. To solve these issues, it is essential to understand immunobiology of cancer patients, particularly mechanisms of action and resistance in the current effective immunotherapy. Pretreatment immune status in tumor associated microenvironments varies among cancer patients, and it correlates with responses to various cancer therapies including immune-checkpoint inhibitors. It may be defined by cancer cell's genetic characteristics (e.g. immunogenic mutations and immunosuppressive oncogenes), patients' immune-reactivity (e.g. SNPs), and environmental factors (e.g. smoking, microbiota, diet, stress). To establish effective combination immunotherapies, in addition to combination with standard cancer therapies such as chemotherapy, molecular target therapy, and radiation therapy, immune-interventions targeting the major regulation points in the anti-tumor T-cell responses and their appropriate combination need to be considered as follows; 1) Use of appropriate tumor antigens such as immunogenic neo-antigens, 2) *in situ* tumor destruction to induce immunogenic cancer cell death, 3) Enhancement of antigen presenting cells' function, 4) *in vivo* activation and expansion of anti-tumor

T-cells, 5) Reversal of cancer-induced immunosuppression (e.g. primary, adaptive, acquired immune-resistance). Personalized combination therapy needs be explored for improvement of current cancer immunotherapies in Japan.

S9-2

Overview of immune-related adverse events

Shigehisa Kitano
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Conflict of interest: Yes

As an adverse event specific to an immune checkpoint inhibitor, an immune-related adverse event (irAE) appears. The characteristics of irAEs include the possibility that they appear in various parts of the body and the difficulty of predicting the onset time. Although rare, some irAEs can be fatal if diagnosis and treatment are delayed. Therefore, it is important to diagnose them earlier by establishing a patient education system and a medical system that crosses medical departments and occupations. In this lecture, the mechanism, diagnosis, management and current problems of irAE will be outlined.

S9-3

Neuromuscular adverse events associated with immune checkpoint inhibitors

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Conflict of interest: None

Neuromuscular adverse events (irAEs) associated with cancer treatment with immune checkpoint inhibitors (ICIs) include diverse clinical subsets. The general features of neuromuscular AEs have not been elucidated because the frequency is generally low, ranging from 1%-2% of cancer patients undergoing ICIs therapy. The diseases affect the central nervous system, peripheral nerves, neuromuscular junction, and muscle. Disease onset and progression may be rapid with a critical clinical course. The clinical presentation may be different from that of patients unrelated to drugs. Brain MRI images or laboratory findings do not always yield useful information, even if cancer patients suffer from severe neurological symptoms. Headache, dizziness, and dysgeusia were relatively common and mild treatment-related AEs. In contrast, representative immune-related AEs such as autoimmune encephalitis, demyelinating polyneuropathy, myasthenia, and myositis were serious. There are guidelines for the treatment of neuromuscular immune-mediated AEs. For all but the minimum neurological symptoms, checkpoint inhibitor therapy should be withheld until the diagnosis of AEs is made. Immune-modulating medication is generally effective for neuromuscular AEs. Correct understanding of neuromuscular AEs is required for the best management of cancer patients.

S9-4

Immune check point inhibitor mediated pneumonitis

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Conflict of interest: Yes

The efficacy of immune check point inhibitors in patients with various type of cancer were demonstrated in huge number of pivotal studies. In terms of adverse events, in general, immune check point inhibitors have a favorable safety profile. However, due to its mechanism of action, immune check point inhibitors are associated with immune-related adverse events, including interstitial lung disease/pneumonitis. Pneumonitis may lead to a fatal outcome and, therefore, requires careful attention. In this symposium, current summary of overview, radiological characteristics, risk factors, treatment in management of immune check point inhibitor mediated pneumonitis will be presented.

S9-5

Rheumatologic complications of immune checkpoint inhibitors

Kimito Kawahata
St. Marianna University School of Medicine

Conflict of interest: Yes

Immune checkpoint inhibitors (ICIs) are the most commonly used immunotherapy drug for advanced stage cancers but can cause a number of immune-related adverse events (irAEs), including a variety of rheumatologic manifestations. Rheumatic irAEs occur in approximately 10-20% of anti-programmed death 1-treated cancer patients. Inflammatory arthritis has been the most commonly reported rheumatic irAE and often require prolonged immunomodulatory therapy. The rheumatic complications of ICIs and their management will be reviewed in this presentation.

S10-1

Destruction and repair of articular cartilage in osteoarthritis: Overview

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Conflict of interest: Yes

Joint is composed of articular cartilage, synovium and joint cavity. Synovial fluid produced by synovial membrane nourishes avascular tissue articular cartilage and functions as shock absorber. Development of noninvasive imaging techniques has provided paradigmshift in studies on articular cartilage destruction in osteoarthritis (OA), and showed that in knee OA, synovitis and osteophyte commonly occur in early stages, suggesting their implications for destruction and progression of OA cartilage. Articular cartilage comprises of chondrocytes and extracellular matrix (hyaluronan-aggrecan network structure and collage fibers), and cartilage destruction progresses by degradation of hyaluronan-aggrecan network structure and subsequent digestion of collagen fibers, and chondrocyte death. Collagens are degraded by collagenolytic MMPs (MMP-1, 8, 13, 14), and ADAMTS4 and ADAMTS5 play a key role in the aggrecan degradation. The expression of these metalloproteinases is regulated by growth factors and cytokines such as IL-1, TNF-α and TGF-β. We have demonstrated that HYBID (KIAA1199/CEMIP) plays a central role in hyaluronan degradation, and is up-regulated by TNF-α and IL-6. On the other hand, the damaged articular cartilage results in incomplete repair, showing osteophyte formation at the periphery of articular surface and chondrocyte cluster formation in the central part. Our studies on chondrocyte cluster in OA cartilage showed involvement of overexpression of ADAM12, motility-promoting and antagonistic effects of VEGF and Semaphorin 3A, and overexpression of inhibitors to MMP and ADAMTS4 (RECK and CCN1). In this symposium, I would like to review the problems in the destruction and repair of articular cartilage in OA, which may include characters of inflammatory reaction specific to articular cartilage, unsolved topics in cartilage destruction, mechanism of incomplete cartilage repair, and functions of osteophytes other than cartilage repair.

S10-2

Maintenance of Articular Cartilage

Taku Saito
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Conflict of interest: Yes

Articular cartilage is continuously exposed to mechanical loading for long time. Property of mechanical loading varies depending on the location of articular cartilage. Characters of articular chondrocytes are different according to the location, and their responses to mechanical loading are different as well. I will introduce recent studies and discuss the mechanisms of articular cartilage maintenance.

S10-3

Mechanisms underlying articular cartilage degradation and the strategies to treat

Takeshi Miyamoto
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Conflict of interest: Yes

Mechanisms underlying articular cartilage degradation are considered different between rheumatoid arthritis and osteoarthritis. Rheumatoid arthritis is characterized by a chronic inflammation, and the expression of extracellular matrix protein degrading enzymes, namely a disintegrin-like and metallopeptidase with thrombospondin type 1 motif, 4 (ADAMTS4), ADAMTS5 and matrix metalloproteinase 3 (MMP3), is induced by inflammatory cytokines. Subchondral bones is also degraded by osteoclasts activated by inflammation. We found that positive feedback loop played a role for such inflammatory cytokine expression in rheumatoid arthritis, and the loop also promoted expression of receptor activator of nuclear factor kappa B ligand (RANKL), which is required for osteoclast differentiation. We also found that signal transducer and activator of transcription 3 (Stat3), a transcription factor, was required for this positive feedback loop. We demonstrated that inhibition of Stat3 could inhibit articular cartilage degradation in a rheumatoid arthritis model in mice. Meanwhile, mechanical stresses were considered promoted articular cartilage degeneration, leading to degradation. We found that oxidative stresses were induced by a mechanical stress in chondrocytes in vitro, in turn induced cartilage degeneration, inflammatory cytokine expression and apoptosis in chondrocytes. We found that articular cartilage degradation could be inhibited by an administration of an anti-oxidant in an osteoarthritis model in mice. I will introduce and discuss about our findings in this symposium.

S10-4

Synovial Pathology in Osteoarthritis

Naoshi Fukui[1,2,4], Nobuho Tanaka[2], Hirotaka Tsuno[2,3], Satoru Ohashi[2,4], Mitsuyasu Iwasawa[2,4], Hiroshi Furukawa[5]
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Conflict of interest: None

In osteoarthritis (OA), synovial changes develop with the progression of the disease. Synovial pathology in OA was previously considered to be a secondary change associated with cartilage degeneration. However, this conventional view has been completely revised in the last two decades, and synovial changes are now considered to play a pivotal role in the pathology of OA. The significance of synovial pathology in OA has been indicated through a series of epidemiological studies on knee OA. Investigations using MRI have revealed that the presence of synovitis and/or effusion is significantly correlated with the progression and symptoms of OA. This correlation was initially recognized with radiographically evident, or established OA, but recent studies have suggested that the synovial pathology may have a similar significance in early OA joints that do not show overt radiographic changes. This finding underscores the importance of clarifying the mechanisms underlying synovial pathology in OA. However, no powerful hypothesis has yet been proposed regarding these mechanisms. Clinically, synovial pathology in OA manifests as joint swelling and/or synovial tenderness. However, in OA joints, these two findings may not always develop together and often appears independently. In many cases, severely painful knees show little swelling, while highly swollen knees have no tenderness around the joints. Again, joint swelling and tenderness may often fluctuate in severity with time, even without any significant treatment. Furthermore, both of these findings often develop with little correlation to the disease severity. Such a complex clinical picture may hamer the dissection of synovial pathology in OA. In this presentation, the current understanding of synovial pathology in OA will be reviewed, and the future direction of research will be discussed. The presenters' attempt to clarify the pathology will be introduced as well.

S10-5

Pathophysiology of osteoarthritis of the knee: knowledge obtained from recent clinical researches

Muneaki Ishijima[1,2,4], Haruka Kaneko[1], Hitoshi Arita[1], Jun Shiozawa[1], Yoshifumi Negishi[1], Masahiro Momoeda[1], Lizu Liu[1,2], Takako Aoki[2], Xiang Ji[2], Adili Arepati[1], Shinnosuke Hada[1], Shin Fukusato[1], Takanori Wakayama[1], Sayuri Uchino[1], Masashi Nagao[1,3,5], Masataka Nagayama[1], Yoshitomo Saita[1], Yuji Takazawa[1,5], Hiroshi Ikeda[1,6], Yoshifumi Tamura[2,7], Hirotaka Watada[2,7], Ryuzo Kawamori[2,7], Yasunori Okada[4], Kazuo Kaneko[1,2,4]
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Conflict of interest: Yes

Osteoarthritis of the knee (knee OA) is an age-related progressive joint disease, which is characterized by degradation and destruction of cartilage, meniscus, subchondral bone and synovium, and results in walking pain and limitation of range of motion of the joint, leading to the disability of activity of daily living. In Japan, it has been estimated that there are 25 million people with radiographic knee OA and speculated that eight million have knee pain. In addition, as the prevalence of the disease increases with aging, >80% of elderly Japanese women have knee OA. Thus, knee OA is a one of the representative age-related chronic motor organ diseases responsible for locomotive syndrome. Pain is the most prominent and disabling symptom of knee OA. Recent development of clinical researches has revealed that elderlies with knee OA, even though they do not complain walking pain, increase risk for mobility impairment, metabolic syndrome, and cognitive impairment. Therefore, when we take the future treatment strategy of knee OA into consideration, we should pay more attention to knee OA subjects without pain in addition to painful knee OA patients. Symptom-modifying therapy is the only available treatment for knee OA and there are currently no disease-modifying osteoarthritis drugs (DMOADs) available for OA. Treatment will succeed, when it is based on the pathophysiology of the disease. Thus, reason for the absence of DMORDs may be due to the misunderstanding and/or inappropriate understanding of the disease. Therefore, it is critical to further deepen our understanding of the pathophysiology of the knee OA. Recent development of both basic and clinical researches for knee OA has advanced the understanding of knee OA. These developments have gradually revealed that current understanding for the pathophysiology of knee OA may not be true. In this symposium, we'd like to introduce recent development of the pathophysiology, especially the developmental process, of knee OA.

S10-6

Regenerative treatment with iPSC-derived cartilage and drug discovery with SIK3 inhibitor for articular cartilage damage and degradation

Noriyuki Tsumaki
Center for iPS Cell Research and Application, Kyoto University, Japan

Conflict of interest: Yes

Articular cartilage lesions are caused by two types of etiology: injury due to trauma which causes focal damage and arthritis, aging and metabolic abnormalities which cause erosion of extended area of articular cartilage. Regenerative cell therapies can be indicated to the focal damage. We are developing a new treatment method in which cartilage derived from human induced pluripotent stem cells (iPSCs) is implanted into the damaged area. Taking advantage of self-renew activities and pluripotency, unlimited amount of hyaline cartilage can be theoretically created. We are considering that iPSC-derived cartilage would directly contribute to the repair tissue, whereas existing cell therapies induce repair tissue through trophic effects. Against wide range of erosion of articular cartilage, drug application would be preferable rather than regenerative implantation approach. Developing drugs that target the molecules responsible for loss of cartilage is under way. These drugs would also be effective to the cartilage

legion in rheumatoid arthritis under the condition in which arthritis is controlled. We found that salt-inducible kinase 3 (SIK3) is one of factors responsible for development of osteoarthritic change in the mouse model. Our experiments indicated that inhibition of Sik3 alleviated the degree of osteoarthritic changes in the mouse model, suggesting that the SIK3 inhibitor could be one of lead molecule for drugs treating erosion of articular cartilage.

S11-1

Toward the revision of JCR guidelines for management of rheumatoid arthritis

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Conflict of interest: Yes

Japan College of Rheumatology (JCR) publicized '2014 JCR Guidelines for the management of rheumatoid arthritis' with the advent of enriched treatment armaments and treatment strategy. The guidelines were developed by using GRADE methods with careful considerations of clinical settings in Japan and benefited from the previously published recommendations/guidelines from EULAR and ACR. The designated research group led by Dr. Nobuyuki Miyasaka and Dr. Hisashi Yamanaka played a central role in the development of the guidelines. Japanese government has taken a series of strategic measures for rheumatoid arthritis (RA) based on the reports from the special committee for rheumatic diseases and allergic diseases of the Ministry of Health, Labour, and Welfare (MHLW). In 2018, the special committee for rheumatic diseases of the MHLW published a new strategic measures for RA and set their goal as 'controlling disease activity of RA by using appropriate treatments, maximizing long-term quality of life, and providing carefully crafted supports for patients' life at workplace and school and for various life events such as pregnancy and delivery'. The report summarized points at issue about standardization of management of RA and read 'the associated medical societies need to collaborate with the government to update the guidelines for the management of RA and spread them throughout the country in order to promote standardization of medical care of the disease'. Based on the requests from the MHLW as well as the launch of new approved drugs for RA and accumulation of evidence in the literature, a new designated research group has been organized since 2018 (principal investigator, Masayoshi Harigai) and revising the JCR guidelines for the management of rheumatoid arthritis in the committee led by Professor Yutaka Kawahito. In this symposium, each speaker will describe relevant features of the revised guidelines.

S11-2

Characteristics and making process of 2020 Japanese guidelines for rheumatoid arthritis

Yutaka Kawahito[1], Masayo Kojima[2], Masataka Kohno[1], Yuko Kaneko[3], Shintaro Hirata[4], Mitsumasa Kishimoto[5], Takahiko Sugihara[6], Akio Morinobu[7], Yohei Seto[8], Masaaki Mori[6], Atsuko Murashima[9], Hiromu Ito[10], Toshihisa Kojima[11], Keiichiro Nishida[12], Isao Matsushita[13], Eiichi Tanaka[14], Mieko Hasegawa[15], Hisashi Yamanaka[16], Masayoshi Harigai[14]
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Conflict of interest: Yes

[objective] To develop RA clinical practice guideline suitable for daily medical care in Japan. [Method] As a project of the Ministry of Health, Labor and Welfare's research group (Harigai group), using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) method, RA clinical practice guideline including the evidence from Japan were prepared. In addition to the update of RA clinical practice guideline 2014, this guideline was created with the treatment of life stage of the elderly, adult transition period, and perinatal period. We consensus by the Delphi method by a panel including specialists of RA treatment and RA patients. [Results] The following items were examined according to the clinical guideline preparation process by the GRADE method. (1) Importance of clinical question (CQ): The importance of outcomes was evaluated by creating a CQ for current medical care. (2) Evidence: A systematic review was conducted after searching the literature, and the existing Cochrane review and RCT were applied, and also the evidence from the cohort study was evaluated. (3) Balance between benefits and harms: Post-marketing surveillance and clinical trial data on RA drugs were considered. (4) Patient values and wishes: With the cooperation of the Japan Rheumatism Friendship Association, patient questionnaires were used as recommended data, and the opinions of patient representatives were incorporated. (5) External validity of costs and interventions: Incorporating evidence from the medical economy, and evaluating the panel. Then Japan original treatment algorithm composed of drug, non-drug and surgical treatment was constructed. [Conclusion] In the future, we will make public announcements through appropriate process. Acknowledgments: I would like to express my deep appreciation to systematic review team and Dr. Takeo Nakayama, Kyoto University School of Public Health, who helped us to create this guideline.

S11-3

Efficacy of biological disease-modifying antirheumatic drugs and other antibody therapy: a systematic literature review informing the 2020 update of the Japanese Guidelines for the management of rheumatoid arthritis

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University Graduate School of Medicine, Kobe, Japan

Conflict of interest: Yes

[Purpose] To review the evidence for the efficacy and safety of biological disease-modifying antirheumatic drugs (bDMARDs) and other antibody therapy in patients with rheumatoid arthritis (RA) to inform the 2020 update of the Japanese Guidelines for the management of rheumatoid arthritis. [Methods] As a project of MHWL study group, new guidelines have been developed, using the newly proposed GRADE (Grading of Recommendations, Assessment, Development and Evaluation) method. For construction of evidence for this issue, we used the Cochrane library systematic reviews and conducted a new systematic review for other supportive evidences. Finally, recommendations with recommended strength as strong or weak were created. A panel discussion was held among specialists of rheumatology, statistics and pharmacoeconomy, together with the representatives of patients association. Modified Delphi method was used for the Occupational therapy the consensus building. [Results] With special interests for therapeutic strategy using bDMARDs, clinical questions for the recommendations (recommended strength/agreement score) were determined. A systematic literature review (SLR) for efficacy and safety of bDMARDs stratified by mode of action (TNF inhibitors vs. non-TNF inhibitors including IL-6 inhibitors, T-cell co-stimulator modifier, etc.), concomitant therapy (combined therapy with methotrexate (MTX) or monotherapy), or response to prior therapeutics (MTX-inadequate response (MTX-IR) or bDMARDs-IR), as well as anti-RANKL antibody therapy were performed. According to meta-analyses with the selected articles, the preliminary recommendations were created. [Conclusion] Preliminary recommendations regarding bDMARDs and anti-RANKL antibody for the guidelines were created.

S11-4

2020 Japanese Guidelines for the management of rheumatoid arthritis

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Conflict of interest: Yes

[Purpose] To establish 2020 Japanese Guidelines for the management of rheumatoid arthritis. [Methods] As a project of MHWL study group, new guidelines have been developed, using the newly proposed GRADE method. For construction of evidence for this issue, we used the Cochrane library systematic reviews and conducted a new systematic review for other supportive evidences. Finally, recommendations with recommended strength as strong or weak were created. A panel discussion was held among specialists of rheumatology, statistics and pharmacoeconomy, together with the representatives of patients association. Modified Delphi method was used for the Occupational therapy the consensus building. [Results] Clinical questions for the recommendations (recommended strength/agreement score) are as follows. 1. Is a JAK inhibitor monotherapy useful for methotrexate-inadequate response (MTX-IR) patients with RA compared to MTX? 2. Is a JAK inhibitor in combination with MTX useful for MTX-IR patients with RA compared to MTX? 3. Is a JAK inhibitor in combination with MTX useful for MTX-IR patients with RA compared to a TNF inhibitor with MTX? 4. Is a JAK inhibitor in combination with MTX useful for biologic agents-IR patients with RA compared to MTX? Thirty eight articles were scrutinized, and preliminary recommendations were created. [Conclusion] Preliminary recommendations regarding JAKs for the guidelines were created.

S11-5

2020 Japanese guidelines for the management of rheumatoid arthritis -non-pharmacological treatment and surgical intervention-

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Conflict of interest: Yes

Objective: We conducted systematic review and meta-analysis for the clinical questions on non-pharmacological treatment and surgical intervention to revise the 2014 Japanese guidelines for the management of rheumatoid arthritis. Methods: A systematic review was performed on articles indexed in the Cochrane Library, PubMed, and Ichushi from 2013 to 2018. The outcomes of the studies searched had been set by Delphi methods in the review team. Then we added the articles used for the previous meta-analysis and ones published in 2019. The bias and the certainty were evaluated, and the results was summarized in each study. Whenever possible, a quantity analysis was made by odds ratios and 95% confidential interval. Results: The results of systematic reviews of 12 CQs on the usefulness of surgical interventions were to recommend the operations. The results vary because of the levels of evidence in each CQ. The CQs of physiotherapy, occupational therapy, and intraarticular steroid injection resulted in recommendation of the treatments by quantitative analysis. The levels of evidence on the risk toward operation or perioperative risks were found low. In perioperative medical management, MTX was not to and bDMARDs were to suggest halting the drugs before operations. Conclusions: The review suggest that non-pharmacological treatment and surgical interventions improve not only the functions of the individual joints but systematic disease activity, physical function, and patient-reported outcomes. On the other hand, appropriate cautions should be paid perioperatively including halting medication to lower perioperative risks.

S11-6

2020 Japanese Guidelines for the management of rheumatoid arthritis -elderly patients, comorbidities, pregnancy-

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Conflict of interest: Yes

Objective: In order to update 2014 recommendations of pharmacological treatment for RA in special situations such as pregnancy, lactation, comorbidities, or aged patients. Methods: We selected clinical questions (CQ), searched relevant literature, evaluated evidences by systematic review and proposed recommendations. Results: 7 CQs were set for the patients with comorbidities, 3 for elderly RA patients, 2 for pregnant or breast-feeding patients, and 1 for the male partner of the patients who has desire for a baby. After literature search on articles indexed in the Cochrane Library, PubMed, and Ichushi from 2013 to 2018, systematic reviews against each CQs were performed. Some important articles published before 2013 or in 2019 were included. Also regarding to CQs for pregnant and breast-feeding women, important articles were cited from database of Japan Drug Information Institute in Pregnancy, National Center for Child Health and Development. The certainty of evidences was evaluated, and the results were summarized in each CQ. Most of the article selected are based on observational studies such as case-control studies and cohort studies. The evidence levels were not so high, especially for CQs for elderly patients and patients with complications. Conclusions: More evidences are required for the treatment of RA patients with specific conditions. The recommendations will be presented after they are voted in the guideline meeting and shaped up.

S11-7

2020 Japanese Guidelines for the management of rheumatoid arthritis-Transitional medical care-

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Conflict of interest: None

Objective: We aim to create a guide for the transition medical care in 2020 Japanese Guidelines for the management of RA, which is based on the evidence as much as possible. Methods: We studied transitional cases of articular juvenile idiopathic arthritis (JIA) with similar pathology to RA with reference to "Transition support guide essential for popularization of transitional medicine". In transitional medicine, the background questions such as knowledge about diseases and transitional medical care are mainly explained. In addition, the results of the library search are mostly commentary and general comments, making it difficult to create evidence tables. For this reason, the transitional chapter is described as a separate chapter from the main body, and pediatric rheumatologists have created CQs as some points that adult clinicians should know in transitional clinical practice. Results: The following five CQs were listed for JIA during adult transition. 1. Does the treatment for transitional articular JIA patients require different considerations compared to adult RA patients? 2. Does articular JIA cause joint destruction in the long term? 3. Can articular JIA cure? 4. Is the uveitis, an extra-articular symptom of articular JIA, necessary to be careful even in adulthood? 5. Which is better for JADAS-27 or DAS-28 as an index for assessing disease activity in patients with transitional articular JIA? We made an answer sentence for each CQ, a bibliographic flowchart, and evidence table if possible, and finally compiled it as qualitative synthesis. Conclusions: Centered on the content of the "Transition support guide", a separate chapter was set up to present it in 2020 Japanese Guidelines for the management of RA in a form that is distinct from the previous guidelines. An answer sentence was also prepared for CQ taking into account the medical situation in Japan. Acknowledgments: We would like to express my deep appreciation to the transition team members in JIA subcommittee.

S11-8

Evaluation of patients' values and preferences

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Conflict of interest: None

In the development process of the new practice guidelines for the management of rheumatoid arthritis 2020, a self-administered questionnaire survey was conducted with the aim of reflecting the patient's perspectives as evidence. The first half asked questions about the current status of rheumatoid arthritis patients, and the second half asked about satisfaction with specific treatments. The survey subjects were 1,600 members of The Japan Rheumatism Friendship Association over 20 years old, randomly selected according to the number of members in each prefecture, and conducted by mail (survey period September 1-20, 2019). There were 1,145 respondents (response rate 71.6%), average age 63.1 ± 11.9 years, patient global assessment average 32.3 ± 23.7, and average medical satisfaction was 75.9 ± 17.2. 446 people (39.0%) have discussed with their doctors about the treatment goals, 387 people (33.8%) have received explanations, and 285 people have answered neither (24.9%). Many patients pay attention to maintain their physical condition by diet (n=547, 47.8%), stretching (n=497, 43.4%), walking (n=355, 31.0%), and resistance training (n=211 people, 18.4%). Although of all pharmacotherapy, benefits exceeded adverse effects, the patients' satisfaction was particularly high for biological products. For anti-RANKL antibodies, 68.3% of the respondents answered "cannot say". Synthetic anti-rheumatic drugs, steroids and JAK inhibitors were relatively variable. Surgical treatments were all satisfactory, and 91.3% of 240 patients answered that they had achieved the expected effect, especially in knee replacement. In the previous survey, we examined the ease of accepting each treatment for patients. This time, we were able to clearly show patients' satisfaction for treatments. Patient questionnaire survey is considered indispensable as a concrete method to reflect patient values in clinical practice guidelines.

S12-1

Treatment strategy of the antiphospholipid syndrome

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Conflict of interest: Yes

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by thrombotic events and pregnancy complications with persistently positive antiphospholipid antibodies (aPL). APS patients suffer from thrombosis in both arteries and veins. According to the guidelines for the management of patients with APS, anticoagulation using warfarin is recommended for secondary prophylaxis of arterial/venous thrombosis. However, a major limitation in the recommendations is that no definitive evidence has been shown to prevent recurrent arterial events. Our longitudinal APS cohort was used to evaluate the benefit of anti-platelet including Dual antiplatelet therapy (DAPT) in patients with a history of arterial thrombosis. We found that the effectiveness of DAPT as a secondary prophylaxis against arterial thrombosis in APS patients was similar to that of Warfarin + aspirin and superior to warfarin alone. However, in any case, antithrombotic therapy is not sufficient to manage APS, considering its high recurrent rate and complicated autoimmune disorders in the affected patients. How to establish the better treatment strategy in this syndrome? The role of aPL in the development of APS manifestations is widely recognized, and the pathogenic mechanisms that lead to thrombosis have been intensively investigated. We and others have shown that the aPL may affect the normal procoagulant and anticoagulant reactions occurring on cell membranes, and may also interact with certain cells, altering the expression and production of procoagulant and/or proinflammatory substances. Furthermore, aPL may activate complement causing and perpetuating APS manifestations. The identification of various candidate cell receptors for aPL-cell interaction and the intracellular signaling pathways mediating pathogenic effects of aPL on different cell types have increased the understanding of the hypercoagulable state of APS.

S12-2

Secondary thrombotic microangiopathy in connective tissue diseases

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Conflict of interest: None

Thrombotic microangiopathy (TMA) is a multiple organ syndrome that results in microvascular occlusion and endothelial injury. It may be seen in association with microangiopathic hemolytic anemia, schistocytosis, thrombocytopenia, and organ failure by microvascular thrombosis. Subtypes of TMA have been pathologically defined on the basis of the pathogenetic factors: thrombotic thrombocytopenic purpura (TTP), typical and atypical hemolytic uremic syndrome (HUS), and secondary TMA. The pathogenesis of TTP involves a deficiency of ADAMTS13 enzyme activity. The pathogenesis of HUS involves uncontrolled dysregulation and excessive activation of the alternative pathway of complement. HUS is usually categorized as typical, caused by Shiga toxin-producing Escherichia coli (STEC) infection, as atypical HUS (aHUS), caused by genetic or acquired defects in the proteins that regulate the alternate complement pathway, as well as autoantibodies that neutralize the function of these proteins. Secondary TMA occur in association with another underlying disease or pathological condition such as connective tissue diseases (CTDs). CTDs often have hypercoagulable state induced by immune activation, such as vascular endothelial injury associated with vasculitis, autoimmune abnormalities that neutralize the function of complement regulatory proteins or ADAMTS13, and complement activation by the alternative pathway. Therefore, a number of CTDs have been reported in association with TMA: SLE, APS, scleroderma renal crisis, Polymyositis/Dermatomyositis, vasculitis and others. Plasma exchange, a treatment that removes inhibitor of anticoagulation is widely used in TTP. Eculizumab, a monoclonal antibody that targets complement protein C5 and prevents the activation of complement system is considered for HUS. Additionally, immunosuppressive therapies for underlying CTDs is also important for secondary TMA. Early diagnosis and appropriate treatment are important to better prognosis.

S12-3

JAK inhibitors for refractory anti-MDA5 Ab positive interstitial lung disease

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Conflict of interest: None

Anti-MDA5 Ab positive interstitial lung diseases (MDA5-ILD) is a critical and frequent condition in Japanese patients, which progress rapidly, is resistant to intensive immunosuppressive therapy and causes poor prognosis. 'Triple therapy', combination therapy of high dose glucocorticoid, calcineurin inhibitors and cyclophosphamide, are widely used. However, the survival rate of MDA5-ILD are still in 50-75%. Thus, the new therapy for this poor condition has been required. We here reported our experience of JAK inhibitor administration against refractory MDA5-ILD. We examined cytokine profiles of MDA5-ILD. IFN-a, IL-15 TNF-a and IL-6 levels were elevated in serum and BAL fluid in MDA5-ILD, which indicated that multiple cytokine over-production was characteristic of this condition. Thus, we selected patients who had poor prognostic factors and failed to respond to the triple therapy immunosuppressive and administrate tofacitinib (TOF), a JAK inhibitor that blocks multiple cytokines. Three poor prognostic factors were identified: serum ferritin level >1000 ng/ml before therapy; ground-glass opacities in all six lung fields before therapy; and worsening of pulmonary infiltrates during therapy. All six patients who had all of the three factors and received triple therapy died before TOF therapy. There were five patients who had all of the three prognostic factors and failed to respond to triple therapy, but were able to receive the combination therapy with TOF; among them, three survived and two died. The survival rate of patients who received TOF was significantly better than that of the historical controls with immunosuppressive therapy

before TOF. The patients who received TOF experienced complicated adverse events, particularly viral infection. Our experience suggests that combination therapy with TOF might rescue patients refractory MDA5 -ILD, although further investigations including validation efficacy of the therapy and determination of proper protocols are required.

S12-4

TAFRO syndrome

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Conflict of interest: Yes

TAFRO syndrome, first reported in 2010, is a systemic inflammatory disorder manifesting as thrombocytopenia; anasarca, including pleural effusion and ascites; fever; reticulin myelofibrosis and/or renal insufficiency; and organomegaly, including hepatosplenomegaly and lymphadenopathy. The annual incidence rate of TAFRO syndrome in Japan has been estimated to be 0.9-4.9 per million individuals, and the nationwide prevalence to be 860-7,240 cases, numbers which are larger than previously expected. Most patients with TAFRO syndrome manifest modest-to-mild systemic lymphadenopathy with characteristic histopathological features resembling those of Castleman disease. Some researchers therefore consider that TAFRO syndrome to be a subtype of idiopathic multicentric Castleman disease (iMCD). However, clinical features of TAFRO syndrome are quite different from those of classical Castleman disease, and we consider TAFRO syndrome to be a distinct clinical entity, although several pathological findings of lymph nodes resemble those in iMCD. In 2015, we proposed diagnostic criteria and a disease severity classification for TAFRO syndrome, which have been widely accepted and cited. Since then, we gained some additional insights and experiences that prompted us to update these criteria and classification as the 2019 version. Recently, we retrospectively analyzed data from 220 patients stored in the database of the Multicenter Collaborative Retrospective Study for Establishing the Concept of TAFRO Syndrome. In that study, we compared clinical features of patients with iMCD, not otherwise specified (iMCD-NOS), TAFRO-iMCD, and TAFRO-without-proven-iMCD (TAFRO-w/op-iMCD). Our analysis clearly demonstrated that iMCD-NOS and TAFRO-iMCD are different clinical entities, whereas TAFRO-iMCD and TAFRO-w/op-iMCD, which were diagnosed without lymph node biopsy, could be considered the same clinical entity, requiring prompt diagnosis and intensive care.

S12-5

Neuromyelitis Optica

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Conflict of interest: Yes

Neuromyelitis Optica (NMO) is a relapsing inflammatory disease of the central nervous system characterized by severe optic neuritis and longitudinally extensive transverse myelitis. The research of NMO had made a remarkable advance following the discovery of NMO-specific aquaporin 4 (AQP4) antibody in 2004~2005. Brain syndrome including area postrema syndrome manifesting intractable hiccup, nausea and vomiting can develop in AQP4 antibody-positive cases, and thus NMO spectrum Disorders (NMOSD) wad proposed as the unifying term for the entire clinical spectrum in the 2015 International Diagnostic Criteria. In AQP4 antibody-positive NMOSD, one core clinical characteristic is sufficient to make a diagnosis if alternative diagnoses are excluded. Meanwhile, multiple conditions should be met for AQP4 antibody-negative NMOSD. Recently, a fraction of patients with AQP4 antibody-negative NMOSD have been found positive for myelin oligodendrocyte glycoprotein (MOG) antibody, and MOG antibody-associated disease has a clinical spectrum distinct from AQP4 antibody-positive NMOSD. Corticosteroids and various immunosuppressive agents have been used to prevent relapses in NMOSD, but none were studied in randomized controlled trials (CRT). Some disease modifying drugs for multiple sclerosis (MS) can exacerbate NMOSD, and thus NMOSD should be distinguished from MS in the early phase of the disease. Recently, first-ever international RCT of three monoclonal antibodies (anti-IL-6R, anti-C5, and anti-CD19) in NMOSD were completed, and the drugs reduced the risk of relapse by 80~94% in AQP4 antibody-positive cases. Due to small numbers of cases, the therapeutic efficacy in AQP4 antibody-negative NMOSD was unclear. In this presentation, clinical, MRI and laboratory features, pathogenesis and treatment of NMOSD including the updated information will be reviewed.

S12-6

Current status and prospects of intractable phenotypes in Behcet's disease

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Conflict of interest: Yes

Behcet's disease (BD) is a rare systemic inflammatory disease with repeated inflammatory attacks of the mucocutaneous region. Both environmental and genetic factors are related to the pathogenesis of the disease. The 2018 EULAR recommendation recommends treatment according to age, gender, type of disease, and severity of organ damage, and the eye, blood vessels, nerves, and gastrointestinal lesions are defined as refractory conditions that require intensive treatment. However, a method for predicting or preventing these intractable conditions has not been established. Recently, we reported that the proportion of patients with complete type and HLA-B51 positivity decreased over time, while those with incomplete and intestinal type increased (Kirino et al, Arthritis Res Ther, 2016). Furthermore, a cluster analysis using 707 BD patients at Yokohama City University and 7,399 patients from the Ministry of Health, Labor and Welfare designated intractable disease database found that the intestinal cluster is a subtype that is difficult to meet the diagnostic criteria and is a group with poor prognosis. We also reported that HLA-B51 negative, joint symptoms, and absence of ocular symptoms were predictors of the intestinal type (Soejima, Kirino et al, submitted). Based on the findings of previous research, we are currently promoting nationwide disease registry research. Prospective detailed clinical data, genetic data, and serological data will be comprehensively and prospectively accumulated to be used for identify prognostic predictors, revision of diagnostic criteria and guidelines, disease activity indicators, etc. In the future, we aim to establish optimized medicine based on BD disease subtype.

S13-1

Clinical guide for ankylosing spondylitis

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Conflict of interest: Yes

Spondyloarthritis (SpA) is a group of rheumatic diseases characterized by axial and peripheral arthritis, enthesitis, extraarticular manifestations, such as anterior uveitis, and association of HLA-B27. Ankylosing spondylitis (AS) mainly affects axial joints, including sacroiliac joints and spine. AS frequently develops in young male having HLA-B27 with inflammatory back pain. Inflammation in AS starts from entheses, then induces consequent bone erosions, repair of erosions with fat tissue called backfill, and new bone formation resulting in bridging between vertebral bodies by syndesmophytes in the long disease duration. Recently, innate lymphocytes and inflammatory cytokines, such as TNF and IL-17, are known to be involved in the pathogenesis of AS, and inhibitors of these cytokines reduce clinical symptoms and possibly slow the new bone formation. Early diagnosis and intervention are strongly necessary. ASAS

(Ankylosing SpondyloArthritis International Society) proposed a classification criteria for axial SpA that can classify non-radiographic axial SpA (nr-axSpA) by the presence of osteitis on MRI or HLA-B27 in combination with clinical features of SpA. However, nr-axSpA does not always progress to radiographic SpA, and it includes mild cases of axial SpA and probably other diseases. Making diagnosis of AS is often difficult due to the initial common symptom of back pain, negative CRP in 30-40% of patients, and relatively slow progression. Because of very low frequency of AS, disease recognition seems poor in Japan. To learn appropriate clinical diagnosis and treatment of SpA, a clinical guide of SpA was published by the study group for SpA granted by the Ministry of Health Labour and Welfare. In this symposium, I would like to discuss about diagnosis and treatment of AS based on this guide.

S13-2

The guidance for the clinical practice of psoriatic arthritis

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Conflict of interest: Yes

Psoriatic arthritis (PsA) is a major disease of spondyloarthritides (SpA) characterized by enthesitis. Although PsA is categorized into peripheral SpA, ~40% of patients develops axial joint involvements. Apart from the axial joint disease in ankylosing spondylitis (AS), it does not always progress in ascending manners from sacroiliac (SI) joints: frequently involvement of cervical lesions and asymmetric/atypical lesions in the spinal bones and SI joints are the features of PsA. Magnetic resonance imaging (MRI) is useful for an early detection of axial joint diseases, while joint ultrasound is suitable for peripheral joint diseases such as enthesitis, arthritis and dactylitis. The CASPAR classification criteria may be of some help for the diagnosis of PsA, although the consideration of various items beyond that criteria and intensive differential diagnosis is necessary before making diagnosis as PsA. In the treatment of PsA, it should be noted that non-steroidal anti-inflammatory drugs (NSAIDs) suppress the formation of syndesmophytes, namely, serve as disease-modifying drugs, and the effectiveness of methotrexate is limited in PsA as compared with that in rheumatoid arthritis, and only in peripheral arthritis. At present, biologics targeting tumor necrosis factor (TNF) or interleukin (IL)-17/23 are highly effective, and Janus kinase inhibitors are expected to be approved for PsA.

S13-3

Imaging in patients with spondylarthritis

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Conflict of interest: None

Spondyloarthritis (SpA) is chronic rheumatic diseases that cause inflammation of the joints of the axial skeleton, such as the spine and sacroiliac joints, and the peripheral skeleton. The former type is classified as axial SpA, and the latter type is classified as peripheral SpA. In the classification of ASAS, axial SpA is further classified into radiographic axial SpA and non-radiographic axial SpA, according to the presence or absence of definite radiographic changes in the sacroiliac joints. Knowledge of the imaging findings of sacroiliac arthritis is most important in the diagnosis of axial SpA. The classification based on modified New York criteria is fundamental on radiograph. Other imaging findings include Romanus lesion, Andersson lesion, and syndesmophyte in the spine. Syndesmophytes are classified as marginal and non-marginal. Ankylosing spondylitis shows symmetrical marginal syndesmophytes which extend along the margins of the vertebral bodies. While psoriatic spondylitis and reactive arthritis typically show asymmetrical non-marginal syndesmophytes which extend 2 to 3mm away from the vertebral bodies. There is no doubt that a radiograph is basic modality in imaging, however it is vital to detect early lesions using MRI before bone changes occur in radiograph, from the viewpoint of early treatment intervention. In the diagnosis of sacroiliac arthritis using MRI, a so-called "fluid-sensitive MR sequences" that water component shows high signals are essential, such as fat-suppressed T2-weighted images and STIR images. T1-weighted images are also required in differentiating the lesions as active inflammation, fat metaplasia, and sclerosing lesion. Backfill is also a specific sign of axial SpA seen on T1-weighted image, which is a predictor of development of ankyloses in the sacroiliac joints of patients with SpA. The differential diagnosis includes inflammatory diseases such as osteitis condensans illi, pyogenic/tuberculous arthritis and spondylitis, neoplastic lesions including metastases, and degenerative lesions such as spondylitis deformans including Modic degeneration. SAPHO syndrome is known as other related disease of SpA. In this session, I review the fundamental imaging findings of SpA, and the differential diagnoses that can be encountered in daily clinical practice.

S13-4

Update on diagnosing and the manage for juvenile spondyloarthritis

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Conflict of interest: None

Spondyloarthritis that develops before age 16 is defined as juvenile spondyloarthritis (JSpA). ILAR classification criteria of juvenile idiopathic arthritis (JIA) has been used for chronic arthritis in children, and "enthesitis related arthritis" "psoriatic arthritis" "Part of the unclassified arthritis" corresponds to JSpA. Note that "reactive arthritis" and "IBD related arthritis" are not included in JIA. SpA is a disease that occurs in young people in their 20's and 40's, and there are many cases in which symptoms begin to appear in childhood and adolescence. The clinical course of childhood onset case is similar to adult onset case when the patient reaches adult age, although there is a difference in the findings in the early stages of onset. Therefore, both diseases are considered to be continuum and the concept of JSpA is often used for seamless medical care and clinical research through adulthood. In the early stage of JSpA, peripheral and unclassified types are common, and they rarely complain inflammatory back pain. After 5 to 10 years, inflammatory back pain and radiographic sacroiliitis appear, and the disease state becomes similar to that in adults, but the progression of the axial lesion is reported to be slower. Diagnosis is comprehensive because blood tests are often negative for autoantibodies and inflammatory reactions and MMP -3 levels are normal to mild. Recently, the usefulness of the musculoskeletal ultrasound examination is expected on the identification of the enthesitis. Treatment for JSpA follows JIA guidelines. In other words, the initial treatment with NSAIDs should be started, if no improvement is obtained, MTX should be started, and if there is no improvement, use of biologics should be considered. Tocilizumab, Enbrel, adalimumab, and abatacept are biologic agents indicated for the treatment of polyarticular inflammation in JIA. The ACR guidelines published in 2019 for sacroiliitis/adhesitis recommend TNF inhibitors.

S13-5

Joint management for IBD-associated spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis is a group of several diseases with similar clinical, serological features and familial and genetic relationship. Inflammatory bowel disease (IBD) is frequently observed in the setting of SpA. Recently the patinets number of IBD has increased in Japan, however, the nationwide actual state of IBD SpA in Japan has not been investigated yet. Cross-sectional collaboration between rheumatologist and gastroenterologist should be promoted in order to improve management of patients with IBD SpA.

S13-6

PAO (Pustulosis associated osteoarthritis)

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Conflict of interest: Yes

PAO manifests as chronic inflammation of bones and joints accompanied by PPP (Palmoplantar pustulosis)) and most often affects the anterior

chest wall. In 1981, Sonozaki et al described PAO that the osteoarthritis, including mainly the clavicles, sternum and stermoclavicular joints, associated with PPP appeared in Japanese patients. Several associations between chronic inflammatory dermatological lesions and osteoarticular lesions were subsequently reported, and Benhamou et al proposed the diagnostic criteria of SAPHO (Synovitis-Acne-Pustulosis-Hyperostosis-Osteitis) in 1988. The latest criteria of SAPHO was proposed in 2003. There has not been validated diagnostic criteria for SAPHO until now, because 15% of the patients have osteoarthritis without skin manifestations, one third of the patients have osteoarticular manifestations precede skin manifestations, and skin manifestations are various. PAO is a part of SAPHO syndrome but each pathogenesis is considered to be different. Both of PAO and SAPHO syndrome are rare diseases in Japan, but PAO is more frequently seen in Japanese than in western countries. Recently, bDMARDs are shown to be effective in the treatment of PAO and SAPHO, therefore, they are now highlighted as a kind of spondyloarthritis. The exact etiology and pathogenesis of PAO remains unclear. A combination of genetic factors, environmental triggers, such as focal infection, tobacco, and metal allergy and so on, induce immunological abnormalities and lead to osteoarticular manifestations. First treatment should be removing theses triggers, which sometimes result in dramatic improvement in osteoarticular manifestations. For patients without improvement, NSAIDs, DMARDs, corticosteroids and bisphosphonates have been used but bDMARDs are preferentially used recently as more effective treatment for PAO. In this symposium, I present patients with PAO in our hospital and review the pathogenesis, diagnosis, and treatment for PAO based on latest knowledge.

S14-1

Rheumatoid arthritis and Lymphoproliferative disorders - Overview and the clinical guide for the diagnosis and management of lymphoproliferative disorders in RA patients under an immunosuppressive therapy

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Conflict of interest: Yes

The recent T2T strategy, using MTX and molecular-targeted drugs brought innovative progress for RA treatment. On the other hand, the increase in sideeffects such as lymphoproliferative disorders (LPD) becomes one of the safety concernin long-term immunosuppressive therapy. In RA, an increased risk of lymphoma compared to the general population, is well established. The etiology and pathogenesis of LPD in RA remained to be resolved, but it has been suggested the involvement of immunodysfunction, caused by aging, immunosenescence, hereditary factor, chronic inflammation and RA-related immunodysfucntion, and long-term immunosuppressive therapy with or without EBV reactivation. LPDs that arise in patients treated with immunosuppressive drugs including MTX for autoimmune diseases are categorized as other iatrogenic immunodeficiency-associated LPD according to the WHO classification. Because it tends to increase in the case repost of RA-related LPD (RALPD) and some confusion regarding incidence, diagnosis and management of LPD in the field of clinical practice, JCR Committee on Research and Study has started a retrospective cohort study to clarify the actual situation of RALPD. In addition, JCR decided to develop a clinical guide for diagnosis and management of RALPD, jointly with Japanese Society of Hematology (JSH) and Japanese Society of Pathology (JSP). To accumulate more evidences of RALPD, another multicenter, retrospective study has conducted by the JCR/JSH/JSP joint working group (WG) and data from 232 cases of LPD, including 40 cases of clinical LPD were collected. On the basis of the results of these clinical studies and evidences from Japan and Western countries regarding RALPD, the WG is in the process of drawing up the clinical guide. In this symposium, we will discuss epidemiology, signs before the onset, clinico-pathological features, clinical course and prognosis, and RA treatment after regression according to the content of the clinical guide.

S14-2

A retrospective, multi-institutional study for lymphoproliferative disorders in patients with rheumatoid arthritis by Japan College of Rheumatology

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Conflict of interest: Yes

Objective: Risk of lymphoma in Japanese patients with rheumatoid arthritis (RA) is 4 to 6 times as high as that of the general population. Risk factors for lymphoma in patients with RA are reported to include age, accumulated disease activity, and immunosuppressed status. Because of spontaneous regression of LPD in some patients after withdrawal of MTX, MTX has been included in the causative drugs for 'other iatrogenic immunodeficiency-associated LPD'. This study was implemented by JCR to reveal clinical and pathological characteristics, incidence, and risk factors of LPD in patients with RA in Japan. **Method**: Research Electronic Data Capture (REDCap) was used to collect data in this retrospective cohort study. We enrolled patients with RA who were >= 20 years old and visited participating hospitals during April 1, 2011 to July 31, 2011. Patients were registered at each site by the order of their first visit during the four months and observed for 3 years. Patients who had been diagnosed as having lymphoma were excluded. Those who developed LPD were further observed for 5 years after the diagnosis. **Results**: Of 11099 patients registered, 10807 patients from 59 sites were analyzed. Mean age was 63 y/o and 79.3% were female. LPD was reported in 91 patients. Of the 71 cases with pathological diagnosis of LPD, 54% were diffuse large B cell lymphoma and 16% were Hodgkin lymphoma. Sites of the lesions were nodal alone in 43%, extra-nodal alone 37%, and both in 20%. A variety of tissues were included in the extra-nodal lesions. Median age at the onset of LPD was 69 y/o, disease duration until the onset of LPD was 12 years, and length of MTX use was 60 months. Current or previous MTX users were 91.7% and median doses of MTX at the onset of LPD was 8.0 mg/week. Mean values of ESR, CRP, LDH, and sIL-2R were 43.9 mm/hr, 4.62 mg/dL, 371 U/L, and 2035 U/mL, respectively. **Conclusion**: Clinical and pathological features of LPD in patients with RA in Japan were revealed.

S14-3

Clinical signs and laboratory findings preceding lymphoproliferative disease in rheumatoid arthritis patients

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Conflict of interest: None

[Purpose] To clarify the risk factors, clinical signs and laboratory abnormalities preceding lymphoproliferative disease (LPD) development in rheumatoid arthritis (RA) patients. [Methods] Among RA patients who developed LPD in participated institutions, clinical characters such as age, gender, duration of RA disease, RA disease activity, medication, and concomitant autoimmune disease were analyzed. We also analyzed the changes in laboratory values such as number of lymphocytes and LDH before and after the development of LPD. [Results] 232 patients were enrolled. Median age at the LPD diagnosis was 67, and 77% were female. The median duration of RA disease was 144 months. The median CDAI at the same timepoint were 3.33 and 4.83, respectively: most of the patients developed LPD under the condition of low RA disease activity. In terms of medication, 95% of patients were administrated Methotrexate (MTX) and 22% used biologic agents. The most common concomitant disease was Sjögren's syndrome and the prevalence rate were 16%. At the onset of LPD, the number of lymphocytes decreased, and increased after MTX cessation: median 1188/μL at 1 year before,1012/μL at LPD diagnosis, and 1365/μL at 4 weeks after MTX cessation. Although the change of lymphocyte were significant in the LPD group in which spontaneous regression of LPD after MTX cessation were observed, the change were not significant in the LPD group without regression. Change of lymphocyte number were similar in each histopathological type of LPD. In addition, LDH and CRP levels were significantly increased at the development of LPD diagnosis. [Discussion] Most patients who have developed LPD were in old age and had a long disease duration of RA. Elevated CRP levels that are not linked to RA activity, increased LDH, and decreased lymphocyte might be considered as a preceding signs for the development of LPD.

S14-4

Clinicopathological Characteristics of Lymphoproliferative Disorders in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Objective: A guide to the diagnosis and treatment of lymphoproliferative disorders (LPD) in patients with rheumatoid arthritis (RA) is currently under development. A database of LPD by the working group of Japan College of Rheumatology was analyzed to identify clinicopathological characteristics of LPD in patients with RA in Japan. **Method:** We enrolled patients with RA who were newly diagnosed as having LPD between January 2000 and March 2017. LPD was divided into two categories: biopsy-proven LPD and clinical LPD. The clinical LPD was defined as LPD diagnosed without biopsy because of prompt regression of clinical manifestation after withdrawal of immunosuppressive therapy. **Result:** Among the 232 patients (median age, 67 years old; 77% women) included, 195 (84%) had biopsy-proven LPD and 37 (16%) had clinical LPD. The median (IQR) duration of RA was 12 (6-20) years. At the time of LPD diagnosis, 219 (94%) patients received methotrexate (MTX). The median (IQR) duration of MTX treatment was 6.0 (2.2-10.0) years. B symptoms were present in 71 (31%) patients and 116 (51%) patients had extranodal involvement. Major extranodal sites were lungs (n=35), oral mucosa (n=27), gastrointestinal tract (n=15), bone marrow (n=14), skin (n=13), and liver (n=10). The median (IQR) lymphocyte count, LDH, CRP, and sIL-2R were 1080 (650-1510) /μL, 236 (195-316) U/L, 1.39 (0.30-3.76) mg/dL, and 980 (650-1930) U/mL, respectively. Of 195 patients with biopsy-proven LPD, 79 (41%) had DLBCL, 21 (11%) had classic Hodgkin lymphoma, 15 (8%) had EBVMCU, 11 (6%) had reactive follicular hyperplasia, and 10 (6%) had follicular lymphoma. Other subtypes included MALT lymphoma, Hodgkin-like lesion, peripheral T-cell lymphoma, etc. EBER-ISH was positive in 74/134 (55%) patients. Compared with biopsy-proven LPD, clinical LPD had fewer extranodal lesions (27% vs 55%, p=0.002) and lower sIL-2R (p=0.02). **Conclusion:** This study revealed the clinicopathological characteristics of LPD in patients with RA in Japan.

S14-5

Clinical course of lymphoproliferative disorders in patients with rheumatoid arthritis

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Conflict of interest: None

Lymphoproliferative disorders in patients with rheumatoid arthritis (RA-LPD) may be categorized into cases associated with RA itself and cases induced by immunosuppressive treatments. In the present study, clinical course of LPD was examined using RA-LPD patient cohort who was followed for more than 1 year (n=188) after LPD onset in 6 Medical University Hospital. Whereas LPD was spontaneously regressed by MTX withdrawal in 94 cases (50.0%), LPD was recurred after spontaneous remission (SR) in 28 cases (14.9%). LPD was treated (e.g., chemotherapy) in 57 cases (30.3%). In 3 cases (1.6%), LPD was stable but not regressed. Unfortunately, 6 cases (3.2%), who should require chemotherapy, were deceased by LPD before treatment. Patient characteristics of SR (n=94) and treatment group (TR, n=57+6=63) groups were examined. RA duration and disease activity at LPD onset were not different between both groups. RA stage and class were high in TR group. Whereas MTX duration and total amount of MTX were not different, MTX dose at LPD onset was higher in SR than in TR group. Deep lymph node and extranodal lesions were frequent in TR group. Diffuse large B cell lymphoma was more frequent in TR, but reactive follicular hyperplasia and EBV-positive mucocutaneous ulcer were more frequent in SR group. In the majority (93.4%) of SR group, LPD lesion was getting smaller during 2 weeks after MTX discontinuation. LPD, however, relapsed in 26.3% of SR group and during 5 years in most cases. In relapsed cases, soluble IL-2 receptor (sIL-2R) at LPD onset was higher than in non-relapse cases. Classical Hodgkin lymphoma was frequent in the relapsed cases. Five-year survival rate of RA-LPD was 78.2% and prognosis of cases with high sIL-2 and LDH at LPD onset was poor. Understanding clinical course of RA-LPD including MTX-associated LPD, which is highly concerned with daily practice, is the important issue in Japan. This is the first report about feature of SR cases with multicenter cohort.

S14-6

Treatment for RA after regression of lymphoproliferative disease in RA patients who were treated with MTX

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Conflict of interest: Yes

Objective In RA, when lymphoproliferative disease (LPD) develops during treatment with MTX, RA treatment after LPD regression is difficult because MTX cannot be resumed. Therefore, it is necessary to clarify what DMARD is recommended after LPD spontaneously regresses or after CR is reached by chemotherapy. Method 232 RA patients who developed LPD between 2000 and March 2017 at 8 hospitals belonging to the LPD working group of JCR. Among patients who resumed RA treatment after LPD regression, risk factors for LPD relapse were analyzed by logistic regression analysis. In addition, the bDMARD-continuation rate in patients after LPD regression was evaluated using Kaplan-Meier curves, and the risk factor for discontinuation was analyzed using the COX proportional hazard model. Results 22 cases (17%) of Regressive-LPD and 19 cases (35%) of Persistent-LPD had relapsed LPD. When pathological diagnosis was DLBCL, 4 of 32 cases of Regressive-LPD and 9 of 29 cases of Persistent-LPD relapsed LPD. In patients with Hodgkin lymphoma (HL) 8 of 12 cases with regressive-LPD and 4 of 8 cases with persistent-LPD relapsed with LPD. Age (under 70 years), sIL-2R ≧ 2300, history of LPD treatment, and HL was shown to be a risk factor for LPD relapse after DMARDs resumed. bDMARDs were used in 61 cases (total 88 cases, TCZ39, ABT20, TNFi 29). The overall one-year continuation rate was 68%. Non-DLBCL, LPD treatment history, high disease activity of RA, non-TCZ, csDMARD non-combination was shown to be a risk of discontinuation of bDMARDs. Conclusion In RA treatment after LPD regression, careful attention should be paid to relapse in patients with LPD regression due to chemotherapy, high sIL-2R at the onset of LPD, and HL. Although bDMARDs contributed to the improvement of RA disease activity, it was shown that the TCZ continuation rate is better than other drugs, and the combined use of csDMARDs other than MTX is desirable, because the high disease activity is an obstacle to continuation.

S15-1

Medical big data research in rheumatology

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Conflict of interest: None

In Japan, various big data initiatives have started, centered on health insurance claims data, and medical big data is being used for the effective utilization of medical resources. If there is no patient refusal, the certified company can collect and anonymize medical institution data and provide these data from May 2018. Medical big data involve NDB, MID-NET, DPC, JMDC, MDV. NDB is the data of almost all insurance medical data in Japan and is comprised of 1.87 billion cases/year of health insurance claims data and 27 million cases/year of Specific Health Checkups and Specific Health Guidance data. However, big data have problems, such as accuracy, validity of disease name, difficulty of data handling, cost of data available and lack of outcome data. Especial, data handling needs the acknowledgment of data science. If the difficulty of data handling was

solved, many researchers will utilize medical bog data. In this lecture, I will talk about medical big data, especially NDB data. Further, I will speak on the research using big data in a collagen disease area, to explain the future of big data research. In April 2018, the Clinical Research Promotion Subcommittee was established in the Japan College of Rheumatology. The mission of this Committee is to promote literacy and clinical research for clinical research by the members to publish higher-quality clinical research from Japan. We are planning to launch seminars, lectures and consulting sessions organized by the Committee in the future, and I would like to inform you about the activities of the Committee.

S15-2

Clinical epidemiology using the NDB: Toward an all-inclusive future

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Conflict of interest: None

Since Fiscal Year 2009, the Ministry of Health, Labour and Welfare has managed a nationwide database of electronic claims from medical institutions authorized to treat patients with public health insurance, the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB). Since Fiscal Year 2011, the NDB has been available for the use of researchers. Because it covers Japan's national health insurance system, researchers can use the NDB to identify all patients who have received medical care through public health insurance and use their data to conduct a wide range of clinical epidemiological research, such as understanding how medical care is actually provided and how effective the treatment would be. However, in the 8 years since researchers have had access to the NDB, only a tiny fraction of clinicians from national research and development agencies and research universities have been able to use the database. In other words, the majority of the clinicians on the front line of medical care have not used the NDB. In addition, although more than 200 applications to use the NDB have been approved, only about 50 academic papers based on the database have been published; i.e., the NDB has been of little use to patients. Establishing a sustainable research system is key to ensuring that more clinicians use the NDB. Specifically, a joint research system needs to be built that includes not only clinicians but a variety of other specialists, including epidemiologists, engineers, and biostatisticians. Universities and medical institutions face particularly high hurdles in hiring engineers solely dedicated to using the NDB. Therefore, fresh ideas are needed, such as providing mid- to long-term training to cultivate professionals with close to engineer-level skills. The NDB is scheduled to be linked to a comprehensive database on long-term care insurance, which will make it possible to investigate such matters as the state of collaboration between medical and long-term care. This promises to create an even richer database. However, the past 8 years have only seen poor research results that are almost useless to patients. We must take this problem seriously if we are to overcome it to create a future where anyone can use the NDB.

S15-3

Further utilization of National Database of Health Insurance Claims and Specific Health Checkups of Japan

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Conflict of interest: None

In 2009, based on Act of Assurance of Medical Care for Elderly People, the Ministry of Health, Labour and Welfare (MHLW) started operating the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB), which accumulates health insurance claims every month and specific checkup data every year. Since 2013, the data of NDB have been open to a third party such as researchers. In the fiscal year 2018, there were 67 offers for the data provision. In addition, since 2016, MHLW publishes NDB Open Data Japan as statistics of healthcare system and specific health checkups in Japan, which was made to be easily comprehensible to the general public. After publishing 1st NDB Open Data Japan in October 2018, MHLW have been enhancing the items in NDB Open Data Japan every year, reflecting requests from the public. Along with these activities, utilization of big data regarding healthcare and long-term care have been discussed on various occasions. The discussion about the connection between public databases, which have been developed recently such as the connection between NDB and comprehensive long-term care insurance database was started in May 2018 and its report was published in November 2018. In the context of the report, the revisions of laws including Act of Assurance of Medical Care for Elderly People, which clarifies the provision of NDB data for a third party including local governments, researchers and private sectors for the purpose of data utilization for public and the data utilization and provision of NDB connected with comprehensive long-term care insurance database, was approved in the diet deliberation. At present, the preparation toward its enforcement has been on going. At this presentation, these approaches toward NDB data utilization will be introduced.

S16-1

Bigdata analyses in autoimmune diseases

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Conflict of interest: None

Next generation sequencing technology has massively provided large amount of omics data in life sciences. Since genetic backgrounds of individuals confer substantial roles in onset of autoimmune diseases, large-scale human genome studies such as genome-wide association studies (GWAS) have been applied. In addition to the case-control association studies to identify disease risk genes, stratified analyses within affected cases have been conducted to elucidate clinical biomarkers and complications. A variety of human omics data is now widely constructed in a tissue-specific way; gene expression (RNA-seq), chromatin immunoprecipitation (ChiP-seq), accessible chromatin (ATAC-seq), metabolome (LC/GC-MS), metagenome (shotgun-seq), and immunophenotype (FACS). Single cell sequencing technologies have successfully explored novel disease-related cell types. Integration of such omics data contributes to understanding of disease pathology. Informatics approaches to interpret omics data have also been developed. By converting omics resources into shared information units, one can indirectly connect omics resources from different samples (i.e., trans-layer omics analysis). Integration of large-scale GWAS results and tissue-specific epigenome data enlightened immune cells related to autoimmune diseases. Application of machine learning methods is a promising approach to understand omics data, including linear, non-linear, and deep learning. One of the final goals of these omics data analysis is implementation of genome-based precision medicine. Polygenic risk score (PRS), which aggregates genetic risk of the genome-wide SNPs, is considered as a powerful tool to estimate individuals' risk on disease. However, to achieve clinically useful prediction for individuals, further tune-up of the PRS methodology is warranted. We would like to report the current progress in the bigdata analyses of autoimmune diseases.

S16-2

Tph cells in human autoimmune diseases

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Conflict of interest: None

Investigations of synovium in rheumatoid arthritis (RA) have revealed immune responses at tertiary lymphoid structures (TLSs), formed in chronic inflammatory sited, play crucial roles in pathogenesis of various autoimmune diseases, in addition to immune reactions at secondary lymphoid organs (SLOs) such as lymph nodes. Follicular helper T cells, expressing chemokine receptor CXCR5, migrate into germinal centers of SLO and exert finely regulated B-cell helper activities with transcription factor BCL6. Human Tfh cells also express characteristic molecules such as PD-1, CXCL13, ICOS, and IL-21, but RA synovium contains a distinct CD4+ T cells expressing these molecules but not CXCR5 or BCL6. Based on the findings that PD-1hiCXCR5-CD4+T cells are also increased in RA

blood and exert B cell helper activities as well as Tfh cells, peripheral helper T (Tph) cells were coined for PD-1hiCXCR5-CD4+T cells as a CD4+ subset exerting B cell helper activities in peripheral tissues. Tph cells are firstly involved in TLS formation via CXCL13, induced by transcription factor Sox4 in response to environmental TGF-β. Subsequently, Tph cells are supposed to exert B-cell helper activities at outside area of lymphoid follicle. Cells that leaked out from inflammatory tissues could be detected as circulating Tph (cTph) cells in the blood. cTph cells correlate with disease activities of several autoimmune diseases such as SLE, IgG4-related diseases, Sjogren syndrome, IgA nephritis and inflammatory bowel diseases. On the other hand, B cell helper activities of Tph cells have been investigated just in RA and SLE. Interestingly, Tph cells are susceptible for inflammatory environment of autoimmune diseases compared to Tfh cells; i.e., IFN-signature genes are enriched in SLE cTph cells, implying Tph cells would exert multiple functions depending inflammatory conditions. Thus, it is expected to figure out further function of Tph cells, a new subset that exert pathogenic roles in peripheral tissues.

S16-3

Cellular and molecular mechanisms underlying the induction of fibrotic responses in the lung

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Conflict of interest: None

The lung has a unique mucosal barrier system that protects the host from the continuous invasion of pathogens. Memory CD4+ T cells are crucial for long-term protection against pathogens in the mucosal tissue. However certain subpopulations of memory Th cells can be pathogenic and drive chronic inflammatory disorders. These memory-type pathogenic Th cells (Tpaths) can be detected in various inflammatory diseases. Our recent research has shed light on the segregation of the pathogenic roles among several subsets of memory-type Tpaths; for example, the IL-5-producing memory-type Tpath subset is critical for the recruitment and differentiation of eosinophils in allergic airway inflammation. Another population of memory-type Tpath2 cells that specifically produces amphiregulin, a ligand for epithelial growth factor (EGF) receptor, is critical for the induction of fibrotic changes in the lung. We also found that these fibrosis-inducing memory-type Tpaths have features of tissue-resident memory T (TRM) cells. Indeed, the CD103lo CD4+ TRM cells were shown to produce effector cytokines and promote fibrotic responses. An assay for transposase-accessible chromatin using sequencing revealed that CD103lo CD4+ TRM cells were epigenetically distinct. To develop new therapeutic strategies for managing intractable allergic diseases, it will be increasingly important to understand the precise features of Tpaths.

S16-4

Insights into the pathogenesis of rheumatoid arthritis from single cell analysis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an autoimmune disease that presents as polyarthritis and subsequent joint destruction. Inflammatory infiltrates as well as the expansion of fibroblasts are the characteristic features in the inflamed synovial tissues, where these cells interact each other to form persistent inflammatory milieu leading to the joint destruction. The advances in high-dimensional technologies in single cell level have revolutionized the study of RA. The analysis of cells in the inflamed synovial tissue as well as the blood in patients with RA using single-cell RNA-sequencing (scRNA-seq) and mass cytometry (CyTOF) have provided comprehensive view of cells that are involved in the pathogenesis of RA. These approaches have identified a variety of novel disease-associated subsets of cells including T peripheral helper cells that help B cells in the inflamed peripheral tissues, synovial fibroblast subsets that have characteristic features of invasive cells and dominant producer of inflammatory cytokines, HBEGF+ inflammatory macrophages that form inflammatory milieu to promote the tissue injury, and arthritis-associated osteoclastogenic macrophages. The Accelerating Medicines Partnership (AMP) RA Consortium have been analyzing the synovial tissues from a variety of patients with RA or osteoarthritis, and generating a large dataset of histology, flow cytometry, CyTOF, bulk RNA-seq and scRNA-seq. The dataset would enable us to classify the patients based on the molecular and cellular characteristics, which would eventually lead to predicting the response to therapies in the individual patients as well as identifying novel drug targets in RA.

S16-5

Functional genome analysis of immune-mediated diseases

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Conflict of interest: Yes

Owing to various recent technological advances, functional genome analysis has become a powerful approach for systemwide analysis of gene expression and protein function using genomic information. Extensive attempts to stratify diseases using functional genome analysis are being carried out all over the world. We constructed a gene expression and eQTL database which consist of >10000 RNA-seq samples from 29 immune cell subsets of >400 donors with 10 immune-mediated diseases (IMDs) and healthy controls. Our data revealed characteristic gene expression signatures across immune cells and IMDs, which largely distinguished autoimmune diseases from autoinflammatory diseases. eQTL analysis showed genetic variants which are associated with gene expressions for more than 60% of protein coding genes in each cell subset, part of which show cell type specific patterns. Some of IMD GWAS variants show colocalization with eQTL variants in an immune cell type specific manner. In SLE, transcriptome analysis revealed not only upregulation of Interferon (IFN) signature but also oxidative phosphorylation (OXPHOS) especially in memory B cells. Notably, OXPHOS, not IFN signature, significantly associated with long term prognosis of SLE. Significant association between several SLE-GWAS risk variants and OXPHOS was identified by Key Driver Genes (KDG) analysis in each immune cell subset by combining GWAS-SNP, transcriptome, eQTL effect, and open chromatin. Consistently, active immunization and imiquimod-induced lupus model in mice deficient for an anti-oxidant enzyme identified in KDG supported a significant role of OXPHOS in lupus pathogenesis. Our results show critical role of functional genome analysis in the identification of disease-related pathways and genes in IMD.

S17-1

Efforts at the University of Tokyo: Utilization of Functional Genome Information at the University of Tokyo Center of Innovation

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Conflict of interest: Yes

At the University of Tokyo, the University of Tokyo Center of Innovation (COI) “Health Society Protected by Oneself” was established as an open innovation platform where all industry, government, academia and stakeholder stakeholders participate equally from the beginning of R & D. The goal is to promote behavioral change through “individualization of health”, and lead to prevention and non-disease response. The University of Tokyo Department of Allergy and Rheumatology has also participated in the University of Tokyo COI and is trying to apply functional genomics to drug discovery, prevention, and non-disease response. In recent years, risk assessment of common diseases using whole genome sequences is becoming practical, and risk assessment combining transcriptome information with genome information may be a more accurate approach. So far, a database of expression quantitative trait locus (eQTL) effects in which gene polymorphisms affect gene expression has been constructed in 105 healthy individuals. We have verified that disease-specific pathways can be identified by combining this with the genotypes of rheumatoid arthritis and healthy individuals. An eQTL database with a larger number of samples than the previous version has been constructed, and this may enable

the identification of specific pathways in various diseases with sufficient genomic information. Such pathways are presumed to be involved in modification prior to the onset of the disease, and can be applied to prevention / non-disease response. In addition, the eQTL database itself reveals which risk polymorphism of the disease affects which gene expression level of which immunocompetent cell, which can be important information in drug discovery. Industry-academia collaboration that uses cutting-edge medical information in this way is considered to be a powerful approach that contributes to future medical development.

S17-2

Activities in Keio University Hospital for new drug development

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Conflict of interest: Yes

1. Support for drug development at Keio University: In 2014, Clinical and Translational Research Center (CTR) was established to facilitate the clinical and translational research. On the basis of CTR, Keio University hospital was approved as Core Clinical Research Hospital in 2016 and carried out the national project for translational research network by MEXT. 2. The case for drug approval by PMDA: Investigator initiated multi-center clinical trials for tocilizumab (8mg/kg, every two weeks) in adult onset still's disease was carried out by Keio University Hospital as a representative site and tocilizumab was approved for adult onset still's disease in 2019 (ARD77:1720, 2018). 3. The case for advanced medicine by MHLW: While hydroxychloroquine (HCQ) is approved for SLE in 2015, there were no plans for clinical trials for RA in Japan. For advanced medicine framework by MHLW, the study plan for HCQ in RA (target number of RA patients=60) at Keio University Hospital was approved in November 2016. At the end of December 2019, the total 60 cases were completed for registration and the results will be open within the year 2020. 4. Longitudinal cohort for systemic rheumatic diseases for clinical information and biomaterial sampling: The study plan for collecting bio-samples such as peripheral blood along with clinical information in individual inception of standard treatment was approved by IRB and the study was carried out. The data obtained was published and open to public as the academic research or joint research with the private sectors. 5. Seeds A/B originated from the seeds search at our cohort: By multi-omics analysis for RA peripheral blood with increased expression, one of the candidates for drug targets would be TIGIT (T cell immunoreceptor with Ig and ITIM domains). It is expressed on the memory T, Tfh, Treg, and NK cells, and inhibits effector T cells, but activates Treg. Thus, we are now developing new treatment focusing on TIGIT on the surface of T cells in systemic autoimmune diseases including RA.

S17-3

Development of new medicines for arthritis based on glycobiology

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Conflict of interest: None

Carbohydrate chain is well known as the important molecule in extra-cellular matrix. However, its overall function in vivo has not been established so far. We believe that the application of carbohydrate chain to development of novel medicine is a promising field. We have been continued to study the arthritis pleiotropically based on glycobiology. High molecular-weight hyaluronan (HA) has a repeated disaccharide structure. HA has been clinically used for the osteoarthritis (OA) and rheumatoid arthritis (RA) patients in daily clinical practice. However, the biological function of HA has not been fully understood yet. We demonstrated that HA can suppress the cartilage degradation induced by mechanical stress or cytokines via the association with its primary receptor CD44. Siglec-9 is an inhibitory receptor of the family that is expressed on a broad range of immune cells of both lymphoid and myeloid origin. Soluble siglec-9 has inhibitory effect on the collagen induced arthritis mice model. Carbohydrate chain has important function in modification of autoantibody. Administration of ACPA induced the development of arthritis in mice but the sialic acid supplemented ACPA did not. Sialic acid supplemented ACPA significantly suppressed the arthritis in collagen induced arthritis mice model. Carbohydrate metabolism has been focused in various diseases. Glycolysis is reported to be increased in OA and RA. We demonstrated that inhibition of glycolysis significantly suppressed the cartilage degradation induced by cytokines. To control the carbohydrate, carbohydrate chain, and carbohydrate metabolism would have the power to regulate pathology of various diseases. However, development of seeds based on glycobiology would be unsuitable for commercial enterprises because the behavior of carbohydrate is sometimes vagary. We will continue to study the glycobiology to develop novel seeds as a role of academia.

S17-4

Initiatives at Kyoto University -Stratification of SLE patients and search for new treatment targets by multifaceted approach-

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Conflict of interest: Yes

Initiatives at Kyoto University -Multilevel approach to stratification of SLE patients and search for new treatment targets- Treatment of systemic lupus erythematosus (SLE), a representative autoimmune disease, is still centered on steroids and classical immunosuppressive drugs, and is still far from a paradigm shift in therapies such as molecular targeted drugs for rheumatoid arthritis. One of the causes is the heterogeneity of SLE pathogenesis, which is due to not only the severity of each patient but also the organs affected, autoantibodies, and cytokine environment. Rather than treating SLE as a whole, attempts have been made to classify SLE into several subgroups, but this has not been successful. In Kyoto University, in addition to the genomic analysis performed so far, the serum and plasma cytokine profiles and the transcriptome of peripheral blood, and the immune cell profile before and after treatment of SLE patients have been analyzed. Attempts to stratify SLE patients have been made from the perspective of what are the most important cells, molecules, or molecular pathways. In SLE, the involvement of type I interferon has attracted attention, but more than half of patients have normal serum IFNα level, and some of these patients have extremely high levels of IL-1β and IL-6. On the other hand, there are many cases where IFNγ is considered to be the main driver. The molecular target unrelated to IFN signature is also searched using the transcriptome of peripheral blood, and several candidate molecules are under consideration. While looking at the direction of aiming for additional indications of off-label approved drugs such as anti-B cell therapy, anti-T cell therapy, anti-cytokine therapy (IL-1β, IL-6, IL-12 / 23, IL-17, GM-CSF etc), JAK inhibitor and also the direction of aiming for completely new therapeutic drugs, we are first trying to grasp the pathophysiology of individual patients and classify patients according to therapeutic drugs.

S17-5

Efforts of Tohoku University

Tomonori Ishii
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Conflict of interest: Yes

In the last 20 years, with the advances in techniques to develop new drugs, many molecular targeted drugs have been developed, and the field of autoimmune diseases, such as rheumatoid arthritis and connective tissue disease, has been most benefited by the development of these drugs. However, because company-sponsored clinical trials inevitably require strategies that will profit companies, little progress has been made in necessary development in many areas of actual clinical practice. For this reason, in the field of rheumatoid arthritis and connective tissue disease, the use of drugs not covered by health insurance is quite often necessary for treating current patients. On the other hand, there are several systems allowing the use of unapproved and unindicated drugs in research. The available systems for conducting clinical trials include the company-sponsored clinical trial, investigator-initiated clinical trial, and extended clinical trial that is a recently added new option of the system. In addition to

these systems, clinical trials are conducted in accordance with the Japanese Advanced Medical Care B program, Patient-proposed Health Services, and Clinical Trials Act. Through these systems, mainly academia is required to conduct clinical trials to incorporate, into actual clinical practice, unapproved and unindicated drugs and medical devices that are incompatible with corporate strategies but required in clinical practice. Tohoku University Hospital has established the Clinical Research, Innovation and Education Center, which plays a role in promoting development of drugs and medical devices and transforming development projects into actual clinical trials, and the Clinical Research Administration Center, which guarantees that trials will be conducted without any problems. At our hospital, the School of Engineering and other schools of Tohoku University are involved in the early development phase for clinical application of seeds developed by them. We present actual examples of the specified clinical trials and investigator-initiated clinical trials that were conducted through these functions at our hospital on drugs and medical devices which were not approved or indicated for rheumatoid arthritis or connective tissue disease.

S18-1

NinJa (National Database of Rheumatic Diseases in Japan)

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Conflict of interest: Yes

Treatment for rheumatoid arthritis (RA) has made significant progress and the prognosis of RA patients has improved significantly overt the past 20 years. However, before launch of biologics, there was no system that could conduct a large-scale survey on the actual situation of RA treatment, monitor and verify the trend in Japan. In 2000, Tokyo Women's Medical University started J-ARAMIS (currently IORRA), which was the beginning of the large-scale RA database in Japan. Two years later, in 2002, to aim to "clarify the current situation and problems of RA patients in Japan continuously", we started the nationwide RA database: NinJa (National Database of Rheumatic Diseases by iR-net in Japan). The most important things for NinJa was "Continuity". Only core information was collected once a year. Initially, 12 facilities (including one outside NHO) and 2800 cases were registered, but the number of participating facilities expanded beyond the National Hospital Organization (NHO), and 29 prefectures from Hokkaido to Okinawa 49 facilities (20 NHO facilities, 12 universities, other community hospitals, clinics) participated in 2018 (NinJa 2018). Over the last five years, more than 15,000 cases have been collected every year, and information has been transmitted as the largest RA database covering 2-3% of RA patients in Japan. NinJa's strengths include the fact that many large and small facilities from all over the country are participating, and the registration is independent of the patient's background such as treatment content and age, but on the other hand, the amount of information collected is limited. In this lecture, I will introduce "Transition and present status of RA treatment in Japan", various analysis results, recent trends of NinJa, future issues of RA treatment that can be read from NinJa. Furthermore, I would like to think about the role that NinJa should play in the future.

S18-2

Importance of Cohort Study in Rheumatoid Arthritis in Japan -Based on the IORRA Cohort

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Conflict of interest: None

The management of rheumatoid arthritis (RA) has been dramatically improved with the introduction of new DMARDs and biologics. There was a significant change in the goal of treatment, from short-term to long-term improvement in quality of life during the past decade, with the fact that achieving "remission" or "low disease activity state" is a realistic therapeutic goal nowadays based on these recent developments in RA treatment. However, it is extremely difficult to quantitatively evaluate such changes in daily practice. The results from randomized controlled trials (RCT) are considered to have a higher evidence level, however, we should be aware that RCTs include strict selection criteria, thus, the patients registered into RCT are usually selected patients but not the representative of patients in daily practice. Furthermore, it is hard to evaluate long-term outcomes in patients with RA using RCT since RA is a chronic disease. Therefore, to understand what is going on in real world, the importance of the observation cohort study that verifies a long-term outcome and safety is emphasized. There was no prospective observational cohort study in Japan until the establishment of the IORRA (Institute of Rheumatology Rheumatoid Arthritis) study. Twenty years have passed since IORRA study was launched in our institute. By accumulating information from approximately 4-5,000 RA patients using patient self-report questionnaire biannually, analysis has conducted to find the way for the better outcome of patients, and many scientific papers have been published. The concept of IORRA is transplanted into all post-marketing surveillance (PMS studies) of biologics, and the IORRA stimulated the establishment of other registry studies of RA in Japan, indicating that importance of cohort study in rheumatology has become greater and greater. In this session, IORRA system, the evidences produced through the IORRA cohort and future plan will be discussed.

S18-3

Safety of biologics in Japanese patients with rheumatoid arthritis: achievements of the REAL study

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Conflict of interest: Yes

The registry of Japanese rheumatoid arthritis (RA) patients on biologics for long-term safety (REAL) is a prospective cohort established to investigate the long-term safety of biological DMARDs (bDMARDs) in RA patients. Enrollment in the REAL database was started in June 2005 and closed in January 2012. Twenty-seven institutions participated in the REAL, and over 2,000 patients were registered. The criteria for enrollment were patients meeting the 1987 American College of Rheumatology criteria for RA, written informed consent, and starting or switching treatment with a bDMARD or starting, adding or switching a csDMARD at the time of enrollment in the study. Main recorded baseline data for each patient included demography, disease activity, comorbidities, treatments, and laboratory data. In addition, follow-up data were submitted every 6 months to the REAL Data Center to report the occurrence of serious adverse event (SAE), current RA disease activity, treatments, and laboratory data. We have published articles using the REAL database as follows; 1. Risk of serious infection (SI) under the treatments with high dose of methotrexate 2. Incidence and risk factors for SI under the treatments with tumor necrosis factor inhibitors (TNFI) in 1 year 3. Incidence and risk factors for SI under the continuous treatments with TNFI over 3 years 4. Drug retention rates and factors associated with drug discontinuation of bDMARDs 5. Comparison of incidence and risk factors for SAE between Japan and Korea 6. Change of risk for SI over time under the treatments with TNFI 7. Risk of herpes zoster 8. Comparison of safety of tocilizumab and TNFI Clinically important evidence had been generated from the REAL database along with emergence of the paradigm shift of RA treatments, when revealing safety of bDMARDs in clinical settings in Japan was one of the most urgent tasks. In this symposium, we will review above studies, and discuss clinical epidemiological research in rheumatology in the future.

S18-4

Kyushu Multicenter Rheumatoid Arthritis Ultrasound Prospective Cohort in Japan

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Conflict of interest: None

Musculoskeletal ultrasound (MSUS) is excellent in the detection of synovitis in patients with rheumatoid arthritis (RA) and the synovitis score well reflects the clinical disease activity [1]. We have been promoting the cohort study for RA patients introduced molecular targeted therapeutic drugs (biologic DMARDs or JAK inhibitors) in collaboration with multi-center in Kyushu region from 2013 [Kyushu Multicenter Rheumatoid Arthritis Ultrasound Prospective Cohort in Japan: UMIN 000012524] [2-3]. In this study, we have evaluated disease activity every 3 months by MSUS, and have analyzed associations between MSUS score, clinical disease activity, radiographic change, and serum biomarkers. In this study, we investigated the relationship between MSUS score, clinical disease activity, radiographic change, and serum levels of biomarkers, focusing on assessment of synovitis every 3 months by MSUS. The strength of this study is that a highly objective outcome can be obtained due to MSUS assessment. As of August 2019, 379 cases have been entered. Although multi-center clinical study using MSUS assessment is rare in the world, standardization of MSUS evaluation is indispensable. Introducing the standardization of MSUS evaluation in this study. Regarding serum biomarker analysis, comprehensive analysis of cytokines and chemokines using a multi-suspension array and autoantibody isotype analysis in collaboration with Professor Huizinga at Leiden University have been performed. Factors associated with the therapeutic response of synovitis detected by MSUS and the differences between the drugs have become clear. In the future, it may be possible to use different drugs according to patient conditions by accumulating cases and integrating multiple evaluations. This symposium outlines the results and future developments of this cohort study. 1) Kawashiri SY, et al. Rheumatology (Oxford). 2011;50:962. 2) Nishino A, Kawashiri SY, et al. Arthritis Care Res (Hoboken). 2018;70:1719. 3) Endo Y, Koga K, Kawashiri SY, et al. Scand J Rheumatol. 2019 in press.

S18-5

ANSWER (Kansai Consortium for well-being of rheumatic disease patients) Cohort -Past and Future-

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Conflict of interest: Yes

The importance of observational studies including patients who are not suitable for randomized control study (such as aged or with complications) is well recognized. We established the Kansai Consortium for Well-being of Rheumatic Disease Patients (ANSWER) cohort, including seven institutes (Kyoto University, Osaka University, Osaka Medical College, Kansai Medical University, Kobe University, Nara Medial University, and Osaka Red Cross Hospital) in 2016. It is a multicenter registry of rheumatic disease patients in the Kansai district of Japan, including both rheumatologist and orthopaedics. Recently, we established general incorporated association called ANSWER Cohort Consortium in 2019, to further promote clinical studies. We would like to present the history, present activities, and future plan of this cohort in this symposium.

S18-6

Clinical research of rheumatoid arthritis in clinical practice - For better treatment of rheumatoid arthritis-

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Conflict of interest: Yes

Treatment of rheumatoid arthritis has made great progress over the last 20 years with methotrexate and molecular targeted therapies (biologics, JAK inhibitors). The effects of new therapeutics have been verified at a high level of evidence. Based on these, treatment guidelines and recommendations have been made from Europe, the United States and Japan. Both interventional and observational research should be indispensable in promoting clinical research. In clinical trials with a high grade of evidence, there is a major limitation that enrolled patients were strictly selected. In the observational study, many institutions and doctors participate, and the results of the treatment in various real clinical cases give a lot of information including the safety and long-term effectiveness. As an observational study, we have been conducting a cohort of patients treated with biologics and JAK inhibitors, named Tsurumai Biologics Communication Registry (TBCR) since 2008, and there are currently about 3,500 cases registered. In addition, we conduct a cohort to identify prognostic predictors in patients with early-onset RA, Nationwide Incentive Cohort of Early Rheumatoid Arthritis in Japan (NICER-J) (funded by Eli Lilly Japan as a doctor-led study; about 200 early RA patients are currently registered). As a doctor-led intervention stud (funding from Chugai), we examined the effect of reducing the dose of methotrexate in the treatment of tocilizumab on maintaining the therapeutic effect of tocilizumab (T-ReX study). Actually, we believe these our researches have provided a great deal of information. We have to conduct more clinical research properly based on real world clinical question.

S19-1

Current status of Surgical treatment for rheumatoid hand

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Conflict of interest: None

Recent trend of surgical treatment for rheumatoid arthritis in japan is characterized by increasing incidence of hand and foot surgeries. The current feature of foot surgeries are the joint preservation procedures, especially for forefoot deformities. Recostruction of tendon or ligament without resection of joint surface have been applied also for the finger deformity of RA. 32 joints were preserved after surgical intervention in recently treated 108 joints. We investigated the patient's satisfaction for surgeries for fingers (41 cases) and forefoot (70cases) with rheumatoid arthritis. The mean satisfaction scores of finger surgeries are 7.2 (total satisfaction), 8.2 (appearance), 6.9 (function) and 8.1 (pain relief) out of ten points. The major procedure for rheumatoid hand is MCP joint arthroplasty with silicon spacers. We performed a systematic review for the silicon arthroplasty for MCP joints reported after 1999 and found that improving range of motion, pain relief and correction of ulnar deformity could be expected. However, we still have non-negligible rate of the implant fracture (2.9-62.5%). We had been performed MCP joint arthroplasties with SWANSON prosthesis before. AVANTA prosthesis was applied in expectation of improved flexion range of motion. Previously, we had reported improved flexion arc using AVANTA. But we still have experienced some cases with insufficient flexion range in their little fingers. Therefore we have used pre-flexed type of AVANTA for only little fingers in all cases recently. Significantly better flexion range was observed in AVANTA preflex group than that of AVANTA straight group. On the other hand, we found seventeen implant fractures (8.3%) in 205 joints during the mean 4.5 years postoperative period. Patient's expectation for the functional or cosmetic results of hand surgeries should be higher in cases under better disease control. Further improvement of procedures or prosthesis is necessary to meet their demand.

S19-2

Pathology and treatment of the rheumatoid forefoot deformity

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Conflict of interest: None

Dramatic improvement in disease activity control due to the development of powerful disease-modifying anti-rheumatic drugs has significantly changed the therapeutic strategy for joint involvements in rheumatoid arthritis (RA) patients. Especially, decreased involvements of large joints in lower limbs have come to shed light on the magnitude of functional

impairment by foot deformity and wide-ranging needs for resolution of foot trouble. Potential high needs of treatment for foot deformities are now appearing as the gradual increase of numbers for foot surgeries in some data base studies. In particular, toe arthroplasty is one of the major forms among the surgeries for foot, and the surgical method is also changing from resection arthroplasty to joint-preserving arthroplasty. In general, some important precautions should be reminded when applying procedures to RA patients as follows: 1) the preservation of joint is possible or not, 2) the disease control status, 3) laxity of the joint. In addition to these points, the presence or absence of mid or hind-foot deformities has an impact on treatment decision making for RA forefoot deformities. Flatfoot is a secondary major form of RA foot deformity after the forefoot deformity; however, both deformities exist together and interact with each other in most of the cases. Recurrent deformity could happen after forefoot surgery when mid- or hindfoot deformity remains or progresses afterwards. Conversely, there could be some cases of spontaneous correction of forefoot deformity after the mid- or hindfoot deformity correction. Although the hallux deformity in coronal plane such as hallux valgus tends to be paid attention to, it should be reminded that the hallux has some deformities in the sagittal plane accompanied with the flatfoot deformity. It is essential to overlook the whole foot or even the whole limb but not focus on the limited area of forefoot for constructing treatment strategies of RA forefoot deformity.

S19-3

The Appearance of Similarity-or Actual Similarity? Rheumatoid Hand and Foot Surgeries: Wrist Joint

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Conflict of interest: None

Some five to six million years ago, an animal considered a member of the human subfamily-a large-brained primate that could easily become bipedal-walked the earth, as a direct ancestor to humans. The ankle and wrist joints had undergone substantial functional and morphological changes until that point. Since the wrist joint is not a load-bearing joint, great muscular strength for movement and bearing weight is not needed. However, stability is more important than mobility for the wrist to get a sufficient grip power. The wrist is a “keystone” of hand function supplemented by the motion of palmar/ dorsi flexion and radial/ ulnar flexion. Also, it is associated with direction adjustment function by the forearm rotation in conjunction with the elbow joint. In the arthritic wrist joints, synovitis causes loosening and tearing of soft tissues, such as ligaments, and dorsal subluxation of the ulnar head at the distal radioulnar joint occurs. Radial rotation, ulnar shift, volar subluxation and supination of the carpal bones and scapholunate dissociation occur at the radiocarpal joint. In contrast, however, the mid-carpal joint is not easily deformed. In functional reconstruction of the wrist joint, malalignment (deformity) is corrected along with synovectomy. We herein present the anatomical differences between the wrist and the ankle as well as differences in function, operative procedure and target setting by addeing reference to the literatures.

S19-4

Ankle

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Conflict of interest: Yes

The hindfoot consists of the ankle joint (talar joint), the posterior subtalar joint (posterior talocalcaneal joint), and the anterior subtalar joint (talonavicular joint, anterior – and middle talocalcaneal joint). These joints support the weight and perform complex movements such as dorsi-/plantarflexion, inward/outward movements, and inversion/eversion around talus as a bearing ball. The ankle mortise, in which the talus is surrounded by the tibial plafond, the medial and lateral malleolus, has bony stability, and the main movement is sagittal dorsi-/plantarflexion. The range of motion is limited to approximately about 70-80 ° due to the impingement of the tibia and talus. We have performed total ankle arthroplasty (TAA) using TNK Ankle, a two-component prosthesis for end-stage arthropathy of the talocrural joint. Unlike the talocrural joints, TNK Ankle is a semi-constrained type constraint, in which the radius of curvature of the talar component surface is slightly smaller than that of the tibial component surface. Consequently, as a result, the degree of freedom is maintained in the appropriate longitudinal direction and during rotation, and the eccentricity of the center of rotation of both components is allowed. The tibial prosthesis coated with calcium phosphate paste and bone marrow obtained by puncture of the iliac bone was fixed to the posterior cortex of the tibia using a small screw, and the talar prosthesis was fixed with cement since 1991 and acceptable clinical results were obtained.

S19-5

Surgery for the Rheumatoid Hand

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Conflict of interest: None

Surgeries of the rheumatoid hand are classified into synovectomy of joints and / or tendons, reconstruction of ruptured tendons, and correction of finger / wrist deformity secondary to joint destruction and / or attenuation of the ligament. In order to obtain best results, not only accurate surgical technique but also prehension of the rheumatoid activity, through meticulous evaluation of the hand, and demand of the patients in the ADL are necessary. In most of cases, we should consider not only evaluation of the hand but also elbow and shoulder. Corrective surgery should not be planned with comparison to the normal hands because the affected hand has already accepted gradually progressed deformity in patients daily life. In the wrist joint, excision of the ulnar head to make synovectomy easier is questioned by some because of possible carpal ulnar translation and unstable a proximal stump of the ulna. So I usually choose a Sauve-Kapandji procedure, which is arthrodesis of DRUJ (distal radio-ulnar joint). In the MP joint, when the joint destruction is minimal, synovectomy is indicated. After gross dislocation and destruction, resection arthroplasty is indicated when the patient does not want implant arthroplasty but the ROM gains are not predictable. There are mainly two types of finger deformity; one is swan-neck deformity, hyperextension of the PIP joint, and flexion of the DIP joint, and the other is boutonniere deformity, vice versa. The former can occur from either hyperextension of the PIP joint or MP joint volar subluxation. The latter can occur mainly from PIP synovitis attenuating dorsal extensor mechanism. To treat this, pathology and condition of each joint should be well understood. To treat extensor rupture in the dorsal wrist, either tendon graft or tendon transfer is chosen. In my preference, tendon transfer produces better results. Whichever one should choose, one should bear in mind not to create extension contracture of the MP joint due to the negligence.

S19-6

Surgical strategy considering tendon’s tension for rheumatoid forefoot deformity

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Conflict of interest: None

Techniques for rheumatoid forefoot surgery have changed in the past decade. Recently, joint-preserving surgeries for rheumatoid forefoot deformities have become popular gradually. Osteotomies of the metatarsal bones are performed to correct deformities during the surgery. Especially for the dorsal displacement of the lesser toes, metatarsal bones are shortened to reposition the displaced toes. However, we consider the decrease in tendon tension after metatarsal shortening as one of the reasons for the development of postoperative rigid toes. We constructed a surgical algorithm considering tendon tension and used it to decide the surgical procedures. The main goal of this algorithm is to form a smooth arc of the metatarsal heads, which makes the second metatarsal head the longest, followed by the first, third, fourth, and fifth metatarsal heads. We decide the surgical procedures depending on the case, on the basis of this algorithm. We perform proximal rotational closing-wedge osteotomy of the first metatarsal

for rheumatoid hallux deformities. As the angle of the wedge depends on the intermetatarsal angle, the postoperative first and second metatarsals locate in parallel. As a result, we can measure the theorical gap between the first and second metatarsal heads preoperatively. We previously showed that callosities often occur on the plantar when the gap is >4.5 mm. On the basis of our results, we perform extensor tendon lengthening to reposition lesser dislocations rather than metatarsal bone shortening when the theorical gap is <4.5 mm. However, techniques without bone shortening may lead to complications such as recurrence of the deformity, delayed wound healing, or circulation disorder of the toe. In this session, I am going to present the details of our surgical strategy for rheumatoid forefoot deformity and discuss the clinical and radiographic outcomes.

S20-1

Physical function of RA patients from viewpoint of locomotive syndrome and movement speed

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Conflict of interest: None

Japan has a rapidly aging population, and elderly rheumatoid arthritis (RA) patients are also a social problem. RA is one of the causative diseases of locomotive syndrome (LS). LS is a high-risk condition that requires caregiving due to musculoskeletal disorders. RA is susceptible to become LS because it can cause physical disability due to rapid destruction of bones and joint structure. Therefore, it is an urgent task to evaluate the physical function of RA patients and intervene properly in order to prevent LS. The Health Assessment Questionnaire (HAQ) is used as a conventional physical function assessment tool for RA patients. The 25-question Geriatric Locomotive Function Scale (GLFS-25) is useful in evaluating the physical function of RA patients. We investigated that GLFS-25 corresponding to functional remission (HAQ remission, HAQ 0.5 or less) was 20 points, which was higher than 16 points of GLFS-25 defined as LS. In other words, RA patients who achieved functional remission may be LS. On the other hand, movement speed (gait speed) is one of the diagnostic criteria for sarcopenia and frail. Timed Up & Go test (TUG) is a physical function evaluation method. It is a useful and simple evaluation method because it can evaluate complex physical functions such as lower limb muscle strength and balance and does not require special equipment. We conducted a multicenter cohort study to register RA patients undergoing surgery as a study from the Ministry of Health, Labor and Welfare. Using TUG, the effect of lower limb joint surgery was examined. The goal of TUG for lower limb surgery was 9 seconds, and the cut-off value for TUG as the timing of surgery was 12 seconds. By setting the goal in this way, it is easy to share information with patients and other medical staff. From the above, in evaluating the physical function of RA patients, as an orthopedic rheumatologist, it is essential to stand from the viewpoint of LS and movement speed.

S20-2

Physical function in patients with rheumatoid arthritis -Focusing on sarcopenia-

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Conflict of interest: Yes

Recently, sarcopenia, flail, and locomotive syndrome are being focused for evaluation of body condition and function for extending healthy life expectancy. Sarcopenia is a syndrome in which muscle loss is linked to functional loss, resulting in physical disability. Previous reports have showed that sarcopenia-associated risk factors involve diet, confinement to bed or sedentary lifestyles, and chronic diseases. RA presents risk factors for sarcopenia development. In our study, the prevalence rate of sarcopenia was 29.6%. Age, BMI, CRP, and hip BMD were significantly associated with the development of sarcopenia. We found that patients with HAQ-DI ≦ 0.5 had significantly different values among these 3 age groups. In contrast, patients with HAQ-DI > 0.5 showed no significant difference among 3 age groups by age. Therefore, we concluded that HAQ-DI was not associated with sarcopenia. However, it is necessary to monitor sarcopenia in patients with functional remission. The relative skeletal muscle mass index was significantly correlated with grip strength. The Japanese Orthopaedic Association has proposed the term "locomotive syndrome" to designate a condition that places a person at high risk for requiring support, nursing care or/and long-term care. In our study, elderly patients with RA have a greater need to suppress joint damage compared to younger patients with RA. The main goals in RA treatment involve the control of inflammation and suppression of joint damage. Moreover, we are now taking physical function into greater consideration than ever before.> Advances in drug therapy have led to an improved control of inflammation. However, maintaining muscle mass requires support from various aspects because of the related aging and improvement of mortality of patients with RA. Hence, rheumatologists should focus and evaluate RA patients' physical functions to increase their healthy life expectancy and reduce their need for care and support.

S20-3

To develop and maintain the function of lower extremity in RA 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 of lower extremity by destruction or deformity could not be 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.

S20-4

Treat-to-target strategy for elderly rheumatoid arthritis and impact of chronic lung diseases and chronic kidney disease on treatment outcomes

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Conflict of interest: Yes

The prevalence rate of elderly RA increases in line with the increasing life expectancy, and the age of onset also shifted to elderly side. Management of chronic lung diseases and chronic kidney disease is important for elderly RA in clinical practice. Comorbidities and adverse events (AEs) after start of the treatment are more common in elderly population than in non-elderly population, and cumulative burden of comorbidities may influence the outcomes of elderly patients. Previous studies showed patients with interstitial ling disease (ILD) were older, and had a higher mortality rate than patients without ILD. Especially, UIP pattern was associated with a higher mortality risk compared to other patterns of RA-ILD. The cause of death was pneumonia, acute exacerbation of ILD and lung cancer. Interestingly, previous prospective study showed active articular RA was associated with an increased risk of developing RA-ILD. Chronic lung disease including ILD increased the risk of serious infections in patients with RA, but low diseases activity or remission should be achieved to prevent progression of ILD. Previous cohort studies showed patients with RA had more chronic kidney disease (CKD) than patients without RA. Renal dysfunction decreased with aging, and about 40 % of elderly RA patients had

CKD. CKD was associated with serious infection. Progression of CKD due to drug-related damage or nephrosclerosis was common in elderly RA, and dose adjustment of MTX should be needed. Our previous prospective study (CRANE) showed that achieving low disease activity (LDA) and structural and functional remission were realistic goals for patients with elderly-onset RA. About 80% of the patients achieved LDA and 50% clinical remission. We focused impact of ILD and CKD on treatment outcomes in elderly patients. We also show clinical features of patients aged 75 years and more, using the data of CRANE cohort and NinJa cohort.

S20-5

Osteoporosis in patients with rheumatoid arthritis and its long-term treatment strategy

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Conflict of interest: Yes

General status of patients with rheumatoid arthritis (RA) has been improved due to improvement of medication to treat RA. However, we face to novel problems and one of them is a problem due to aging of RA patients. Aging increases the rate of dementia, osteoarthritis, and so on. Osteoporosis (OP) is representative disease due to aging. Arthritis and joint damage due to RA decreases physical functions and OP also decreases physical functions due to fragility fracture. That is why we have to treat both RA and OP together. OP in RA patients has complex pathology derived from not only postmenopausal status but activation of osteoclast due to inflammatory cytokines, disuse due to joint pain and concomitantly-used glucocorticoids. We aim to treat RA early and to reach remission according to treat to target strategy and also to evaluate OP as early as posiible. RA patients with OP should be treated properly. Information of past fracture, familial history of fracture of proximal femur, X-ray photos of thoracic and lumbar spine and measurement of bone mineral density (BMD) at lumbar spine, tpotal hip and femoral neck are necessary at least to diagnose and evaluate OP. We suggest meal guidance, living guidance and follow-up in patients with osteopenia. Anti-resorptive drugs such as bisphosphonate and denosumab with activated vitamin D3 are prescribed in patients with OP. Teriparatide or Romosozumab is use in patients with OP at high risk of fracture. One of the important things is evaluate BMD and fragility fracture using DEXA and X-ray of spine and evaluate the efficacy of medication of OP. Alyhough we often continue same drugs for OP for two years except for occurence of adverse event, change of medication is proposed to patients if not effiective. Goal-directed treatment has been proposed from ASBMR-NOF. If treatment goal is set using BMD (T-score>-2.5), it should be reached within 3 to 5 years. Effective strategy of sequential therapy in OP medication is most necessary.

S20-6

Do anti-rheumatic drugs improve sarcopenia in rheumatoid arthritis patients?

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Conflict of interest: Yes

Rheumatoid arthritis (RA) patients have increased risk of sarcopenia due to inflammatory cytokines such as TNF or IL-6. TNF has a direct catabolic effect on muscle by impairing protein synthesis. IL-6 acts directly on skeletal muscle and inhibits the anabolic activities of IGF1. TNF and IL-6 also reduce IGF-1 concentration in the body. Thus, bDMARDs which directly inhibits these inflammatory cytokines may have an effect to inhibit sarcopenia. Also, recent studies identified that JAK-STAT signaling is involved with the loss of regenerative capacity of muscle satellite cells. Therefore, JAK inhibitor also could be useful to reduce sarcopenia. Glucocorticoid could also reduce sarcopenia by inhibiting inflammatory cytokines if it was used in short term for RA patients with high disease activity. On the other hand, however, glucocorticoid has a direct catabolic effect on muscles (steroid myopathy), therefore the long term use of glucocorticoid may lead to the progression of sarcopenia. Indeed, the ANSWER cohort study revealed that glucocorticoid transiently improve health assessment questionnaire (HAQ) in a short term but progressively deteriorate HAQ if it was used for the long term. Thus, treatment strategy to achieve remission by bDMARDs or JAK inhibitor and reduce the use of glucocorticoid may contribute to extending healthy life expectancy. However, the “real world” evidence to support these hypotheses is still lacking and more clinical researches on the association between RA and sarcopenia is needed.

Educational Lecture

EL1

Skin manifestation of rheumatic diseases

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Conflict of interest: None

Rheumatic diseases are characterized by tenderness of joints, muscles, and bones. Those patients with rheumatic diseases, showing skin eruption visit dermatologist. An internal medicine doctor or orthopedic surgeon would try to diagnose the patients from examining the arthritis, however, we dermatologists would try to diagnose the patients mainly from the skin rash. The major skin diseases with arthritis include collagen diseases such as systemic lupus erythematosus, systemic sclerosis, dermatomyositis, Sjögren's syndrome, and vasculitis such as IgA vasculitis or periarteritis nodosa, and others such as adult-onset Still's diseases, psoriatic arthritis and pustulotic arthro-osteitis. There are many diseases, which are included in this category. Here, rheumatic diseases, which are frequently seen in dermatology clinic would be covered.

EL2

Reproductive issues in Rheumatic disorders among patients of childbearing age

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Conflict of interest: None

Due to recent advancements in treatment, more women who suffer from connective tissue and rheumatic diseases could have a chance to become pregnant and deliver their health babies. Pregnancy and child-rearing are major processses of life that nurtures new generation in their body. At the same time, it is an irreplaceable experience that spurs emotional and physical growth. Men also experience a great deal of joy and growth from becoming fathers. Pregnancy or childbirth in patients with connective tissue and rheumatic disease is an inevitable and important theme in the present time in which medical treatment not only seeks to treat disease but also to improve QOL. Since 2016, guidelines on the management of rheumatic and connective tissue disease during pregnancy have been published in Europe and Japan. In 2018, contraindications during pregnancy on three kinds of immunosuppressants were lifted in Japan. Over the past few years, men and women suffering from connective tissue disease have become able to control their condition, and this has increased the possibility of delivering a healthy baby. The following four points are listed in the European and US consensus papers as "principles for the management of patients with rheumatic diseases at childbearing age". The first point is preconception care. This includes the assessment for the effects of pregnancy on primary disease activity and the effects of the disease on pregnancy outcome. It also includes teaching birth control when taking teratogenic drugs and sharing accurate information with patients about drugs that should be immediately terminated after pregnancy. The second point is the clarification of "treatment goals during pregnancy." High maternal disease activity during pregnancy could lead to obstetric complications such as premature birth and fetal growth restriction. Appropriate drug treatment is necessary to control disease activities. The third point is an objective risk assessment of drug use during pregnancy. Finally, it is advisable to select a drug based on agreement between the physician, patient, family, and related medical staff. It is anticipated that the management of patients with rheumatic diseases during reproductive age will be carried out with these principles in mind.

EL3

Treatment of gout

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Conflict of interest: None

Clinical manifestation of gout is characterized by acute monoarthritis, however, the main pathogenesis is persistent deposition of monosodium urate crystals inside the joint. In 2008, Becker MA et al discussed the management of gout management. They pointed that "paucity of management guidelines", "incomplete patient education about gout and the aims and modalities of management", "suboptimal patient adherence" and "limited urate lowering alternative" were the obstacles to pursue better management (Becker MA, Chohan S. Curr Opin Rheumatol. 2008;2:167). Since then, guidelines and recommendations of gout has been published in many countries and areas. The life styles including dietary pattern to affect the development of gout has been revealed by the prospective epidemiological studies in a large scale. Introduction of new imaging modalities as ultrasonography and dual-energy CT provide the useful information of pathology in gout. New drugs to suppress xanthine oxidoreductase and uricosurics have been developed. These progresses in gout contribute to the better management of gout.

EL4

Self-achievement of joint assessment with musculoskeletal ultrasound

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Conflict of interest: None

Joint assessment is the most important and specific aspect in management of inflammatory arthritis. "Arthritis" usually represents joint synovitis, whereas it is important to distinguish with other synovial pathology such as tenosynovitis and bursitis, extrasynovial inflammation including enthesitis, and degenerative change (with or without mild inflammation) for the measurement of precise disease activity. Musculoskeltal ultrasound enables detection and localization of inflammation and structural damage and occasionally disease-specific findings in non-invasive and real-time manner. It is useful for the physicians' achievement in clinical joint assessment skill to compare clinical and ultrasound findings. Tips and limitation of clinical assessment are to be introduced.

EL5

Rehabilitation for rheumatoid arthritis patients

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Conflict of interest: None

The result of progression in RA treatment, the aim for RA treatment becomes not only decrease disease activity and also ADL improvement. Many RA patients have less joint inflammation by biologics, however, biologics cannot improve contracture and muscle weakness, therefore, we need rehabilitation therapy to improve them. In addition, splint and orthosis is useful for joint protection and deformity in RA patients. In this lecture, I will show the situation of rehabilitation for RA patients in Japan and evidence of physical therapy, occupational therapy, splints and orthosis.

EL6

Aspirational ethics for scientists' well-being

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Conflict of interest: None

Although ethics often tends to be in the tone of "not to do", ethics that deals with the pros and cons of individual behavior based on precedents is called preventive ethics. This preventive ethics should be acquired as a member of society, In addition to this, however, we scientists are required to have aspirational ethic that considers what to do as an expert. Rules and laws are agreements to avoid repeating the same problems and inconveniences. On the other hand, our scientists place importance on originality, elucidate what no one knows yet, solve problems that nobody can do yet, and provide society with new knowledge and convenience. However, as is

clear from pollution and drug side effects, new knowledge and convenience almost always bring new problems and inconveniences. If ethics is interpreted as ethics that teaches the pros and cons of individual behavior, it is difficult to reach the stage where scientists think about how to face new problems. Scientists themselves are the first to be aware of the new problems that arise as a result of scientists' activities, and are able to take countermeasures most efficiently, and scientists should also propose new rules necessary for this. Kohlberg considers the formation process of human ethics in three stages. The first is "pre-conventional level" in which the right or wrong is judged by being praised or punished, and the action is selected by profit or loss. The second is "conventional level" that considers actions that are recognized as good by others as good actions. The third is "post-conventional level" in which one recognizes actions following one's own conscience are good. The idea of giving priority to profit over rules is only the same ethical level as that of preschoolers. Rules and laws actually correspond to this level. As people grow up, they follow rules and majority decisions, understand public order and morals, and reach to the conventional level that considers their surroundings. However, this is not enough for scientists. Because it is necessary to understand the background of rules and authority's words, and to predict problems related to the creation of knowledge and convenience and propose new rules to prevent them. In higher education institutions, we professors should focus on teaching students to propose rules rather than encouraging students to follow the rules, which is one of the most important things that we should do. And doing this will contribute to the social safety and security of which everyone recognizes value, and will lead to well-being of ourselves and students.

EL7

New era of complement research- need-to-know points for rheumatologists

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Conflict of interest: None

Complement is considered to be one of the most difficult fields to understand for physicians. However, we have to change our mind and need to understand and learn more about complement, because an anti-complement drug, eculizumab, has contributed to the improvement of various intractable inflammatory disorders. We here present a number of basic and clinical points of complement that the rheumatologists should know in daily clinical practice. This is a joint program of the Japan College of Rheumatology and the Japanese Association of Complement Research. Activation of complement system eventually lead to the activation of complement C3, which culminates in the formation of bioactive complement fragments such as C3a and C5a, as well as membrane attack complex (MAC). Congenital defects of complement components cause various types of inflammatory disorders other than increased susceptibility to infection. These disorders include such diseases as atypical hemolytic uremic syndrome (aHUS) and hereditary angioedema. Eculizumab is a humanized anti-human C5 monoclonal antibody that binds to C5 and inhibit its activation. Eculizumab has indications of paroxysmal nocturnal hemoglobinuria, aHUS, generalized myasthenia gravis and neuromyelitis optica spectrum disorder (NMOSD). Clinical studies are being carried out to obtain additional indications of eculizumab. In Nov. 2019, the effectiveness of CCX168 (avacopan), an orally-administered selective C5a receptor inhibitor, for ANCA-associated vasculitis was announced based on the pivotal Phase III ADVOCATE trial. Dysfunction of complement is now revealed to cause many intractable disorders including autoimmune diseases. We are facing a new era of complement research.

EL8

How we should deal with patients with rheumatoid arthritis and sleep disturbance? diagnosis, sleep hygiene and pharmacotherapy

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Conflict of interest: Yes

The previous reports showed the prevalence of sleep disturbance in patients with rheumatoid arthritis is high, and sleep disturbance causes decrease of QOL, increase of sensitivity to pain, impairment of the immune system, and increase of the comorbidity of other mental and physical diseases and mortality. Sleep disturbance has been shown to affect the body, brain and mind. Thus, improvement of sleep disturbance is important for maintaining both physical and mental health. When encountering a patient with sleep disturbance, we should consider specific sleep disorder including sleep apnea syndrome, restless legs syndrome, etc., and pay attention to the presence of snoring and complain of lower limbs at bedtime. In addition, large sleep and body movements that is reported from family members suggest REM sleep behavior disorder, and examine the possibility of Lewy body dementia. In addition to Lewy body dementia, almost all neuropsychiatric disorders are accompanied by sleep disturbance, especially considering the high frequency of depression in patients with rheumatoid arthritis and we should consider the possibility of depression. After excluding specific sleep disorders and neuropsychiatric disorders, it is necessary to encourage a review of lifestyle habits to adjust the rhythm of sleep and awakening. For example, it is desirable to give advice on sleep hygiene such as getting up at a certain time in the morning, exposed to external light, and increasing daytime activity. In particular, guidance regarding bedtime is a point to be noted during treatment. In other words, insomnia occurs when trying to go to bed earlier than the original bedtime. It is also necessary to place importance on the setting target of sleep itself. This lecture will summarize how to deal with patients with rheumatoid arthritis and sleep disturbance, especially focusing on diagnosis, sleep hygiene and pharmacotherapy.

EL9

Knowledge of foot and ankle surgery useful in treatment of rheumatoid arthritis

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Conflict of interest: None

Recent improvement of drug therapy for rheumatoid arthritis enabled suppression of joint inflammation and destruction. This has greatly changed the patient profile, and what patients want from medical professionals has also changed. Regarding the lower limbs, operating patients because they can't walk is over. It is an era to meet the needs of patients who are able to walk but want more. In this situation, the foot and ankle is a hot spot and are attracting attention. In order to respond to this need, it is necessary for medical professionals to have general knowledge of rheumatism, of course. Knowledge of "rheumatoid foot" is also necessary. In addition, in this age when disease status of patients is getting milder, the knowledge of general foot and ankle surgery is becoming more important. The problem of rheumatoid foot and ankle is solved by combination of the general knowledge of foot and ankle. However, the chance of gaining knowledge of foot and ankle surgery in general is rare for both orthopedic surgeons and rheumatologists. In this lecture, the common sense known in foot and ankle surgery, the common treatments being performed, and their concepts will be explained. I aim to tickle the audiences' intellectual curiosity and to increase the depth of knowledge that is the basis for rheumatologists when talking to patients.

EL10

Cervical spine disorder which rheumatologists should know-focused on spinal sagittal alignment-

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Conflict of interest: None

Rheumatoid arthritis is known to exhibit various cervical spine lesions in addition to limb joint lesions. In particular, rheumatic lesions that occur in atlantoaxial vertebra joints start from atlant axial subluxation (AAS) and progress to vertical subluxation (VS), and the middle and lower cervical vertebrae also undergo changes such as sub axial subluxation (SAS). The natural course of RA cervical spine lesions varies, and in some cases, AAS may spontaneously heal. In addition, cervical spine lesions vary de-

pending on the RA type, and there is no unified strategy for surgical treatment. However, among the systemic disease type classification proposed by Ochi et al., the most destructive cervical lesion mucilans type (MUD) showed AAS + SAS + VS in all cases, and their life prognosis were pessimistic. In these cases, preoperative Halo vest fixation is performed to improve the general condition and neurological improvement, and fixation from the occipital bone to the thoracic spine is often performed. The number of cases requiring fixation from the occipital bone to the thoracic vertebra was clearly reduced as a result of better control of RA. However, RA patients may have lumbar lesions associated with cervical spine lesions, especially kyphosis with vertebral fractures. Treatment is more difficult if the patient presents with cervical and lumbar lesions. It is necessary to treat the spinal disorder with particular emphasis on sagittal alignment. This time, I will discuss points that rheumatologists should be careful not to miss the presence of spinal disorders.

EL12

Epidemiology of rheumatoid arthritis

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Conflict of interest: None

Epidemiology is a discipline that clarifies how health-related events within a population vary. By using reliable and well-validated tools of evaluation, epidemiology can clarify the relationship between various factors and outcomes numerically and enable us to realize effective strategies of health promotion. So far, we have conducted a series of epidemiological studies on patients with rheumatoid arthritis (RA), and confirmed that none of the physical and psychological quality of life of RA patients has a significant association with rheumatic disease activity, but psychosocial factors have deep influence on it. It was also found that both CRP and depression were independently associated with pain (5). These findings are consistent with the results of the patient survey conducted during the development of the Rheumatoid Arthritis Clinical Practice Guidelines 2014, which revealed the complaint of the RA patients that they want to understand their sickness that does not reflect clinical data to the doctors. Physical diseases associated with pain, deformity, and dysfunction are thought to cause affective disorders such as depression and anxiety due to high psychological stress. RA is a fit for these conditions, and psychological factors enhance pain and other physical symptoms and affect medical acceptance behavior and relationships with others. The QOL of RA patients is thought to be determined by complex intertwining of physical symptoms and psychological and social factors, and a holistic approach is indispensable. Recent advances in treatment with the advent of biologics are remarkable, and by starting treatment at an early stage of onset, it has become possible to achieve remission with little destruction of the joint. However, further psychosocial considerations are necessary especially for poorly controlled patients. Flailty is defined as a state in which vulnerability to health problems has increased due to various functional changes accompanying aging and a decrease in reserve ability, and is considered to be a pre-stage of dependency. Flailty is closely related to sarcopenia and locomotive syndrome, and RA patients are considered to be high-risk populations of frailty. In recent years, RA patient population are aging, and there is an urgent need to establish effective preventive strategy for frailty in RA patients.

EL13

Management of infections in patients with rheumatoid arthritis and collagen disease

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National Center for Global Health and Medicine

Conflict of interest: Yes

The risk of infection is high in patients with rheumatoid arthritis (RA). This is due to the use of immunosuppressive drugs. In particular, patients using biologics have been found to be at a higher risk of infection. In addition, patients with RA are at increased risk of respiratory infections, especially bacterial pneumonia. This is thought to be because RA patients may have airway lesions such as bronchiectasis and bronchiolitis and repeat infection in such chronic airway lesions. It has been found that among cases that were previously considered bacterial pneumonia, cases of infection with RS virus and human metapneumovirus were actually misidentified. Since cellular immunity is reduced in patients with RA, opportunistic infections such as Legionellosis, Nocardiosis, and Pneumocystis pneumonia are also seen. It is necessary to identify the causative microorganism. As it is often difficult to detect those organisms, accurately assuming the causative microorganism is crucial to individually and specifically select a test method for accurate identification. Prevention of infectious diseases is important because respiratory viral infections such as viral upper respiratory tract inflammation and influenza become serious in immunocompromised persons. Wearing a surgical mask by a patient is effective. From Oral care will be important in the future. Vaccinations such as influenza vaccines and pneumococcal vaccines are also important. There is a view that the vaccine effect is insufficient in patients with immunodeficiency, but it is necessary to try to prevent infection by putting the vaccine around the family to ultimately prevent patients from infection. Oral ST is effective in preventing Pneumocystis pneumonia, but it is necessary to individually examine which patient is required. In patients who use biologics, it is necessary to take measures such as prior assessment and treatment of latent tuberculosis when necessary.

EL14

Epidemiological studies of RA in the last 20 years

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Conflict of interest: Yes

Treatment of Rheumatoid arthritis (RA) has been remarkedly improved over the last twenty years. Development of new classes drugs has strong impact; however, we should not forget the improvement of therapeutic strategy to utilize new drugs in the daily practice. Randomized controlled trials (RCTs) is necessary in clinical studies of drug development, on the other hand, observational studies based on the daily practice is required for the development of new therapeutic strategy. However, in the year 2000, just before the breakout of new drugs in RA treatment, no systematic disease cohort of RA was present in Japan. Considering the requirement of the data in the daily practice, we have established a disease cohort named J-ARAMIS in Institute of Rheumatology, Tokyo Women's Medical University. J-ARAMIS was established based on ARAMIS cohort conducted in North America, however, by adding the physician's data and the laboratory data to the patient's data of ARAMIS system, J-ARAMIS has become a more powerful database. J-ARAMIS was renamed to IORRA, and has published more than 140 English, peer-reviewed publications and reported the changes of daily practice of RA management and also unrevealed the issues of the RA treatment. Also, establishment of IORRA has stimulated the clinical studies of RA in Japan, including the Ninja study conducted by National Hospital Organization. Recently, trend of clinical studies in medicine has shifted from RCT to observational studies, and the words as Real World Data (RWD) or Real World Evidence (RWE) have been used frequently, I may regard IORRA as a pioneer of RWD and RWE in Japan. I deeply feel that the times finally has caught up to our spirit. In this educational lecture, I would like to review the development of epidemiology of RA management in the last 20 years, mainly using the achievement of IORRA, and discuss the essence necessary for the establishment of clinical studies in rheumatology.

EL15

New mechanism of autoimmune diseases mediated by neoself

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Conflict of interest: Yes

Misfolded proteins localized in the endoplasmic reticulum are degraded promptly and thus are not transported outside cells. However, misfolded proteins in the endoplasmic reticulum are rescued from protein degradation upon association with MHC class II molecules and are transported

to the cell surface by MHC class II molecules without being processed to peptides, suggesting that MHC class II molecules function like a chaperon to transport misfolded proteins. Because structures of misfolded proteins associated with MHC class II molecules are different from normal proteins, antigenicity of the misfolded proteins are different from that of normal proteins. Studies on the misfolded proteins rescued by MHC class II molecules have revealed that misfolded proteins associated with MHC class II molecules are specific targets for autoantibodies produced in autoimmune diseases. Furthermore, a significant correlation has been observed between autoantibody binding to misfolded proteins associated with MHC class II molecules and the risk of autoimmune diseases conferred by each MHC class II allele. These findings suggest that misfolded proteins rescued from protein degradation by a chaperon-like function of MHC class II molecules are involved in the abnormal immune response observed in autoimmune diseases, which will provide a new insight into the pathogenesis of autoimmune diseases.

EL16

Updates on Pathologies of the Neuromuscular Junction and the Skeletal Muscle for Rheumatologists

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Conflict of interest: None

The neuromuscular junction (NMJ) is an essential organ where an action potential of the spinal motor neuron is converted into muscle contraction. The NMJ is a target of autoimmune disorders including myasthenia gravis, Lambert-Eaton myasthenic syndrome, and Isaacs' syndrome, and is also a target of congenital myasthenic syndromes and Schwartz-Jampel syndrome due to germline mutations in genes expressed at the NMJ. In addition, bacterial toxin botulinus, snake toxin alpha-bungarotoxin, spider toxin latrotoxin, shell toxin conotoxin, organophosphate pesticides, chemical weapon sarin, and chemical weapon VX also affect the NMJ. The skeletal muscle is the largest organ in human, and is also a target organ of autoimmune myopathies, as well as of fugu toxin tetrodotoxin and snake toxin myotoxin. In myasthenia gravis, four autoantibodies have been reported. Examinations of anti-acetylcholine receptor antibody and anti-MuSK antibody are covered by health insurance. In addition, anti-LRP4 and anti-agrin antibodies are likely to the cases of myasthenia gravis, although their pathogenicity has not been fully elucidated by developing an active immunization model and a passive immunization model. Lambert-Eaton myasthenic syndrome is caused by anti-P/Q-type calcium channel that is expressed at the nerve terminal and also in a concurrent malignant tumor. Isaacs' syndrome is caused by autoantibody against volage-dependent potassium channel that is expressed at the motor nerve terminal. Isaacs' syndrome is also called neuromyotonia, and is characterized painful and sometimes painless myokymia due to excessive depolarization of the nerve terminal. Isaacs' syndrome is frequently misdaignosed as fibromyalgia or complex regional pain syndrome (CRPS). Immune checkpoint inhibitors in the classes of anti-PD-1 antibodies, anti-CTLA-4 antibodies, and anti-PD-L1 antibodies sometimes provoke adverse autoimmune events in many organs, and the NMJ and the skeletal muscle are not exceptional. The educational lecture will cover normal physiological process of how the NMJ signal transmission takes place and how the signal is transduced to the muscle contraction, and also cover pathologies due to autoimmune mechanisms, germline mutations, and natural/artificial toxins.

EL17

Positioning of anti-fibrotic agents in the treatment of interstitial lung disease associated with connective tissue disease

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Conflict of interest: Yes

The majority of the causes of death except for malignancy and infection are attributed to fibrotic diseases, and overcoming pathogenic fibrosis is a major issue remaining in modern medicine. When tissue damage occurs, the repair machinery works, but, in fibrotic conditions, dysregulated mechanisms in this process result in excessive accumulation of extracellular matrixes, leading to distortion of the normal tissue architecture. Typical fibrotic conditions in the field of connective tissue disease (CTD) include systemic sclerosis (SSc) and interstitial lung disease (ILD). Current treatment regimens aim primarily at suppressing inflammation and immune activation, but not at suppressing fibrotic process. Recently, therapeutic agents that inhibit fibrotic process have been actively investigated and introduced into clinical practice. The disease concept of chronic fibrosing ILD with a progressive phenotype (PF-ILD) is proposed for ILD that causes restrictive lung impairment due to progression of fibrosis in the lung parenchyma. In idiopathic pulmonary fibrosis (IPF), which is a typical form of PF-ILD, anti-fibrotic agents pirfenidone and nintedanib have already been introduced and are shown to suppress respiratory function decline. Clinical trials of anti-fibrotic agents targeting ILD associated with rheumatoid arthritis and SSc also showed the same inhibitory effect on progression of restrictive lung function. We have an entirely new treatment option of antifibrotic therapy, in addition to immunosuppressants and molecular targeted therapies. However, there are still many issues to be solved, such as in what cases, at what timing, when to use them properly or in combination, and long-term safety profiles. This lecture features the positioning of anti-fibrosis therapy in CTD-ILD based on updated information of pathogenesis of CTD-ILD, clinical trial data, and clinical experience with IPF.

EL18

Clinical Significance of Myositis-Specific Autoantibodies

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Conflict of interest: None

To date, a variety of myositis-specific autoantibodies (MSAs) have been identified and their clinical significance has been elucidated. MSAs can help us not only to make diagnosis of idiopathic inflammatory myopathy (IIM) but also to classify IIMs and to predict disease course and prognosis. Patients with anti-aminoacyl-tRNA synthetase (ARS) antibodies often present such manifestations as called "anti-synthetase syndrome (ASS)"; myositis, interstitial lung disease (ILD), arthritis, mechanic's hand, fever and Raynaud's phenomenon. Among these manifestations, anti-ARSs show the strongest association with ILD. Anti-melanoma differentiation-associated gene 5 (MDA5) is also strongly associated with ILD. However, ILD with anti-ARSs is often chronic progressive with frequent recurrence, but ILD with anti-MDA5 is often rapidly progressive reading high mortality in early disease phase. Thus, it is important to treat patients in accordance with their predicted clinical course. Dermatomyositis-specific autoantibodies are anti-MDA5, anti-transcriptional intermediary factor 1-γ (TIF1-γ), anti-Mi-2, anti-nuclear matrix protein 2 (NXP2) and anti-SUMO-1 activating enzyme (SAE) antibody. Anti-TIF1-γ and anti-NXP2 are associated with malignancy in adult IIM, the latter of which is associated with subcutaneous calcinosis especially in pediatric patients. Anti-TIF1-γ and anti-SAE are associated with dysphasia and anti-Mi-2 is associated with relatively fair prognosis. Anti-signal recognition particle (SRP) and anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) are associated with immune mediated necrotizing myopathy. Anti-SRP-positive patients tend to show severe muscle weakness, dysphasia and high creatine kinase (CK) level, and anti-HMGCR-positive patients often have episode of statin exposure. In this lecture, clinical significance and application for clinical practices of MSAs are discussed with showing our own research data.

EL19

New development of autoinflammatory disease: From new classification/new disease to transitional medicine/regional collaboration

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Division of Respirology, Neurology, and Rheumatology, Department of Medicine, Kurume University School of Medicine

Conflict of interest: None

As elucidation of the pathophysiology of autoinflammatory diseases progresses, new autoinflammatory diseases and their disease genes are identified each year. Currently, a narrowly defined autoinflammatory dis-

ease in which more than 30 disease genes have been identified has been reported and its classification has been reviewed. Many autoinflammatory diseases are caused by abnormalities in the giant protein complex inflammasome, but in recent years, the function of each inflammasome (NLRP3, NLRP1, NLRC4, AIM2, Pyrin) has been elucidated. Pyrin inflammasome activation in familial Mediterranean fever (FMF) patients with the highest number of autoinflammatory diseases reveals the existence of an activation mechanism by gain of function rather than the previously considered loss of function. There are many reports of FMF-related diseases caused by *MEFV* mutations other than FMF. In recent years, it has been proposed to newly classify diseases caused by *MEFV* mutations including FMF as pyrin-associated autoinflammatory diseases (PAAD). In some diseases, research on autoinflammatory diseases is important in considering the pathogenesis of rheumatic and collagen diseases. A20 haploinsufficiency showing symptoms similar to Behcet's disease, ADA2 deficiency exhibiting symptoms of polyarteritis nodosa, and Aicardi-Goutières syndrome showing symptoms similar to systemic lupus erythematosus (AGS). Thus, although the number of patients with autoinflammatory syndrome is small, the role of inflammation-related molecules elucidated from clinical studies on autoinflammatory diseases is important as a contact point with rheumatoid and collagen disease. In recent years, there has been a demand for promotion of transitional medicine and regional cooperation in autoinflammatory diseases. In particular, collaboration between pediatricians and physicians, dermatologists, and ophthalmologists is an issue for the future. Furthermore, problems due to the recognition of autoinflammatory diseases, such as the method of requesting genetic tests and the necessity of medical consultation, have arisen. In this lecture, I would like to discuss these new issues.

EL20

Revision of the diagnostic criteria for sarcopenia (AWGS2019)

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Conflict of interest: None

With the aging of society, there is an increasing interest in the pathological conditions that increase with age, and sarcopenia is one of them. Sarcopenia is a concept proposed by Rosenberg in the United States in 1988, and the incidence of sarcopenia increases with age. Therefore, there is concern about the prognostic effect of sarcopenia in older patients with rheumatoid arthritis. Regarding the diagnosis of sarcopenia the European Working Group on Sarcopenia in Older People (EWGSOP) published an operational diagnostic algorithm for sarcopenia in 2010, and research on sarcopenia has made great progress since then. We felt the need for diagnostic criteria for Asians, formed the Asian Working Group for Sarcopenia (AWGS) in 2013 and announced diagnostic criteria for Asians in 2014. The AWGS criteria followed the approach adopted by the EWGSOP and proposed cutoff values for grip strength, walking speed, and skeletal muscle mass based on Asian data. Later, EWGSOP announced the revision of diagnostic criteria in October 2018, and published a paper in 2019 (EWGSOP2). AWGS planned to publish a revised version in 2019. In January 2019, the first meeting was held in Nagoya to revise diagnostic criteria followed by the second meeting in Hong Kong in May, when we confirmed the policy for the revision. The diagnosis process was proposed so that the measurement of the skeletal muscle mass can be maintained in the diagnostic criteria, but the diagnosis can be performed in the area where the measurement of the skeletal muscle mass is difficult to measure, such as in the primary care setting. In addition, we conducted a systematic review for epidemiology of sarcopenia along with the review for case finding, skeletal muscle mass, and muscle strength, physical function. We then determined the cut-off values based on the review. In this lecture, I will introduce the latest knowledge about aging rheumatoid arthritis and sarcopenia along with the outline of AWGS2019.

EL21

IgG4-related disease: diagnosis and treatment

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Conflict of interest: None

IgG4-related disease (IgG4-RD) is a recently established systemic disease that is characteristically associated with elevated serum IgG4 levels and believed to be caused by autoimmune mechanisms. The clinical features of IgG4-RD include (1) systemic distribution, (2) imaging findings of swelling, nodules, and/or wall thickening, (3) high serum IgG4 levels, (4) abundant IgG4-bearing plasma cell infiltration in affected organs, (5) a favorable response to corticosteroid therapy, and (6) coexistence with other IgG4-RD manifestations. The concept of IgG4-RD was established based on the culmination of specific discoveries, including a close association between autoimmune pancreatitis (AIP) and high serum IgG4 levels, massive IgG4-bearing plasma cell infiltration in pancreatic tissues affected by AIP, and systemic other organ involvements in AIP with similar IgG4-bearing plasma cell features, which opened the gateway from AIP to IgG4-RD. AIP exhibits the typical clinical features of IgG4-RD: elderly male preponderance and obstructive jaundice / pancreatic swelling, which may mimic pancreatic cancer. The disease spectrum of IgG4-RD seems to be capable of spreading every organ, including well-established members of AIP, lacrimal and salivary gland lesions, respiratory diseases, sclerosing cholangitis, kidney diseases, and retroperitoneal fibrosis, and other additional new members. The algorithms developed for the Comprehensive Diagnostic Criteria for IgG4-RD, 2011, by Japanese researchers have remarkably increased detection sensitivity. 2019 ACR and EULAR Classification Criteria for IgG4-RD is established, which will make IgG4-RD diagnosis on a global standard. Oral glucocorticoids are the first-line agents for remission induction and maintenance therapy. Originally, IgG4-RD had been considered reversible and to have a good prognosis; however, long-term afflictions sometimes result in transition to advanced-stage conditions with dysfunction and/or complicating malignancy.

EL22

Clinical Ethics for Clinician; Practical Approach to Problem- Solving

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Conflict of interest: None

Clinical ethics is a practical approach to ethical problems in clinical medicine. The four principles of medical ethics (respect for autonomy, non-maleficence, beneficence, justice), case conference sheet and ethics consultation are useful tools for ethical problem-solving. I present how to use the tools when you encounter the problems in clinical practice.

EL23

Diagnostic imaging of spondyloarthritis

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Conflict of interest: None

The inclusion of MRI, given equal weight as radiographic sacroiliitis, is a crucial advancement in 2009 ASAS classification criteria of axial spondyloarthropathy (SpA). MRI is highly sensitive for detection of sacroiliitis, mainly via demonstration of bone marrow edema (BME) representing early stages of inflammation; however, the findings are often nonspecific. Familiarity with the anatomy, anatomic variants, and physiologic changes of the sacroiliac joints is important for correctly interpreting findings and avoiding misdiagnosis. 1) MR imaging protocol For sacroiliac joint, T1-weighted images and fat suppressed T2-weighted or short tau inversion recovery (STIR) images parallel and perpendicular to the joint are obtained. For the spine, T1-weighted images and STIR images are obtained. Contrast enhanced fat-suppressed T1-weighted images may be useful in detecting synovitis at early stage, but not required for demonstration of bone marrow edema. 2) Anatomy of sacroiliac joint Sacroiliac joint is composed of synovial and fibrous components, and bone marrow edema is dominant at a synovial component. 3) MRI findings of sacroiliac joint and spine in SpA MRI of sacoilliitis include BME in the subchondral bone (osteitis), erosions, fatty conversion of bone marrow, osteosclerosis, synovitis and enthesitis. In spine, inflammatory changes are commonly seen in the corner or endplate of the vertebral bodies or facet joints. Fat suppressed T2-weighted or STIR images are sensitive in demonstrating BME as areas of high signal intensity, which represents increased water content associat-

ed with inflammatory cellular infiltration of bone marrow (osteitis). 4) MRI criteria of active sacroiliitis To diagnose active sacroiliitis, BME (osteitis) should be present in at least two consecutive planes or more than one focus in a single plane regardless of its size. Structural lesions identified on MRI are excluded from the diagnostic criteria. However, it is contradictory whether size/extent of BME as well as structural lesions without BME should be included in the diagnostic criteria. 5) Differential diagnosis MR finding are often nonspecific and BME can be seen in various situations. The diagnosis should be based on not only MRI, but also plain radiography and clinical findings.

EL24

Considerations for medical care of patients with cognitive impairment

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Conflict of interest: None

The number of the older adults with dementia is increasing with population aging, and the patient population with dementia is also aging. Therefore, many departments now often treat older patients who have dementia, and clinicians engaged in the medical care of older patients are expected to be able to detect cognitive impairment at an early stage and provide the appropriate care. Dementia of the Alzheimer type is characterized by severe memory impairment, with relatively good recall of past events but difficulty remembering new events. Therefore, during examinations, clinicians may be able to detect early cognitive impairment by asking patients their age. When patients have difficulty remembering new events, they often divert to confirming their date of birth (recalling an old event) instead of directly giving their correct age (recalling a relatively new event). Assessing temporal orientation is also useful (e.g., by asking the present date) because memory impairment is accompanied by disturbance of orientation, especially temporal orientation, in early-stage dementia of the Alzheimer type. Thus, incorrectly answering the present date suggests disturbance of temporal orientation, and clinicians should suspect cognitive impairment. If a condition deteriorates after having been stable with oral medication in older patients, clinicians need to consider non-adherence to treatment due to increasing forgetfulness. In this case, the patient's family should be asked about treatment adherence and should check for unused prescription drugs. If cognitive impairment is confirmed, clinicians should simplify the medication regimen as far as possible and request family support to ensure adherence. Also, they should consider entering the patient into the long-term care insurance system and then introducing helpers and day services after the patient is certified to need long-term care.

EL25

Overall picture of patient safety—Correspondence of usual condition and emergency Situation—

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Conflict of interest: None

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

EL26

Instructions and Management of Self-injection Treatment in Patients with Rheumatoid Arthritis

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Conflict of interest: None

In addition to a conventional syringe-type injector, a pen-type autoinjector with a retractable needle which are easy to use has been used broadly for self-injection treatment of rheumatoid arthritis (RA). There are many differences among products in terms of presence of the button, location of them and administration time, so outpatient nurses need to understand the product-specific structure and dosage in addition to the administration interval and action mechanism. As in the guidelines of the Japan College of Rheumatology "Self-injection treatment should be introduced after clarifying whether patient is suitable for self-injection procedure and adequate instruction for using an injector", it is necessary to assess patient individual skills and comprehension of the treatment and to detailed explanation about the timing of medication withdrawal before an introduction of the treatment. Patients sometimes feel it difficult to use the device in usual way because that RA patients usually finger deformity and disability, so appropriate individual instruction which is suitable for each patient is necessary. There have been reported several adverse events related to the pen-type autoinjector. One case was that the needle bit in the bone through the skin in using for skinny patients and the other case was that the needle stuck in the finger because it was used upside down. Medical staff should take care of patient adherence and capability to maintain self-injection treatment even after introduction. In our hospital, we carried out an original simple checklist for all patients undergoing self-injection to confirm their skills and knowledge. We believe that this checklist is useful for driving continuous communication among patients and medical staff and also provides an opportunity to determine the appropriateness of the self-injection treatment. This presentation includes information of practical issue about self-injection treatment for RA patients in our hospital.

Meet the Expert

MTE1

Pulmonary arterial hypertension

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

Conflict of interest: Yes

First of all, I would like to compare the world with Japan for epidemiological information such as the frequency of pulmonary hypertension associated with connective tissue disease (CTD). Pulmonary arterial hypertension (PAH) is known to have a variety of pathologies other than those related to CTD. Among them, there are pathological conditions with clear pathological differences. In clinical practice of patients with CTD, there are clinical symptoms suspected of PAH. We will also examine clinical symptoms that can be seen without using instruments such as stethoscopes, electrocardiograms, and ultrasonography. In addition, it is important to regularly measure serological and physiological indicators in order to find PAH at an early stage. We will devise necessary indicators for regular measurement. For diagnosis, cardiac ultrasonography and right heart catheterization have become essential and gold standard. No cardiac catheterization may be possible at any facility. After all, it is important to consult with a PH-special hospital that can diagnose PAH quickly, with the ability to presume that patients with CTD may have PAH or PH at an early stage. Regarding the treatment, the treatment policy differs depending on whether it is accompanied by systemic sclerosis (SSc) or other cases of CTD. The usefulness of immunosuppressive drugs is not observed in PAH and PH, which have SSc as a basic disease. The only treatment is to detect early and use pulmonary vasodilators early. However, there are many reports that the effectiveness of pulmonary vasodilators is low compared to PAH related to pathologies other than SSc. At the time of diagnosis, it is considered difficult to improve in cases where the average pulmonary artery pressure exceeds 40 mmHg or the pulmonary vascular resistance exceeds 10 WU. In addition to therapeutic interventions that have pulmonary vasodilatory effects, we believe that it may be necessary to use treatments with antifibrotic effects in the future.

MTE2

How to treat childhood rheumatic diseases? What to know for adult rheumatologists

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Conflict of interest: None

Childhood rheumatic diseases are extremely rare compared to adult rheumatic diseases. The estimated number of patients with rheumatoid arthritis is approximately 600,000 to 700,000, but the number of children with juvenile idiopathic arthritis is only around 5,000. Similarly, the total number of patients with systemic lupus erythematosus is about 60,000 to 100,000, but the number of patients under 15 years old is about 1,500. Unfortunately, fewer than 100 pediatric specialists have a board of rheumatology, and there are still many areas absent pediatric rheumatologists. Therefore, patients have been treated with the cooperation of adult rheumatologists in many regions. However, except for rare autoinflammatory diseases, Kawasaki disease, giant cell vasculitis, and rheumatic vasculitis, the disease composition of rheumatic diseases are almost the same. Therefore, it is possible for an experienced adult rheumatologist to treat patients with pediatric rheumatic diseases if they keep in mind several points and cooperate with pediatricians. To treat children with rheumatic diseases better, there are some important points, 1) Differences between adults and children by disease, 2) Treatment goals in children, 3) Drug use, tolerability, side effects, 4) Transitional care and medical support systems, 5) Significance and joy in pediatric rheumatology. I hope this seminar will be useful for adult rheumatologists who are involved in the treatment of pediatric rheumatic patients.

MTE3

Diagnosis of spondyloarthritis-SpA examined by rheumatologists

Shigeyoshi Tsuji
NHO Osaka Minami Medical Center

Conflict of interest: Yes

For diagnosis of spondyloarthritis, screening using the ASAS classification criteria is desirable. However, there is a possibility of misdiagnosis if overconfidence of ASAS classification standard. For example, there are MRI findings in the ASAS classification standard "imaging arm" (the presence of two high-intensity regions on the same plane in STIR images or the same high-intensity region in consecutive slices). The change is known to occur in 30% of the elderly. Emphasis on images can lead to misdiagnosis. In this lecture, while presenting the case, I would like to explain the points to be noted in the "clinical symptoms, blood biochemistry, and images" necessary for "diagnosis of spondyloarthritis".

MTE4

Early treatment of tenosynovitis with conventional synthetic disease-modifying antirheumatic drugs other than methotrexate prevents the progression of preclinical rheumatoid arthritis

Tomomasa Izumiyama
Higashisendai Rheumatic Disease Clinic

Conflict of interest: None

The earlier we initiate treatment the better it is for the patient, and preclinical RA (pre-RA) can be the best stage to start drug therapy. However, as pre-RA can only be retrospectively defined in the absence of currently available clinical definition, presumable cases cannot be verified as being pre-RA if the treatment is effective and the would-be RA resultantly stops progressing to established RA. Mankia et al. have reported that many patients who possess a risk to progress to established RA actually do not, but it is impossible to distinguish those who progress from those not. I have experienced a case in which the patient progressed to established RA after 37 years from his seroconversion of rheumatoid factor. Predisposed individuals may or may not encounter environmental factors that finally precipitate arthritis. Therefore, a drastic revision in the definition of pre-RA is required. Since RA is a syndrome of systemic synovial inflammation, arthritis is not necessarily its essential component. Accordingly, its treatment must aim at systemic synovitis instead of arthritis alone. Tenosynovitis can be an initial symptom of RA and can cause erosions of adjacent bones. Thus, this pathology can be useful in making an early diagnosis of RA and itself can be a treatment target. Patients with multiple tenosynovitis should be regarded as RA cases even without arthritis. Tenosynovitis can cause severe pain and morning stiffness especially when it affects flexor tendons of hands. At our clinic conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) other than methotrexate (MTX) are effective in treating such cases. Ultrasonography is especially useful in diagnosing tenosynovitis and is widely available in Japan. Further, many csDMARDs other than MTX can be used in this country. Taking these advantages, I hope that we can lead the world in detecting and treating RA without arthritis and in preventing its progression to established RA.

MTE5

Basic knowledge of typical orthopedic diseases for the treatment of rheumatic diseases

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Conflict of interest: None

Rheumatoid arthritis (RA) is characterized by multiple arthritis which causes bone destruction. There are many orthopedic diseases that cause pain in the hand fingers, wrist joints, feet, and other limb joints that are particularly frequent in arthritis by RA. Along with advances in drug therapy, an early diagnosis before the appearance of bone destruction and tight control of inflammation is required. Therefore, in order not to mis-diagnose these conditions as RA and also to evaluate the disease activity correctly during treatment, it is necessary to know representative orthopedic diseases. The following are representative orthopedic diseases due to routine medical treatment that causes pain in the limb joints. These diseases can understand pathology from the anatomical structure and function of the site. Hand fingers, wrist joints: 1) finger tendonitis and de Quervain

tenosynovitis, 2) osteoarthritis (Heberden nodule, Bouchard nodule, CM arthropathy) 3) ulnar plus variance, triangular fibrocartilage complex injury Foot: 1) plantar fasciitis, 2) Achilles tendinopathy Elbow: 1) lateral epicondylitis (tennis elbow) Shoulder: 1) frozen shoulder 2) bicipital tenosynovitis Knee: 1) osteoarthritis, 2) popliteal cyct In elderly onset RA, there are many cases where osteoarthritis is present. Multiple arthritis is an important future of RA. It should be taken into consideration, in the elderly, there are many pain sites. Plantar fasciitis and pain around the heel are also important to diagnose spondylarthritis. In this lecture, we aim to deepen our knowledge including diagnosis of these diseases, pathology, examination methods, differences from RA.

MTE6

Methods for evaluating idiopathic inflammatory myopathies

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Conflict of interest: None

Idiopathic inflammatory myopathy (IIM) is an autoimmune disorder with a diverse phenotype characterized by chronic inflammation of the skin, fascia, muscle, or lung. The treatment response and prognosis differ depending on the phenotype. It is thus important to comprehensively evaluate the disease condition early for an appropriate treatment. I will first describe classification criterion including the latest 2017 EULAR/ACR IIM classification criteria and European Neuromuscular Centre classification criteria focusing on muscle pathology. Furthermore, for the treatment of IIMs, clinicians must evaluate the disease activity, extent of disease, complications, and prognosis using various evaluation methods including imaging tests. Magnetic resonance imaging (MRI) and ultrasonography are particularly useful noninvasive modalities, in contrast to the more invasive electromyogram and muscle biopsy, and allow for the accurate assessment of myositis and fasciitis. I will therefore show the utility of imaging tests in IIMs and discuss characteristic MRI findings for each myositis-specific antibody. Finally, I would like to describe the prognostic factors in clinically amyopathic dermatomyositis (CADM). Anti-MDA5 antibody-positive CADM with rapidly progressive interstitial lung disease leads to a poor outcome. Therefore, it is critically important to assess the prognostic factors and disease activity in CADM for early intervention.

MTE7

Management of Shoulder Pain in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Participants of this program will learn: 1) pathologic events in rheumatoid shoulders, 2) physical examination and imaging diagnosis of the shoulder, 3) how to do corticosteroid injection, 4) how to order rehabilitation program, and 5) how to explain surgical options. <What is the problem of the rheumatoid shoulder? > In advanced RA, the shoulder joint is destroyed in half of the patients. Rotator cuff tear occurs frequently in RA because the insertion of the rotator cuff is located close to the bare area. So the major problems in the rheumatoid shoulder are: 1) synovitis and inflammatory pain; 2) impairment of shoulder motion due to joint destruction; 3) loss of power due to rotator cuff tear. <Tips for physical examination> Pain at rest (particularly night pain) suggests synovitis or the presence of rotator cuff tear. Tender points and range-of-motions are "must" of physical examination. Tenderness over joint spaces suggests synovitis or secondary arthrosis, while tenderness over the greater tuberosity suggests rotator cuff tear. Both active and passive range-of-motions should be measured to differentiate contracture from weakness. <How to make an intraarticular injection?> Intraarticular corticosteroid injection is indicated for longstanding pain uncontrolled by medication. The author prefers an injection from posterior in a sitting patient. <How to order rehab program?> Isometric exercises of the rotator cuff muscles and relaxation of the scapulothoracic muscles are recommended, because these procedures do not worsen pain. <How to explain surgical options?> For patients with advanced joint destruction, total shoulder arthroplasty is indicated if painful or if the ADL is highly impaired. Anatomical shoulder arthroplasty is recommended when the rotator cuff is preserved, whereas reverse shoulder arthroplasty is recommended when the rotator cuff is seriously torn. Arthroplasty is not indicated in case of severe glenoid bone loss.

MTE8

The assessment of nailfold capillary changes in clinical settings

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Conflict of interest: None

Systemic sclerosis (SSc) is a multisystem autoimmune disease characterized by vasculopathy and fibrosis of the skin and various internal organs. Although its etiology remains unknown, recent clinical and basic studies have achieved a progress in the understanding of its developmental process. SSc-associated organ fibrosis occurs as a result of constitutive activation of dermal fibroblasts followed by vasculopathy and autoimmune inflammation; therefore, the assessment of vasculopathy is quite useful for the early diagnosis of SSc without fibrotic changes, as well as for evaluating its disease stage and severity. SSc vasculopathy consists of the functional and structural abnormalities, the latter of which can be evaluated by looking at nailfold capillaries. Generally, skin vasculature forms capillary loops in the papillary dermis, which runs parallel to the epidermis in the areas around nailfold. The nailfold capillary changes associated with SSc vasculopathy is characterized by capillary dilation or loss, which can be observed by naked eyes when the changes are severe. Dermoscopy and capillaroscopy help us observe the nailfold capillary changes much more precisely. Especially, there is a scoring system of nailfold capillary changes, and the evaluation of blood flow velocity is possible in capillaroscopy-based evaluation. Indeed, we experienced the improvement of numeric parameters in capillaroscopy-based assessment in SSc patients treated with disease-modifying drugs, suggesting that capillaroscopy may be useful for evaluating disease modifying effects of new drugs against SSc. In my talk, I will present our cases who were longitudinally followed up with capillaroscopy, and explain the underlying pathogenesis of SSc vasculopathy.

MTE9

Visualizing arthritis bone destruction 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. 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 and tissue dynamics.

MTE10

Total ankle arthroplasty through a lateral approach

Katsunori Ikari
Tokyo Women's Medical University

Conflict of interest: Yes

In 2018, new total ankle arthroplasty (TAA) system has been launched

in Japan. It is to be used through a lateral transfibular approach. The existing TAA systems in Japan have been performed through an anterior approach, but it is subject to soft-tissue complications. On the other hands, a lateral transfibular approach provides direct visualization of the center of rotation of the ankle, allowing less bone resection with anatomically curved resections as well as more accurate reconstruction of the joint alignment. It requires an external alignment frame that is a rigid coordinate system for bony resections. The purpose of this program is to show the surgical technique for the new TAA system.

MTE11

Corticosteroids and psychiatric symptoms

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Conflict of interest: None

Corticosteroids are widely used as a therapeutic drug in various diseases including autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). On the other hand, 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 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%. In addition, the prevalence of depression in RA patients is high, with a report of about 16%. 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.

MTE12

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.

MTE13

Synovial fluid hands-on workshop: "one-drop assessment" by physicians

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Conflict of interest: None

Microscopic examination of synovial fluid provides very helpful information in the differential diagnosis of inflammatory arthritis. Crystal identification by microscopy is a classic, simple diagnostic procedure but remains to be a gold standard for the definitive diagnosis of crystal arthritis. Microscopic examination of a drop of synovial fluid can provide a prompt assessment of the presence or absence of inflammation and crystals and help avoiding excessive tests and treatments. We held the first synovial fluid examination workshop in 2019 and trained 30 participants using 4 ordinary microscopes (with UGAN) and 3 polarized microscopes. This is the second hands-on workshop. **Teaching points** 1) A clinical diagnosis of crystal arthritis is provisional. The definite diagnosis of crystal arthritis should be made by microscopic examination of the synovial fluid. 2) Physicians should look at every synovial fluid by microscopy. It is very important that rheumatologists become acquainted with crystal analysis; besides becoming able to diagnose crystal arthritis at the first visit, they search with knowledge of the clinical picture, and their interest in the search is clearly higher than that of a lab technician. Centrifuging is not necessary. Important clinical information such as presence or absence of inflammation, monosodium urate (MSU) and calcium pyrophosphate (CPP), will be obtained immediately. 3) Ordinal microscopy is acceptable. By the ordinary microscope, crystals are well distinguished and identified as MSU or CPP easily by shape. The polarizing light observation is helpful, showing the strong brilliance of most MSU crystals and the weak to absent of CPP. Polarized microscope may be helpful to identify small crystals in synovial fluids. Acknowledgement: The rental fee of the microscopes was paid by JCR.

MTE14

Efficient strategy of data accumulation and analyses for medical doctors

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Conflict of interest: None

Advancement of data processing by CPU and expansion of data storage has been helping medical knowledge to expand in an unprecedented scale. A doubling time of medical knowledge was 3 and a half years in 2010 and is estimated to be 73 days in 2020. There is a huge demand to efficiently and accurately accumulate and analyze medical data especially under the view point of medical doctors. 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 across statistical models -to get familiar with basic knowledge of machine learning

MTE15

Pharmacoeconomics in Rheumatoid Arthritis

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Conflict of interest: None

The introduction of biologics has resulted in significant advances in treatment strategies for rheumatoid arthritis (RA). On the other hand, rising RA care costs have caused concern, placing a heavy burden on society as well as RA patients. The IORRA study has also shown that RA patients' financial burden is increasing and that direct and indirect costs associated with progression of functional impairment or decline in quality of life (QOL). This suggests that inhibiting the progression of functional impairment through aggressive control of RA may help reduce lifetime healthcare costs. Pharmacoeconomics is the scientific discipline that evaluates both the clinical benefits and economic efficiency of a drug to determine whether it is worth the cost. In Japan, cost-effective assessment was started for some expensive drugs in 2016. In pharmacoeconomic studies for chronic diseases like RA, cost-utility analysis is mainly used, in which "cost" and "effectiveness" are separately quantified for the study and control health technologies to evaluate the incremental cost-effectiveness ratio (ICER). Effectiveness is usually expressed in quality-adjusted life years (QALYs). We have analyzed the cost-effectiveness of biologics in the treatment of RA and found that the use of biologics in Japanese RA patients is justified in the long term from an economic perspective. These results suggest that, although biologics are expensive, their proper use in eligible RA patients may also be socially beneficial by helping maintain QOL for a long time and allowing patients to have a social life including workforce participation without difficulty. At this Meet the Expert seminar, I will first share health economic issues and the importance of pharmacoeconomic evaluation and then explain cost-effectiveness in real-world settings. In addition, since I was in charge of biosimilars and pharmacoeconomics for the revised guidelines for the management of RA, JCR 2020, I would like to talk about them.

MTE16

Rehabilitation and custom orthotic interventions for patients with rheumatoid arthritis for rheumatologist of physician

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Conflict of interest: None

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

MTE17

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.

MTE18

Psychiatric symptoms in patients with neuropsychiatric systemic lupus erythematosus (NPSLE): A management strategy for rheumatologists

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Conflict of interest: None

Neuropsychiatric systemic lupus erythematosus (NPSLE) is associated with poor prognosis, extensive cumulative organ damage, and low quality of life. Therefore, rheumatologists consider adequate management of NPSLE important for patient outcome. However, it is often difficult to evaluate and manage psychiatric symptoms in patients with SLE. Typically, the psychiatric differential diagnosis of medically ill patients includes syndromic and etiologic components. Regardless of the etiology, psychiatric manifestations are classified into 4 major syndromes: cognitive, including delirium and dementia; psychotic; mood; and anxiety. These categories were adopted by the American College of Rheumatology in 1999 to define NPSLE cases. The second step, the etiologic differential diagnosis, is often very difficult in SLE patients for the following reasons: (1) it is difficult to distinguish NPSLE from psychiatric disorders due to other etiology, such as corticosteroid-induced psychiatric disorders, solely on the basis of symptoms; (2) no disease-specific diagnostic markers or gold standard for NPSLE has been established; and (3) NPSLE may occur independently of the systemic activity of SLE. Therefore, the first step of the etiologic diagnostic work-up should involve excluding non-SLE-related conditions. The correct diagnosis is derived from careful analysis of the clinical, laboratory, and imaging data on a case-by-case basis. The choice of psychotropic drug for symptomatic treatments is based on the above-mentioned syndromic diagnosis. However, patients with SLE often develop stress-related psychological distress that manifests as depression or anxiety and requires stress management or supportive psychotherapy. This program reviews the status of the diagnosis and management of psychiatric symptoms in SLE patients, which will be useful for rheumatologists to establish a management strategy for NPSLE. The beneficial collaborative partnership with psychiatrists is also discussed.

MTE19

Assessment of plain X-ray imaging for rheumatic diseases

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Conflict of interest: Yes

Recent progress in clinical imaging technology with novel modalities

have contributed to diagnosis and management, as well as investigation of pathophysiology in rheumatic diseases. Indeed, plain X-ray is a "legacy" modality utilized for more than 120 years since discovery of X-ray by Wilhelm Conrad Röntgen in 1895. Nevertheless, plain X-ray is the most frequently used modality at both diagnosis and follow-up, especially for bone/joint and chest, in rheumatology to date, since plain X-ray is simple, inexpensive, and suitable for repeated test. Various findings are identified on bone/joint X-ray in rheumatic diseases. Erosion, joint space narrowing, and luxation/subluxation are common in rheumatoid arthritis (RA); especially, erosion is highly diagnostic. van der Heijde's modified total Sharp score (vdH-S score, mTSS) has been the standardized index for joint destruction in clinical trials for RA. Pencil-in-cup appearance, sacroiliitis, or bamboo-spine are characteristic for spondyloarthritis (SpA) including psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Linear calcification in joint space is characteristic for pseudogout. Various findings are observed on chest X-ray, as well. Interstitial lung diseases (ILDs) are common in several connective tissue diseases; however, degree of infiltration and fibrosis varies; infiltration is dominant in polymyositis/dermatomyositis (PM/DM) whereas fibrosis is dominant in systemic sclerosis (SSc). Pleuritis and pericarditis are often observed in systemic lupus erythematosus (SLE), airway lesions including bronchiolitis are often found in RA. Indeed, chest X-ray is quite important for screening infectious disorders including tuberculosis and pneumocystis at initiation and follow-up of immunosuppression with DMARDs or glucocorticoids, etc. In the session, active discussion with attendees will be encouraged about assessment of plain X-ray imaging for rheumatic diseases, viewing representative images.

MTE20

A primer of statistical analysis for clinical researches using R and EZR

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Conflict of interest: None

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

MTE21

Clinical significance and interpretation of the autoantibody testing in systemic autoimmune rheumatic diseases

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Conflict of interest: None

Anti-nuclear antibodies (ANA) are autoantibodies against nuclear proteins or nucleic acids (e.g., DNA) and high titer of ANA is one of the important clues for systemic autoimmune rheumatic diseases (SARD). ANA is sometimes recognized in sera from patients with rheumatoid arthritis (RA), but usually low titer. High positive ANA, therefore, may be useful for differential diagnosis of RA from other SARD. Anti-CCP antibody (Ab) positive RA patients may have other SARD if Raynaud's phenomenon and/or systemic organ disorders are evident along with high titer of ANA. New EULAR/ACR classification criteria for systemic lupus erythematosus (SLE), in which positive ANA (>= x80 using HEp-2 cell) is entry criteria, shows that SLE is SARD characterized by high titer of ANA. Interestingly, whereas a variety of ANA is found in an individual with SLE, single positivity of disease-specific ANA is usual in patients with polymyositis/dermatomyositis or systemic sclerosis. Determination of ANA, therefore, is important for making diagnosis and/or specific manifestations, or predicting prognosis in such SARD. Anti-MDA5 and anti-TIF1-γ Abs are associated with life-threatening interstitial lung disease and cancer-associated DM, respectively. In mixed connective tissue disease, anti-U1RNP Ab, which may be linked with pulmonary arterial hypertension or aseptic meningitis, is high positive. Also, in anti-synthetase syndrome (ASS) characterized by positive anti-aminoacyl tRNA synthetase Abs, interstitial lung disease is frequent. Thus, ANA seems to be more specific for disease manifestations than cytokines. Their pathogenesis, however, is not clear. Although neo-natal lupus syndrome (NLS) associated with anti-Ro/SS-A Abs strongly suggests their pathogenesis, a detailed mechanism of NLS is not evident. In this conference, history, measurement methods, and clinical utility of ANA testing will be presented and pathogenic role of a certain subset of ANA may be discussed.

MTE22

Clinical and immunological characteristics of macrophage activation syndrome: From the results of serum cytokine profile analysis

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Conflict of interest: None

Macrophage activation syndrome (MAS) is defined as secondary hemophagocytic lymphohistiocytois related to rheumatic diseases. Excessive activation and expansion of cytotoxic T cells and macrophages, and overproduction of proinflammatory cytokines play a central role in the pathogenesis of MAS. Although MAS has been associated with most rheumatic diseases, in pediatrics it is most common in systemic juvenile idiopathic arthritis (s-JIA). The genetic defects contributing to the development of cytolytic dysfunction including perforin, and chronic interleukin (IL)-6 and IL-18 exposure inducing secondary suppression of cytolytic function are also closely associated to the development of MAS. A trigger of MAS such as infection activates macrophage by interferon-γ, further amplifies the inflammatory response, leading to excessive production of cytokines and ultimately creating cytokine storm. MAS is a potentially fatal complication, and a proper diagnosis of MAS is essential to start appropriate therapeutic interventions. Once the complication of MAS is suspected, careful monitoring of platelets counts, serum AST, ferritin levels and coagulation test is necessary. We analyzed serum cytokine profile in patients with MAS associated with s-JIA. Serum IL-18 levels in patients with s-JIA were extremely high, in particular, in those with MAS. These levels reflected disease activity of s-JIA and MAS. Serum IL-18 levels were useful to predict MAS development. There were two distinct subsets on the basis of serum IL-6/IL-18 levels in s-JIA. Serum neopterin and sTNFRII/I ratio were useful for the diagnosis of MAS. In this lecture, we will learn the pathogenesis of MAS. Furthermore, we will discuss how we should diagnose MAS and how we should treat the patients with MAS through the case presentations.

MTE23

DNA Event Recording Biology

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Research Center for Advanced Science and Technology, Japan

Conflict of interest: None

Mammalian development, tumorigenesis, and other dynamic progressions of heterogeneous cell systems remain largely unclear. My laboratory has been developing "DNA event recording" technologies by which high-resolution molecular and cellular information is progressively stored in "DNA tapes" within synthetic chromosomal regions in individual cells. At the time of observation, the past information of cells of a target system

can be read out by high-throughput sequencing. This will resolve the current limitation in biology where high-resolution snapshots of cells in a complex system can only be analyzed at the time of observation. As a landmark goal, we aim to deliver synthetic mouse lines which contain high-performance DNA event recording systems in order to obtain a whole-body cell lineage and cell type differentiation trajectories of mammalian development at the resolution of single cells. I will talk about how we develop different biotechnologies to sense, record, store, and readout massive cellular histories by harnessing genome editing, DNA barcodes, genetic circuits and mouse engineering technologies as well as robotics.

Luncheon Seminar

LS1-1

Pathophysiology of rheumatoid arthritis from the viewpoint of T cell regulation

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an autoimmune disease that causes inflammation in systemic organs, especially joints, but may be an immunologically heterogeneous population. For example, there is a significant clinical difference between ACPA-positive rheumatoid arthritis and ACPA-negative rheumatoid arthritis, and the therapeutic response of the drug (for example, the ACR 70 response rate are similar by biologics despite various mechanisms (Nat Rev Rheumatol. 2015: 276-289.), and biologics with different mode of action are more effective than 2nd TNF for 1st TNF failure (JAMA. 2016; 316: 1172-1180.), etc.). And so on, there is a possibility of classification into groups such as T-cell or B-cell or innate immunity dominant. ACPA is an antibody against citrullinated peptide and is an antibody produced in a T cell-dependent manner. Consistent with such knowledge, it has been reported that abatacept, an agent that inhibits the interaction between antigen-presenting cells and T cells, is successful in ACPA-positive and high-value cases. Class 2 MHC HLA-DRB1, which is a disease susceptibility gene for rheumatoid arthritis, has a strong ability to bind citrullinated peptides in its risk genotype (mostly also called Shared Epitope; SE), thereby strongly activating T cells. It is also known that ACPA is a high titer among risk genotype holders. Considering the above, we reported that HLA-DRB1 genotype is related to efficacy of abatacept in Rheumatoid Arthritis (Ann Rheum Dis. 2018; 77: 1234-1236.). In this report, the efficacy of abatacept can be predicted more accurately by using risk genotype positivity than by the titer of ACPA. Approve of Abatacept and its analysis of clinical effects have enabled us to consider the pathophysiology of rheumatoid arthritis itself. We consider the possibility of precision medicine considering the immunological background of individual rheumatoid arthritis patients, along with knowledge such as ACPA and RF used in actual clinical practice.

LS1-2

T cell: a major protagonist in infection,cancer,and autoimmunity

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Conflict of interest: Yes

The host defense of higher vertebrates consists of two types of immune responses, innate and adaptive immunity, the latter of which is characterized by high specificity and immunological memory. Adaptive immunity is further classified into cellular and humoral immunity, in which T and B cells play a central role. Immunity is important in infectious diseases caused by intracellular and extracellular pathogens. The patients with primary immunodeficiency diseases that cause T cell dysfunction are often susceptible to both pathogens, thus suggesting that T cell is a major protagonist in such diseases. Moreover, given that the incidence of malignancies is high in immunodeficiencies and the HLA gene is closely associated with susceptibility to autoimmune diseases, T cells are again crucial in these diseases. T cells express an antigen receptor that recognizes the MHC peptide complex, and its downstream signal is fine-tuned by signals via many co-stimulatory/co-inhibitory molecules on the same cell. Therefore, co-stimulatory signals in autoreactive T cells potentially lead to the development of autoimmune diseases, while co-inhibitory signals in tumor-specific T cells are related to the development of malignancies. Based on these findings, inhibition of co-stimulation by CTLA4-Ig in autoimmune diseases and abrogation of co-inhibition by anti-PD-1 antibody in malignancies are both currently available in daily practice. In recent years, it has become possible to analyze gene/protein expression at the single cell level even in human samples. It is becoming evident that various T cell subsets with different functions are defined by expression of co-stimulatory/co-inhibitory molecules and involved in the pathogenesis of infectious diseases, cancer, and autoimmune diseases. In this seminar, I will discuss the role of T cells in the pathogenesis of these diseases, with a particular focus on recently

identified novel T cell subsets.

LS2-1

New insight of the PsA treatment in biologics era

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Conflict of interest: Yes

Psoriatic arthritis (PsA) is one of the spondyloarthritis which exhibits skin and nail psoriasis, peripheral arthritis especially in distal and proximal interphalangeal joint, dactylitis, enthesitis, sacroiliitis or spondylitis. The PsA concurrence rate of the skin psoriasis patient in Japan is thought to be about 10~15%, and a skin lesion is often seen before the PsA onset in about 70% of patients. The diagnosis of PsA is made in reference to CASPER classification criteria, composed of arthritis, spondylitis, enthesitis, negative for rheumatoid factor, current or past existence of skin psoriasis, typical nail symptom, erosion or whiskering in X-rays views of hands and feet. Once joint destruction of PsA became irreversible, the QoL of the patient would dramatically drop. It is necessary to be checked up and treated appropriately as soon as possible. It is well known that inflammatory cytokines such as TNF, IL-17, IL-23 play important roles in PsA. Biologic agents are applied clinical practice, including anti-TNF antibody, anti-IL-17A antibody, anti-IL-17 receptor antibody, and IL-23 inhibitor (anti-p40 antibody or anti-p19 antibody). Certolizumab-pegol, anti-TNF antibody combined with pegol, newly acquired adaptation for PsA. The choices of the PsA treatment increased, and treatment environment improved remarkably. We should decide how to treat patients based on enough talks with them, standing on the individual backgrounds; including a skin, bone and joint lesions, coexistence exhibitions such as uveitis, and comorbidity. There is no perfect treatment strategy for PsA with various clinical manifestations, and it still remains as a quest to cure completely both skin and joint. In this lecture, I would to like to discuss unclarified problems in PsA treatment.

LS2-2

The Possibility of Using Certolizumab Pegol for PsA Treatment

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Conflict of interest: Yes

Psoriasis is a typical disease classified as inflammatory keratosis and occurs in 0.34% of people in Japan. Psoriatic arthritis, characterized by arthritis, spondylitis, dactylitis, and enthesitis, occurs in about 10% to 15% of psoriasis. Compared with psoriatic lesions alone, psoriatic arthritis often coexists with symptoms related to metabolic syndrome (obesity 26%, hyperlipemia 43.9%, diabetes 15.1%, hyperuricemia 20.9%, hypertension 23.2%, and abnormal liver enzymes 29.2%). Furthermore, skin symptoms develop first in 70% or more patients with psoriatic arthritis, and the quality of life (QOL) is significantly compromised in many patients not only due to joint symptoms but also skin symptoms psoriatic lesions alone. Therefore, it is necessary to consider treatment aiming to achieve a balance between improvement of joint symptoms and skin symptoms when treating psoriatic arthritis. What will be the best treatment to achieve better QOL for patients with psoriatic arthritis? First, improving diseases related to metabolic syndrome by proactively providing basic instructions, such as lifestyle guidance, exercise therapy, and nutritional guidance, is considered to be one of the keys that can maximize the benefits of drug therapy and contribute to increasing the adherence rate. Another treatment option is medication. Biological products for psoriasis and psoriatic arthritis have been covered by the national health insurance plan in Japan since 2010, which has dramatically changed the treatment of psoriasis and helped improve the patients' QOL. However, the current treatment with biological products cannot be said to be fully effective for both joint and skin symptoms. In 2019, certolizumab pegol, a TNF inhibitor, was newly approved for coverage by the national health insurance plan for treatment of psoriasis and psoriatic arthritis. In this lecture, I present the latest findings on psoriatic arthritis, and the positioning and possibilities of certolizumab pegol.

LS3

The remaining problems for rheumatoid arthritis

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Conflict of interest: Yes

Advances in the treatment of rheumatoid arthritis have significantly increased the proportion of patients who can achieve their therapeutic goal such as clinical remission or low disease activity. On the other hand, there are some patients who cannot reach that goal even in the standard treatment. Moreover, recent advances in sensitive imaging such as ultrasound and MRI have revealed that there are some patients with residual active synovitis even in well controlled disease activity. These days, patients who cannot suppressed disease activity or with remaining active synovitis, it is expressed as difficult-to-treat rheumatoid arthritis (refractory rheumatoid arthritis). The cause of refractory rheumatoid arthritis is considered multiple, but one of the problems is adherence of the drug. MTX is one of the most difficult drugs to improve adherence because of the various adverse events. In addition, self-injection biologics with a long interval tends to have higher adherence and a higher therapeutic effect. Furthermore, in patients who have difficulty in self-injection, biologics are administered by injection or infusion in-hospital, but the frequency of administration and the simplicity of the administration method are important factors in the continuation. Furthermore, biologics that can be increased the dose or shortened the interval in cases with insufficient effect may be useful for intensive drug treatment in order to prevent development of refractory rheumatoid arthritis patients. Moreover, although the therapeutic effect of drug treatment has been improved, how to restore the joint function that have already been destroyed should be also considered. To improve a patient's lost ADL, it is necessary to pay attention at the joint level, such as joint protection guidance, brace therapy, and surgical therapy. In this session, I would like to discuss the remaining problems for rheumatoid arthritis to prevent development of refractory rheumatoid arthritis patients.

LS4

Proper use of biologic product for Rheumatoid Arthritis in view of self-pay burden of medical expenses

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Conflict of interest: Yes

Owing to the advent of biologics for rheumatoid arthritis (RA), the treatment for patients with RA has dramatically improved, with clinical remission becoming a realistic goal. However, because of high self-pay of medical expenses, there are still many patients who cannot benefit from biologics. Once the disease has been controlled, dose reduction and prolongation of dosing intervals (spacing) are considered to reduce the cost of the drugs. We prolonged the standard dosing intervals by 1.5 times in patients whose disease activity was controlled to the low level with three drugs with different mechanisms of action TCZ, GOL, and ABT, and compared continuation rates of individual treatments for up to 104 weeks in study. The results revealed that treatment with prolonged spacing could be continued for up to 104 weeks in about 70% of patients treated with TCZ or GOL. However, in those treated with ABT, relapse of disease activity was observed at week 52, and the continuation rate for up to 104 weeks was about 50%. Another way to reduce the self-pay burden of medical expenses is the use of biosimilars (BS). The drug prices of BS are stipulated to be 70% of the prices of their respective reference products (RP) less price maintenance premiums (about10%); thus, the actual prices of BS are limited to about 60% of the prices of RP. In Japan, BS of two drugs (IFX and ETN) for RA are already marketed, and the ADA-BS is planned to be launched. The properties of BS, in comparison to RP, are required to satisfy the following: the amino acid sequence must be the same as that of RP; there are no differences in the appearance rate between anti-drug antibodies and neutralizing antibodies; and ADCC activity due to differences in sugar chain structure should be within an acceptable range. Both IFX-BS and ETN-BS already marketed satisfy these criteria, and no differences in

their efficacy were observed when the original IFX and ETN were switched to IFX-BS and ETN-BS, respectively

LS5

Progress with the use of belimumab for the treatment of systemic lupus erythematosus

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is pathologically characterized by immune complexes consisting of antigens, activation of dendritic cells and autoreactive T cells and overproduction of autoantibodies secreted from activated B cells, which cause severe inflammation in various organs. B cells play a pivotal role in autoimmunity not only by producing pathogenic autoantibodies but also by modulating immune responses via production of cytokines and chemokines. BAFF promotes B cell survival and differentiation and thus plays a prominent role in the pathogenesis of SLE. Recent clinical trials demonstrated the efficacy and tolerability of belimumab as a novel biologic agent for the treatment of SLE. Belimumab has a potential, not only for the suppression of disease activity, but also for the prevention of the exacerbation of disease activity and steroid sparing effect. We analyzed the relationship between the phenotype of peripheral immune cells with clinical manifestations and responsiveness to the treatment in patients with SLE. The data indicated that belimumab has positive effects in sparing glucocorticoids and improve control of disease activity without significant side effects. By immunophenotypic analysis, we found that belimumab inhibits the differentiation of B cells, as well as the activation of pathological T helper cells, indicating that the reconstitution of the B cell compartment results in the inhibition of T cell activation by memory B cells, which might lead to the sustained remission of SLE. However, many questions remain to be addressed about the ideal combined therapy with belimumab for the long-term outcomes of this disease. In this seminar, we highlight recent advances that pertain to this topic and the impact of targeting BAFF in the treatment of SLE.

LS6-1

Assessment of bone mineral density and treatment of osteoporosis in rheumatoid arthritis -the significance and implications-

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Conflict of interest: Yes

Recent advancement in the treatment of rheumatoid arthritis (RA) has dramatically improved the disease activity and functional impairment in patients with RA. However, it is reported that the ratios of fragility and insufficient fractures has not significantly been reduced in RA. Those fractures drastically worsen life expectancy as well as activity of daily life and quality of life in the patients, and the preventive measures for the fractures are critical in daily clinical practice. Therefore, improvement in bone metabolism is imperative for the purpose of decreasing the chances of those fractures. On the other hand, bone mineral density has been utilized as a surrogate marker in management of osteoporosis, but the values of assessing bone mineral density may not be limited to the purpose. A reliable report shows that, even after adjustment with the incidence of fracture and age, patients with lower bone mineral density expects shorter life expectancy. Moreover, osteoporosis and low bone mineral density are potently related with pathophysiology and clinical manifestation of RA including joint destruction. In this seminar, the presenter will show the significance and implications of osteoporosis treatment and assessment of bone mineral density in RA by literature review and data from our institute to try to help clinical practice of RA.

LS6-2

The inhibitory effect on bone erosion progression with denosumab

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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) treatment.

LS7-1

Current situations and challenges in RA treatment from NinJa Registry; Looking also at potentials of tofacitinib;

Shigeto Tohma
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Conflict of interest: None

Advances in the treatment of rheumatoid arthritis (RA) such as introduction of methotrexate (MTX) and many biologics (bDMARD) enhanced diagnostic technique, enabling early diagnosis and provision of appropriate treatment in early stage, and treatment in accordance with the treat-to-target (T2T) strategy made achieving clinical remission realistic. In order to clarify the present state and issues of RA patients in Japan, the National Database of Rheumatic Diseases in Japan (NinJa) continuously performs epidemiological and observational research and evaluates the trend. The changes over time show an increase in the percentage of latter-stage elderly patients and higher mean age of the patients. Disease activity decreased over time, clinical remission rate increased, and patient QOL improved. For treatment, the use rates of steroids and NSAIDs decreased over time, whereas the use rates of anti-rheumatoid drugs including bDMARDs and JAK inhibitors increased over time. The use rates in 2018 were 60.6% for MTX, 27.1% for bDMARDs, and 2.9% for JAK inhibitors. How should JAK inhibitors be used for patients with such background? Although JAK inhibitor tofacitinib is an oral drug, it has high antiinflammatory effect and showed efficacy in combination with MTX or as monotherapy in patients with various backgrounds in clinical studies. As the advantages of using tofacitinib, tofacitinib is expected to have an onset of efficacy in early stage; is an oral drug; is not prone to cause anti-drug antibody; and has the evidence of monotherapy. It has been over 6 years since tofacitinib became available in 2013; with the market launch of several JAK inhibitors, JAK inhibitors are drawing a lot of attention. For the positioning in RA treatment, JAK inhibitors were initially the third treatment option for inadequate responders to MTX and bDMARDs. However, with the accumulation of long-term efficacy and safety data, the position was recently elevated and JAK inhibitors were added as a treatment option along with bDMARDs in Phase II in EULAR recommendation (2016). On the other hand, consideration to safety is needed similarly to bDMARDs; it is critical to perform screening prior to treatment and careful monitoring and ensure systemic management.

LS7-2

Safety Information Update: Tofacitinib for Rheumatoid Arthritis Treatment

Kimito Kawahata
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Conflict of interest: Yes

Tofacitinib citrate became available as a therapeutic drug for rheumatoid arthritis (RA) for "RA in patients who have not adequately responded to conventional treatments" in Japan on March 25, 2013. This oral drug has a mechanism of action that regulates the activated cytokine network in RA patients by inhibiting the signaling of multiple cytokines which use the Janus kinase (JAK) pathway. While this drug with a novel function of immunoregulation was expected as a new option for RA treatment, a Special Investigation (all-cases surveillance) has been conducted in RA patients to verify the safety due to safety concerns, especially the onset of serious infection and malignant tumor. In 2019, it has been six years since the launch; more than 10,000 RA patients have used the drug after the market launch, gradually unveiling the safety profile. In Proper Use Information Vol. 12 provided by Pfizer, the occurrence status of adverse drug reactions (ADRs) at 6-month observation and the baseline characteristics of patients at the start of the survey were tabulated for patients who were enrolled in the Special Investigation (all-cases surveillance) for RA and whose data were fixed by August 31, 2018 (patients included in safety analysis: 6,567 patients in the tofacitinib group and 2,389 patients in the control group). In addition, with the progression of data lock for followed-up patients, data have been accumulated on changes in cumulative incidences in long-term follow-up (from the start of administration to Month 36) and changes in incidences by follow-up category (from the start of administration to Month 1, Month 2-3, Month 4-6, Month 7-12, Month 13-18, Month 19-24, Month 25-30, Month 31-36) per 100 persons/year for serious adverse events (AEs) to XELJANZ, i.e., serious infection, herpes zoster, malignancy tumor, and interstitial pneumonia. On the day, I plan to introduce the safety information at 6-month follow-up of the tofacitinib group, for which the approval conditions for the enrollment of all RA patients were lifted by the Ministry of Health, Labour and Welfare (MHLW) as of September 2, 2019.

LS8-1

Reconsider the effectiveness of the new csDMARDs in the era of Biologic agents. ~From the view point of the utility of musculoskeletal ultrasound~

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Conflict of interest: Yes

Treat to target (T2T) concept and treatment strategy based on T2T has also established in rheumatoid arthritis (RA) as well as other diseases. Biologics (Bio) have significantly altered both clinical outcome and prognosis of RA, however not all of Bio are available as a first line RA-treatment with csDMARDs. All of the RA-treatment guidelines such as ACR, EULAR and JCR recommend the csDMARDs including MTX as an initial therapy. Iguratimod (IGU) is one of the csDMARDs invented in Japan, but IGU is not listed in the JCR treatment recommendation up to now, IOW Rheumatologist in Japan have the precious treatment arm by using IGU and have the possibility to elucidate the novel evidence about IGU. Musculoskeletal ultrasound (MSKUS) in one of the best tools for RA in aspect of non-invasive and real-time examination. MSKUS can depict the subtle subclinical findings, contribute not only to early RA-diagnosis, but also to treatment strategy concerned with avoiding the bone destruction, i.e. structural remission. It is suggested the therapeutic evaluation under the MSKUS-examination could distinguish from clinical remission, partial response and treatment failure with visualization to some extent. Moreover, it is the time to show our stuff how to compose the treatment strategy for the patient not achieved T2T purpose even if Bio is administered. Although dose increasing, period shorting or switch of Bio and then some; next treatment candidate focused on Bio are apt to be selected, adding other csDMARDs seems to be one of the best interest in terms of medical economy. It is already reported that many refractory RA cases can be ameliorated by adding IGU with Bio or MTX, and personally it seems to be a credible method that co-treatment with IGU judged by MSKUS findings is noteworthy. In this session, I'll introduce the efficacy and safety of IGU combination therapy with Bio or MTX based on MSKUS evaluation as a novel treatment strategy not precedent in the world.

LS8-2

New development of RA treatment with csDMARDs - Latest findings from clinical use -

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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has changed significantly in recent years with the advent of oral anti-rheumatic drugs (csDMARDs) centered on methotrexate (MTX), biological agents, and JAK inhibitors, and has undergone a paradigm shift. Active administration of these drugs was recommended from the early stage of onset, and it was possible to achieve remission and low disease activity at a high rate. On the other hand, an increase in medical costs has also been a problem in recent years. In addition, Japan entered an aging society in the 1970s, and entered a super-aged society in 2010. The sudden increase in medical expenses and social security costs associated with it is a social problem. It is difficult to take MTX in a sufficient amount due to an increase in the number of cases and an increase in the prevalence of comorbidities such as chronic kidney disease and pulmonary disease associated with aging of RA, and it is difficult to treat often experienced. Salazosulfapyridine (SASP), bucillamine (BUC), tacrolimus (TAC) and iguratimod (IGU) are csDMARDs that have been widely used in daily clinical practice for patients who have difficulty taking MTX or who have insufficient MTX effects. Is also very important from the viewpoint of RA disease activity control and medical economy in daily medical care. Among them, IGU suppresses NF-κB (nuclear factor-kappa B) activity, inflammatory cytokine production in macrophages and synovial cells, antibody production centering on rheumatoid factor in B cells. It is the only new csDMARDs that have been proven to have an equivalent therapeutic effect. In this presentation, I will discuss the combined effects of MTX in IGU, clinical effects as 1st csDMARDs and steroid spring effect, and the possibility of IGU in daily practice in the future.

LS9-1

Interleukin-6 as a Pathogenic Factor of Systemic-onset Juvenile Idiopathic Arthritis

Takako Miyamae
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Conflict of interest: Yes

Systemic juvenile idiopathic arthritis (sJIA), one of the subtypes of JIA, is considered as a polygenic autoinflammatory disease. The prominent systemic inflammatory manifestations, the marked elevation of inflammatory markers, and the absence of autoantibodies make this disease very different from the other JIA forms. The overproduction of inflammatory cytokines, IL-6 and IL-1, of innate immunity is a typical feature of sJIA. Remarkable effects have been observed with inhibitors against these cytokines both in clinical trials and in real life. sJIA patients refractory to conventional treatments previously suffered from a variety of growth disorders. Inflammation and glucocorticoid therapy are the major factors involved in growth retardation seen in children with severe forms of sJIA. Growth disorders in sJIA are associated with increased production of pro-inflammatory cytokines, such as IL-1 β, TNF- α and IL-6. Catch-up growth was observed in patients who required less or no corticosteroid during tocilizumab treatment. Long-term outcomes of sJIA are highly variable. Between 40% and 50% of patients have a self-limited course, either monocyclic or polycyclic. On the contrary, some s JIA patients begin with a highly inflammatory febrile phase that converts over time to an afebrile phase characterized by chronic arthritis requiring extended anti-inflammatory therapy, even into adulthood. It is important to understand the pathology of the afebrile chronic arthritic sJIA will help to identify which strategy is associated with the best outcome though a hypothesis has been reported that sJIA could evolve from a disease of predominantly au-

toinflammatory character into one sustained by autoimmunity.

LS9-2

IL-6 blocking therapy in adult Still's disease

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Conflict of interest: Yes

The concept of adult (≧16 years old) Still's disease (ASD) includes adult-onset Still's disease and carry over of systemic juvenile idiopathic arthritis, which is characterized by fever, rash and arthritis. Recently, the reports on elderly-onset Still's disease have been increasing. An intensive differential diagnosis is prerequisite for the diagnosis as ASD with referring to Yamaguchi criteria: (sepsis and viral) infections, (hematological) malignancies and (vasculitic) rheumatic diseases. Although the precise pathogenesis of ASD has been unrevealed, systemic hyperproduction of pro-inflammatory cytokines usually leads to the marked elevation of serum ferritin level in ASD. Consequently, biological agents targeting pro-inflammatory cytokines such as tumor necrosis factor, interleukin (IL)-1ß and IL-6 have been examined for ASD, and tocilizumab, an anti-IL-6 receptor monoclonal antibody, is the first-in-the-world biological agent approved for ASD in May 2019 in Japan. Tocilizumab shows rapid and high efficacy for ASD, although it should be co-administered with glucocorticoids for active disease with sufficient dosing amounts and intervals to avoid the development of macrophage activation syndrome because of hyperproduction of the above various pro-inflammatory cytokines.

LS10

Forefront of diagnosis and treatment for Sjögren's syndrome: Topics in 2020

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Conflict of interest: Yes

Sjögren's syndrome (SS) is an autoimmune disease which affects salivary and lacrimal glands, accompanied with various autoantibodies and extra-glandular manifestations. In this seminar, we introduce 1) comparison of different sets of diagnostic and classification criteria, 2) assessment of disease activity, 3) clinical practice guidelines for SS in all over the world, and 4) usefulness of new therapeutic strategy by biologics and targeted synthetic drugs for SS. 1) The research team of MHLW clarified that the revised Japanese Ministry of Health criteria (1999) had acceptable sensitivity and specificity (both over 75%) for diagnostic criteria, while it's sensitivity was lower than that of ACR-EULAR criteria (2016). 2) Two tools such as ESSDAI which is based on objective evaluation by physicians, and ESSPRI which is a patient reported outcome have been developed for assessment of disease activity of SS. ESSDAI≧5, which is a definition for moderate disease activity, is usually used as inclusion criteria in RCT as well as severity criteria for designated intractable disease in Japan. In our cases, 58% of SS patients had ESSDAI≧5. 3) Adding to the treatment guideline by SS Foundation in USA, the management guideline by British Society for Rheumatology, and clinical practice guideline for SS 2017 developed based on Minds by the guideline committee of MHLW, EULAR recommendations have been published in 2019. Pilocarpine is recommended for the treatment for dry mouth in these guidelines. 4) Effectiveness of rituximab and abatacept has been revealed in RCT and open label studies, and these biologics are suggested for some cases in the guidelines described above. Belimumab and anti-CD40 were effective in an open label study and in RCT, respectively, while TNF inhibitors, baminercept, anti-BAFF-R, and anti-ICOS-L were not effective in current RCT. RCT for combination of belimumab plus rituximab, or tocilizumab, or targeted synthetic drugs against BTK, SYK, and JAK1 is now ongoing.

LS11-1

The role of IL-6, interferon gamma, and autophagy in rheumatoid arthritis

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Conflict of interest: Yes

Janus kinase (JAK) inhibitors have been successful in the treatment of rheumatoid arthritis (RA) with their high anti-inflammatory and joint protective effects. The JAK inhibitor baricitinib has a selectivity for JAK1 and JAK2 among the members of JAK family including JAK1, JAK2, JAK3 and TYK2. Since IL-6 and interferon (IFN) γ recruit a heterodimer of JAK1 and JAK2 in their signal transduction, the effect of baricitinib may be through the inhibition of these cytokines. The pathogenic role of IL-6 in RA has been supported by a number of basic studies and the clinical effect of anti-IL-6 receptor antibodies, including tocilizumab and sarilumab, whereas it remains to be elucidated how IFNγ contributes to the development and progression of RA. Recently, we have shown an emerging role of IFNγ in the pathogenesis of RA. Following stimulation with IFNγ and induction of autophagy by starvation or proteasome inhibition, vimentin, whose citrullinated form is one of the major autoantigens targeted by anti-citrullinated peptide antibodies, was more citrullinated and subsequently recognized by MHC class II in synovial fibroblasts (Sugawara E, Kato M, et al. Autophagy in press). Moreover, single-cell transcriptomics demonstrated the abundance of MHC class II, IL-6 and IFNγ-inducible protein 30 upregulated fibroblasts in RA synovial tissues (Zhang F, et al. Nat Immunol 2019). In this seminar, I would like to discuss how baricitinib exerts a high therapeutic effect for RA by focusing on the pathogenic role of IL-6 and that of IFNγ.

LS11-2

Role of JAK inhibitors for the treatment of rheumatoid arthritis

Motomu Hashimoto
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Conflict of interest: Yes

JAK inhibitors simultaneously inhibit multiple cytokine signaling, different from bDMARDs which inhibit only one cytokines such as IL-6 or TNF. Although IL-6 signaling is inhibited by both bDMARDs (IL-6 receptor antibody) and JAK inhibitors (gp130 inhibition), some important cytokines such as GM-CSF or IFN-α are not inhibited by previous bDMADS, although they play important roles in the pathogenesis of RA. GM-CSF, transmitted through JAK2 homodimer, is a common effector cytokine for Th1 and Th17 cells and it was shown that some inflammatory condition could be suppressed by GM-CSF inhibition but not by IFN-γ or IL-17 inhibition in animal models. GM-CSF signaling is also involved in the perception of pain, therefore JAK inhibitors might be useful to relieve pain who have intractable pain even after previous treatments. Also, there is an equilibrium between IFN-α and TNF in the body and TNF inhibition by bDMARDs (anti-TNF antibody) increases IFN-α signature, which could lead to the treatment resistance by TNF inhibitors. Because RA patients are very heterogenous, some patients may be more suitable to be treated by JAK inhibitors which simultaneously inhibit multiple cytokine signaling including IL-6, GM-CSF and IFN-α. In this seminar, the role of JAK inhibitors in RA and suitable patients to be treated by JAK inhibitors will be discussed.

LS12

Update on Familial Mediterranean Fever

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Conflict of interest: Yes

Familial Mediterranean fever (FMF) is caused by MEFV gene mutations, which induce dysregulation of pyrin inflammasome. The clinical symptoms consist of periodic fever lasting 12 to 72 hours and serositis. Typical type of FMF patients usually have MEFV gene variants residing

on exon 10 and respond to colchicine very well. Long lasting inflammation due to FMF cause AA amyloidosis that induce organ damage such as renal failure, thus FMF patients that do not respond to or do not tolerate colchicine need to be treated with other drugs. Recently, humanized anti-human IL-1β mAb, canakinumab has been approved to such patients. The canakinumab has improved dramatically treatment strategy for colchicine-resistant or colchicine-intolerant FMF patients. On the other hand, some issues regarding FMF have been raised. Another type of FMF, called FMF atypical type, has been proposed in Japan, whose clinical profile includes different duration of fever than typical type of FMF, less prominent serositis, less specific clinical symptoms of FMF, and good response to colchicine. FMF atypical type has been described in the clinical guideline of the autoinflammatory disease 2017, but the recommendation for its treatment is not mentioned. Accumulation of evidence is needed to propose the recommendation for FMF atypical type. In addition, Pyrin-Associated Autoinflammation with Neutrophilic Dermatosis (PAAND) has been described as an MEFV-related autoinflammatory disease. Now the new disease term Pyrin-associated autoinflammatory disease has been proposed for all the MEFV-related autoinflammatory diseases. The guideline for the diagnosis and treatment for these diseases also needs to be explored. In this luncheon seminar, I will summarize the recent updated information on MEFV-related autoinflammatory diseases including the pyrin inflammasome. I hope this seminar could promote the undersanding of FMF to achieve the better care for the FMF patients.

LS13

Pathophysiology and management of psoriatic arthritis

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Conflict of interest: Yes

Psoriatic arthritis (PsA) is one of the diseases comprising spondyloarthritis (SpA) and the most prevalent disease classified as peripheral SpA. In PsA, inflammation initially occurs at various entheseal sites and frequently expands to the surrounding soft tissues and the bone. These inflammatory lesions are clinically recognized as peripheral arthritis, spondyloarthritis, enthesitis, or dactylitis and result in the characteristic mixture of osteolytic and osteoproliferative bone changes. Enthesitis in PsA develops under genetic and environmental backgrounds and involves various types of cells related to innate-/acquired-immunity or inflammation and various cytokines. IL-23/IL-17 axis is an important treatment target pathway in the pathogenesis of PsA and is considered to play a central role particularly in the skin lesion and enthesitis. Recently, different roles of IL-23 and IL-17 between peripheral and axial diseases have been reported, the underlying mechanism of which has become of research interest. Finally, early intervention against immune/inflammatory dysregulation is necessary to prevent structural damage and functional impairment in PsA. On the other hand, a wholistic approach is important, taking into account the other possible organ involvement and the risks of adverse events.

LS14-1

Clinical features and diagnosis points of elderly RA patients

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Conflict of interest: Yes

Japan is facing an aging society and patients with rheumatoid arthritis (RA) have been aging with improved prognosis due to the use of biologics and JAK inhibitors in addition to methotrexate. Also, the number of elderly onset RA (EORA) is increasing, and it is not uncommon that more than half of rheumatic outpatients are older than 65 years. The cause of EORA in elderly people with immunosenescence is unknown, but the aging immune system may be involved. The diagnosis and treatment of RA have been changed with aging of RA patients. In recent years, the concept of T2T (treat to target) appeared. Early diagnosis and speedy intensive therapy have become an important treatment strategy to improve the prognosis of RA. However, the diagnose of EORA is difficult because of its symptom manifestations and immune responses unlike RA. The frequency of seronegative EORA patient that is negative for rheumatoid factor and anti-CCP antibody is high, and the diagnostic sensitivity of the classification criteria of ACR / EULAR, a tool for early diagnosis of RA, is low. As EORA can develop from the shoulder joint, it is often difficult to differentiate from polymyalgia rheumatica (PMR). We also need attention to temporal aortitis associated with PMR, RS3PE, arthritis due to paraneoplastic syndromes. It means that differential diagnosis is very important. EORA is characterized by high levels of inflammatory mediator such as IL-6 and CRP, high disease activity, and early progressive joint destruction. Since IL-6 has an ability to induce the differentiation of osteoclasts from bone marrow cells and synovial cells, the increase of IL-6 has a possibility to progress bone destruction. In addition, the knee joint is frequently damaged in EORA, it tends to fall into a “frailty” or the decrease of ADL due to irreversible physical function. So intensive treatment after early diagnosis is required. However, it is necessary for elderly people to consider various complications such as the decrease of organ function and the increase of risk of infection. In this luncheon seminar, we will outline the points of diagnosis of EORA, focusing on its clinical features and differential diagnosis from other diseases.

LS14-2

Therapeutic strategy for the elderly with rheumatoid arthritis

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Conflict of interest: Yes

In recent years, aging of patients with rheumatoid arthritis (RA) is remarkable in Japan. In elderly people, when they result in a state of immobility, their physical and cognitive functions quickly decline, and activity of daily living (ADL) hardly recovers even if the causative event is resolved. Features of elderly-onset RA include subacute-to-acute onset, predominant involvement of large joints, and concomitant wasting conditions such as weight loss, leading to disability. Therefore, it is necessary to improve ADL promptly in such patients. To achieve this goal using disease modifying anti-rheumatic drugs (DMARDs), we need to take account of characteristics of the elderly, including the impaired physiological function and dysfunctional acquired immunity. In elderly people, metabolism, inactivation, and excretion of low-molecular compounds are delayed because of decreased kidney and liver function. Furthermore, drug interactions are common in the elderly due to polypharmacy. Therefore, side effects caused by low-molecular compounds are more likely to occur in the elderly than in younger people, and dosage adjustment and frequent monitoring are required. Also, risk of metabolic side effects by corticosteroid use is more prominent in the elderly. On the other hand, biologics are not affected by kidney or liver function. Use of corticosteroids, methotrexate, biologics, and JAK inhibitors further increase the risk of serious infections due to impaired acquired immunity. On the other hand, recent cohort studies have shown that disease activity of RA correlates with the risk of serious infection, and that DMARD treatment can reduce the risk of infection as a result of suppression of the disease activity. Considering the physical characteristics of the elderly, there is advantage in the use of biologics over corticosteroids and low-molecular compounds. It is a good time to develop the therapeutic strategy specific to patients with elderly-onset RA.

LS15-1

The significance of neutralizing TNF-alpha for the Patients of Rheumatoid Arthritis from the synovium point of view

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Conflict of interest: Yes

With the emergence of biologics and JAK inhibitors that target specific pathological molecules, the main goals of treatment of rheumatoid arthritis (RA) are now (1) induction of clinical remission, (2) suppression joint destruction and functional disability, (3) maintenance of remission, (4) improvement of life prognosis. However, the remission rate of RA at present is still 50-60%. To improve remission rates, biomarkers that reflect the patient’s situation are needed. Recently, along with the advancement of biopsy techniques and technological innovations such as single cell analysis, attention has been focused on the search for biomarkers based on the

analysis of synovium, which is the site of inflammation. In the first half, we will outline the molecular basis assumed as a process of the formation of Chronicity as RA and the formation of pannus, which is a synovial tissue oriented to bone and cartilage destruction, which has been clarified from recent synovial research. Clinically, when selecting a molecular target drug to suppress joint destruction, it is necessary to consider sequentially: (1) How quickly the effectiveness of the drug can be determined; (2) Optimizing the switching. When introducing biologics at our facility, be sure to be hospitalized using a clinical path, conduct screening tests such as CT for risk assessment, determine indications, and follow-up evaluation of patients So we have managed effectiveness and safety as the FIRST registry. This time, focusing on TNF inhibitors, in particular, I would like to take the opportunity to rethink the significance of TNF inhibition by summarizing previous clinical studies and the data from the FIRST registry.

LS15-2

Clinical efficacy of certolizumab pegol in rheumatoid arthritis patients in daily clinical practice

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Conflict of interest: Yes

Methotrexate is a key drug in the modern treatment strategy for rheumatoid arthritis (RA). When a sufficient dose of MTX is used in combination, as shown in the various guidelines, all biologics and JAK inhibitors demonstrate similar effectiveness. However, when the dose of concomitant MTX is insufficient, it is necessary and important to select an appropriate agent in consideration of each drug characteristic. In the previous reports, certolizumab pegol (CZP) demonstrated significant suppressive effect on joint destruction in the patients with low dose concomitant MTX. In the data from Japanese clinical trials, CZP suppressed the delta mTSS to less than 0.5 points/year in C-OPERA study (high dose MTX), J-RAPID study (low dose MTX), and HIKARI study (no concomitant MTX). It is unclear why CZP provided the MTX dose-independent effects on joint destruction. Possible reasons are the very high trough serum concentration of CZP and the small molecular weight of CZP compared to full-size antibody preparations, easy to migrate to arthritic tissue. Furthermore, CZP can demonstrate the stable suppressive effect on joint destruction even in the patients with high titer of rheumatoid factor (RF). Since RF is an antibody recognizing the Fc region of denatured IgG, the trough serum concentration and the effect of full-size antibody agents can be affected by RF. On the other hand, CZP has no Fc region and this structural characteristic could result in the stable effect of CZP independent of RF titer. The aging of RA patients has been emerging as a clinical problem in recent years. The number of patients who can use only low dose or no MTX because of the decreased renal function has been increasing and will be increased in the future. The agent like CZP of which effectiveness is independent on MTX dose would be useful treatment option in such patients.

LS16-1

Role of co-stimulation inhibition for ACPA positive rheumatoid arthritis-focusing on RA-ILD and immune aging-

Motomu Hashimoto
Department of Advanced Medicine for Rheumatic Diseases, Kyoto University

Conflict of interest: Yes

ACPA is a representative diagnostic marker for RA and have a direct joint destructive effect. ACPA is produced by the help follicular helper T cells (Tfh) which interact with germinal center B cells in the lymphoid follicles of the lymph nodes of spleen. Because co-stimulatory molecules such as CD80/86 and ICOS is critically involved with the differentiation of Tfh, Abatacept, a T cell co-stimulation inhibitor, reduce Tfh and is more effective in ACPA positive RA compared with ACPA negative RA. In RA, ectopic lymphoid follicles are present in the joint tissue or the lung. In interstitial lung disease (ILD) associated with RA, ACPA is produced at the site of ectopic lymphoid follicles in the lung. Abatacept may inhibit the development of ectopic lymphoid follicles and could inhibit the progression of RA-ILD. In elderly RA patients, naïve T cells are reduced by the atrophy of thymus and limited number of T cells are expanded and differentiated into effector/memory T cells through homeostatic proliferation. Because self-reactive T cells are selectively expanded through homeostatic proliferation, elderly RA patients have increased number of self-reactive T cells and high titer of ACPA. Increase of effector / memory T cells and high titer of ACPA is associated with treatment resistance to various anti-rheumatic drugs. In this regard, Abatacept inhibit effector /memory T cell differentiation and ACPA production, thus is equally effective to elderly RA as well as young RA. In this seminar, the pathogenic mechanism of ACPA and usefulness of Abatacept for ACPA positive RA, in particular RA-ILD and elderly RA will be discussed.

LS16-2

Therapeutic strategy of rheumatoid arthritis targeting osteoclasts

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Conflict of interest: Yes

Recent advances in therapeutics have enabled better control of disease activity in patients with rheumatoid arthritis (RA), and appropriate use of methotrexate, biologics, and JAK inhibitors can induce remission. We have reported that total knee arthroplasty and total hip arthroplasty have greatly decreased over the past 10 years, based on a study using the national database (NinJa). On the other hand, the number of operations for osteoporosis has not decreased. RA patients are known to have a high rate of osteoporosis, which is caused not only by inflammation but also by steroid use, immobility, and lack of vitamin D due to short sunshine hours. The osteoclast differentiation factor RANKL (receptor activator of nuclear factor kappa B ligand) plays a central role in RA bone destruction, and anti-RANKL antibody denosumab not only increased bone density in RA patients but also suppressed the progression of bone erosion. We have shown that CTLA4-Ig abatacept inhibits RANKL-induced osteoclast formation from mouse bone marrow cells by suppressing intracellular calcium oscillations. In this seminar, I would like to introduce recent topics focusing on the effects of abatacept on RA disease activity and osteoclast differentiation.

LS17

Risk of Hepatitis B Virus Reactivation after Immunosuppression/ Chemotherapy and Countermeasures: Current Evidence and Future Perspectives

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Conflict of interest: Yes

Reactivation of hepatitis B virus (HBV) has been reported as a complication following immunosuppression/chemotherapy, resulting in fulminant hepatitis in some cases with a fatal course. In the past, many cases have been reported in hepatitis B surface antigen (HBsAg)-positive patients, but reactivation (de novo hepatitis B) in HBsAg-negative patients (patients with history of HBV infection) has been reported after introduction of molecular-targeted drugs such as anti-CD20 antibody and anti-TNF antibody. Recently, a multicenter, prospective observational study of patients with anamnestic infections showed the risk of HBV reactivation (defined as an increase in HBV DNA) to be 10% and 5% following treatment with anti-CD20 antibodies and anti-TNF antibodies, respectively. In addition, given the increasing number of reports of de novo hepatitis B associated with novel molecular targeted drugs, the risk of HBV reactivation following immunosuppression/chemotherapy may change in clinical practice in the near future. In accordance with the Guidelines for the prevention of HBV reactivation in patients receiving immunosuppressive therapy or chemotherapy described in the in the JSH Guidelines for the Management of HBV Infection, which was revised as Ver.3.1 in March 2019 by the Japan Society of Hepatology, the risk of HBV reactivation should be evaluated by hepatitis B core (HBc) antibody, HBs antibody, and HBV DNA quantitation in addition to HBsAg test performed at screening, and the antiviral drug should be administered for HBsAg positive patients, and measures should be taken by monitoring HBV DNA in patients with past history of infection. In this lecture, the latest evidence on

the risk of HBV reactivation after immunosuppressive therapy/chemotherapy and countermeasures are outlined, and future prospects are described.

LS18

TNF inhibition and crosstalk between TNF-producing cells and receiving cells in the inflamed joint of rheumatoid arthritis

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Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), treatment results are dramatically improved by the use of molecular targeted drugs, and clinical remission can be achieved in about half of patients. However, in about half of the remaining cases, the therapeutic effect is insufficient, and we often experience patients who show rapid progress of bone destruction. Therefore, it is necessary to understand detailed pathological conditions of RA and select appropriate treatment. The heterogeneity of the therapeutic reactivity of RA suggests participation of various immune cells and immunological pathways. In recent years, a number of state-of-art technology, mass cytometry, single cell analysis, and functional genome analysis, are being applied to analysis of RA. As a result, it is rapidly clarified by what cells the inflammatory cytokines are produced in joint and what kind of cells the inflammatory cytokines act on. For example, the gene expression and phenotype of synovial fibroblasts is related to their location between blood vessels and synovial lining. Lining synovial fibroblast express genes that are associated with osteoclast induction. In addition, monocytes stimulated with TNF-α and synovial fibroblasts express EFGR ligand, and EGFR ligand-expressing monocytes enhance invasiveness of synovial fibroblast. Functional genome analysis suggests association between these pathways and genetic risk of RA. Understanding of the local immune response of the RA joint would be useful in stratification and treatment selection. In this seminar, based on the latest knowledge of integrated analysis in RA, I would like to discuss the pathogenesis and treatment of RA.

LS19

Past and future of rheumatoid arthritis treatment

Kensuke Oryoji
Center for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: Yes

Rheumatoid arthritis treatment is started with methotrexate if there are no contraindications according to the guidelines. If the effect is insufficient or the drug cannot be used due to side effects, a biologics agents or JAK inhibitors should be used if there are poor prognostic factors (Anti-CCP antibody / RF positive, High disease activity, Early joint destruction). Until recently, there was recommended that biologic agents were prioritized over JAK inhibitors, but the EULAR2019 recommended that the positioning of biological agents and JAK inhibitors would be same. JAK inhibitors inhibit the JAK family of JAK1, JAK2, JAK3, and TYK2, thereby suppressing T cell proliferation and type I interferon in addition to various interleukins including IL-6. They have the potential to meet the unmet needs of conventional therapies because it works widely on the natural immunity / acquired immunity. In this presentation, I will outline the pathophysiology, autoantibodies, and changes in time phase of rheumatoid arthritis, and describe the position and expectations of JAK inhibitors in the future treatment of rheumatoid arthritis.

LS20-1

Latest topics on EGPA

Yoshinori Komagata
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Conflict of interest: None

“Eosinohil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia. ANCA is more frequent when glomerulonephritis is present. ” In the conference, the name of the disease was also changed from Churg-Strauss syndrome. Most patients have adult-onset asthma or rhino-sinusitis, and it takes several years to develop EGPA after the onset of asthma. Severe eosinophilia causes peripheral neuropathy, heart and gastrointestinal diseases by infiltration of eosinophils. Thus, early diagnosis and early treatment are very important. Only one-third of the patients have ANCA, and their presence seems to differentiate between two phenotypes of EGPA, with different clinical characteristics, genetic background and etiology. In Japan, Research Committee on Intractable Vasculitides of MHLW has released a new treatment guideline of EGPA in March, 2020. In patients with non-severe disease, they conditionally recommend GC only or plus cyclophosphamide for remission induction. In patients with active severe EGPA or who have relapsed, they conditionally recommend adding mepolizumab. On the other hand, ACR is also making a new treatment guideline almost at the same time, and a draft has been released last year. In Western countries, other agent such as rituximab (RTX) can be used which is not covered by health insurance in Japan. ACR guideline conditionally recommend RTX for remission induction. The differences between two guidelines will be discussed in this session.

LS20-2

Advances in diagnosis and treatment in EGPA

Masami Taniguchi
Shonan Kamakura General Hospital

Conflict of interest: Yes

EGPA belongs to ANCA-related systemic vasculitis, severe asthma and eosinophilic sinusitis preceded for several years, with a marked increase in peripheral blood eosinophils, eosinophil inflammation and blood vessels in systemic organs It develops with an inflammatory condition (organ ischemia). The etiology is unclear, although women have many middle-aged onsets. At the onset of vasculitis, the peripheral blood eosinophil count increases markedly (usually 50% or more). In addition to ischemic symptoms caused by vasculitis such as fever, muscle pain, and sudden weight loss, polyneuropathy Is accepted at 90% or more. The basis of treatment is steroid + cyclophosphamide, but IVIG is well suited for hypocardia and peripheral neuropathy. Mepolizumab (anti-Il-5) in 2018 Although it was covered by insurance, the combination of eosinophils markedly decreased, resulting in steroid weight loss and stabilization, and it is becoming the basic drug for this disease.

LS21-1

Treatment strategy of PPP/PsA of Rheumatologist

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

Conflict of interest: None

The incidence of psoriatic arthritis (PsA) has been increasing, and more rheumatologists are interested in treating the patients as we have more therapeutic options in the past several years. Earlier diagnosis is achievable as imaging studies are more readily available, such as musculoskeltal ultrasound and MRI. As the initial medications, non-steroidal anti-inflammatory drugs and methotrexate are used, and biologics such as TNF inhibitors, IL-17 inhibitors and anti-IL-23 monoclonal antibodies are utilized based on the intensity of dermatological and rheumatological manifestations, co- morbidities, the risk of infections and the patients’ preference. IL-23 is one of the most important cytokines related to the pathogenesis, and anti-IL-23 monoclonal antibody therapy is reported to be relatively safe with attractive dermatological efficacy and comparative effectiveness in musculoskeltal manifestations. Palmoplantar pustulosis (PPP) and the related Pustulotic arthro-osteitis (PAO) is also the entity which guselkumab is useful. The new armamentarium is discussed in the session.

LS21-2

Treatment strategy of psoriatic arthritis and palmoplantar pustulosis as Dermatologist

Akimichi Morita

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Conflict of interest: Yes

The medical treatment for psoriasis has been changed drastically compared to the former generation. Especially, the treatment outcome of psoriasis has significantly improved due to the introduction of biological drug in 2010. Nowadays, we can use 8 kinds of biological drug, which enable us to maintain tight control toward psoriasis symptom on skin such as PASI90/100. The aspect of psoriasis as a systemic inflammatory disease has attracted attention, and comorbidities of psoriasis having impact on long-term prognosis such as arthritis, arteriosclerosis, diabetes, cardiovascular disease, liver disease have gained greater interest. Therefore, dermatologists today should treat psoriasis not only from dermatological point of view but also from internal medical one in long-term perspectives. In addition, associating with other departments including rheumatology to cater to the needs from patients and make decision on treatment policy is expected more than before. The disease modifying therapy, which can directly treat disease, has been anticipated to play important role. These days, it became possible to treat plantar pustulosis, an intractable disease, with biological drug, which place high expectation. In this seminar, I would like to talk about decision making on medication in wide range of options with considering mechanism and characteristic of each biological drug and how to use Guselkmab regarding the treatment strategy of psoriatic arthritis and plantar pustulosis.

LS22

Biosimilar-a savior for treatment of rheumatoid arthritis?

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Conflict of interest: Yes

Biological drugs have revolutionised the treatment of rheumatic diseases, but expensive costs represent a significant economic burden to healthcare systems worldwide. Since biosimilars are similar and more affordable versions of previously licenced biotechnologicals, they are expected to contribute to healthcare system sustainability and reduce inequities in treatment access. The recent expiry of the patents for many biological agents has generated considerable interest among pharmaceutical companies, and led to the marketing of highly similar, low-cost versions known as biosimilars. The increasing trend of switching patients from effective but expensive drugs to their biosimilar counterparts will have a considerable economic impact in the coming years. Although this will greatly extend patient access the latest treatments, clinicians and the patients themselves have expressed a number of concerns about their long-term efficacy and safety, as well as the consequences of potentially multiple switches being dictated by economic pressure rather than medical needs. In Japan, biosimilar of two drugs (infliximab and etanercept) for RA are already marketed, and the adalimumab-BS is planned to be launched. The properties of BS, in comparison to RP, are required to satisfy the following: the amino acid sequence must be the same as that of RP; there are no differences in the appearance rate between anti-drug antibodies and neutralizing antibodies; and ADCC activity due to differences in sugar chain structure should be within an acceptable range. Both IFX-BS and ETN-BS already marketed satisfy these criteria, and no differences in their efficacy were observed when the original IFX and ETN were switched to IFX-BS and ETN-BS, respectively.

LS23

Approach to CTD-PH -Importance of early diagnosis and early treatment

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Conflict of interest: Yes

Pulmonary hypertension (PH) is often observed as complication in various CTD such as SSc, MCTD, SLE, and SS, and is one of life threatening complication in CTD. Furthermore, CTD-PH is different from other forms of PH in terms of the presence of organ lesions associated with CTD, which leads to several types of PH. Because of the presence of organ lesions associated with CTD, CTD-PH has a poor prognosis compared with other etiologies. However, the prognosis of CTD-PH has been improved by the early diagnosis of PH, the development of various pulmonary vasodilators, and the new treatment strategies such as upfront combination therapy and immunosuppressive therapy. In clinical practice, early clinical symptoms associated with PH are also found in underlying disorders. Thus, we need to realize that PH occurs frequently in CTD patients. It is important to make an early and accurate diagnosis in clinical practice of CTD-PH. For SSc patients, periodic screening for PH is important, while for non SSc patients, it is important to confirm there is no scleroderma spectrum disorders and immediate evaluation of PH when they describe symptoms associated with PH. Especially for non SSc-PAH patients, appropriate and quick decision is extremely important for each case whether immunosuppressive therapy is effective. Although, the prognosis of many patients with PH has been improved thanks to various pulmonary vasodilators, it is necessary to keep in mind that easy use of pulmonary vasodilators to CTD-PH might worsen PH because of presence of various organ legions. In this seminar, I will outline the specific features of CTD-PH and importance of its early diagnosis and treatment strategies.

LS24

New directions of IL-6 blockade in the treatment of rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is developed and maintained by complicated network communications of various immune cells mediated by cytokines. Among those cytokines, interleukin (IL)-6 plays a crucial role in the pathogenesis of RA. We have reported that IL-6 is a useful biomarker of RA disease activity while tumor necrosis factor (TNF) is a prognostic marker of RA. Further, we have speculated the difference between anti-IL-6 (ligand) antibody and anti-IL-6 receptor antibody from the viewpoint of variations in their molecular expression levels. Sarilumab, the first fully-human and high-affinity anti-IL-6 receptor biological disease-modifying antirheumatic drug (DMARD), has demonstrated considerable efficacy in domestic and global clinical trials irrespective of the patients characteristics such as a concomitant use of conventional synthetic DMARDs or a prior use of anti-TNF and other biological DMARDs. The safety profiles of sarilumab are comparable to those of tocilizumab, a humanized anti-IL-6 receptor biological DMARD developed in Japan, without any novel concerns. We should take care of the development of infectious diseases during the treatment with sarilumab, although it is not associated with neutropenia. The importance of IL-6 blockade in the management of rheumatic diseases are supported by recent approval of tocilizumab for large vessel arteritis and adult Still's disease. In this seminar, the clinical positioning and future perspectives of IL-6 blockade will be discussed with introducing the results from our recent translational researches and several clinical trials.

LS25-1

Treatment of Lupus Nephritis: Clinical Guideline and Future Prospects

Keiju Hiromura
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Conflict of interest: Yes

Lupus nephritis is an important complication of systemic lupus erythematosus (SLE), that is frequently associated and is involved in patient prognosis. The Japanese Society of Rheumatology published the clinical guideline of SLE in 2019, in which treatment algorithms of SLE, including lupus nephritis, are presented. For the induction therapy of ISN/RPS Class III/IV lupus nephritis, moderate to high-dose glucocorticoids (GC), combined with either mycophenolate mofetil (MMF) or intravenous cyclo-

phosphamide (IVCY), are recommended as the first-line therapy. For Class V lupus nephritis, moderate dose of GC with MMF is recommended. When remission is achieved, maintenance therapy, using either MMF, azathioprine, or tacrolimus in combination with a small amount of GC, is recommended or proposed. In the treatment of lupus nephritis, not only immunosuppressive therapy but also adjuvant therapy, is important to reduce cardiovascular complications and protect deterioration of renal function. The clinical guideline also recommends the use of adjuvant therapy, such as antihypertensive treatment, lipid-lowering treatment, and antithrombotic treatment. The administration of hydroxychloroquine (HCQ) was also described in the guideline. HCQ is widely used overseas for SLE and cutaneous lupus erythematosus. Several cohort studies have shown the efficacy of HCQ on lupus nephritis. HCQ also showed multiple clinical benefits in the treatment of SLE, through its pleiotropic effects. However, there are some severe side effects, such as retinal toxicity and drug eruption. In addition, HCQ was approved in Japan for the treatment of SLE, just recently. Based on these concerns, the guideline indicates low-grade recommendation to use HCQ in the treatment of SLE, including lupus nephritis. In this seminar, treatment of lupus nephritis will be explained based on the recent Japanese clinical guideline of SLE. In addition, future prospects of the treatment of lupus nephritis will be discussed.

LS25-2

Cutaneous lupus erythematosus: classification and treatment

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Conflict of interest: None

The classification criteria of 2019 EULAR / ACR (European League Against Rheumatism/American College of Rheumatology) have been proposed recently. The category of mucocutaneous lesions includes acute cutaneous lupus erythematosus (ACLE), subacute CLE (SCLE), discoid LE (DLE), oral ulcers, and non-scarring alopecia. Therefore, it is necessary to understand each mucocutaneous lesion when using this criteria. ACLE is generally found in patients with SLE and correlates with SLE activity. On the other hand, DLE, the main form of chronic CLE (CCLE), often develops in patients without SLE and visceral lesions tend to be mild in SLE patients with DLE. SCLE exhibits intermediate properties between ACLE and DLE. Regarding treatment, it is recommended that hydroxychloroquine (HCQ) is considered as a first-line drug for all organ lesions other than skin in Japanese SLE clinical practice guideline published in 2019. For patients with skin lesions, steroids or tacrolimus should be used as the first choice, and HCQ should be considered when the topical treatment is resistant. Because ACLE is usually active at the time of exacerbation of SLE, systemic treatment for SLE can relieve skin symptoms. However, DLE often develops in patients who do not require systemic treatment. Additionally, DLE leaves scars in more than half cases. Furthermore, patients with widespread DLE often progress to SLE, even if they do not initially have systemic symptoms. Therefore, it is important to give adequate treatment including HCQ early in the disease in patients with DLE. Four years have passed since the HCQ was approved in Japan. There is a concern that chloroquine retinopathy may gradually increase around 5 years after internal use. Currently, the dose of HCQ is determined based on the ideal body weight in Japan. However, there are some reports that the risk increases if the dose was 5 mg/kg of actual body weight is or more per day or if the kidney function is poor. Therefore, treatment planning for the risk of retinopathy is important. In addition, drug eruption is observed in about 10% of cases, but there are some reports that re-administration was possible in cases that developed mild drug eruption. I would like to give an overview including other adverse skin events of HCQ such as pigmentation.

LS26

Treatment algorithm of interstitial lung disease associated with systemic sclerosis in Japan

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Conflict of interest: Yes

Systemic sclerosis (SSc) is an intractable condition, which is characterized by chronic inflammation, vascular remodeling, and excessive fibrosis. SSc affects many critical organ systems, including lung, kidney, heart, and gastrointestinal tract. Of these, interstitial lung disease (ILD) is the leading cause of morbidity and mortality. Pathogenic process of SSc-ILD includes migration of lymphocytes, macrophages and mesenchymal precursors into the lung parenchyma due to endothelial dysfunction, and subsequent differentiation of myofibroblasts, leading to accumulation of extracellular matrixes and distortion of the normal lung tissue. Currently, treatment with immunosuppressants is the mainstream of the treatment of SSc-ILD. On the other hand, in patients with idiopathic pulmonary fibrosis (IPF), a typical form of ILD with progressive fibrotic phenotype, anti-fibrotic agents are shown to prevent lung function decline. Because of common underlying pathophysiology between IPF and SSc-ILD, such as excessive fibrosis, efficacy and safety of nintedanib has been evaluated in placebo-controlled, randomized, comparative phase III clinical trial (SENSCIS). In this trial, nintedanib significantly reduced the annual rate of decline in forced vital capacity compared with placebo. We now have at least two options of treatment for SSc-ILD, i.e., immunosuppressants and nintedanib, but there are many future issues, such as in what cases, at what timing, when to use them properly, or in combination. Recently, Japan Respiratory Society and Japanese College of Rheumatology have jointly proposed the treatment guide for ILD associated with connective tissue disease. The treatment algorithm of SSc-ILD in this guide will be introduced and discussed in this seminar.

LS27-1

The Role of Carers in Rheumatoid Arthritis Management

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Conflict of interest: Yes

Effective management of rheumatoid arthritis (RA) requires the coordinated efforts of a multidisciplinary team with the patient as its central focus and it´s importance is implemented in JCR 2014 RA management guideline and EUALR RA management recommendation. Patient-reported outcomes (PROs) are at the core of assessing RA treatment response. However, PROs have inherent limitations, such as under-reporting of symptoms, minimization or exaggeration of symptoms, and mis-reporting of medication adherence. Furthermore, they are often influenced by patient's personal beliefs and fears. For patients with RA, carers may be key to addressing these limitations. Given their time investment, carers may offer important insight into the patient's true health status. As first-hand observers, carers may provide rheumatologists with a more complete picture of the patient's physical and emotional status. They may also help patients understand and adhere to their treatments, keep track of their appointments, follow nutritional guidelines and manage other aspects of life. In addition, the role of carers involves providing physical, emotional and financial support. However, studies evaluating their role in RA are scarce. Current management paradigms for RA tend to neglect the views of carers. This first-of-its-kind regional, multinational, multi-stakeholder study was conducted to enrich our understanding of the roles and potential impact of carers on RA management in the Asia Pacific region. In this session, we aim to illustrate our understanding of the role of and potential impact carers on RA management.

LS27-2

The Role of Nurses in a Team Approach to Health Care

Midori Suzaki
Souseikai PS Clinic

Conflict of interest: None

A Team Approach to Health Care is essential to provide the best quality specialized medical services to patients. It is most important to share the therapeutic purpose and patient information between staff of different expertise. Medical staff should integrate such shared information and put the patients and their families at the center of the medical practice. Treat-to-Target of RA Therapy ideally leads to remission or low disease activity. However, RA treatment is not the same for every patient. Some drugs for

RA require careful administration, special medication methods, and self-injection. The medical staff needs to provide guidance to help patients continue their treatment safely. In the medical team, nurses are involved in patients' diagnosis, treatment, and care. It is easy for nurses to cooperate and interact with patients and the medical staff, thus realizing the patient's problems quickly, providing psychological support, and explaining about various types of medical expenses and rehabilitation options. Also, it is possible for nurses to quickly assess the information they obtained from patients and then share that information with the medical staff, so that the changes or revisions in treatment are done in a timely manner. In other words, nurses are the key in the medical team. The Certified Nurse by Japan Rheumatism Foundation aims to contribute to the health and welfare of the people by cultivating nurses in the care of rheumatic diseases, and by collaborating with the other medical staff. Collaboration with other specialized medical staff will enable patients to receive more information about specialized treatments. The role of nurses in the medical team is to fully understand patients' needs, demonstrate specialized knowledge and skills, and connect patients and the medical team through their communication skills.

LS28-1

The Ultrasound technique of small joints for beginners

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Conflict of interest: Yes

Musculoskeletal ultrasound (MSKUS) is one of the crucial examination tools for many connective tissue disease (CTD), especially for rheumatoid arthritis (RA). The origin of MSKUS was dating back to 1970s as a huge probe for OBGYN was attached to knee joint. The group of OMERACT undertake various role of MSKUS, however MSKUS technique has gradually spread also in Japan since around 2009. Recently high-frequency probe make it possible to depict precise structures of small articular joint in addition to pathological findings not detected by physical examination. Moreover, we have precious textbooks about procedure technique of MSKUS and pathological atlas from JCR committee, paid attention from all over the world. The benefits derived from MSKUS have innumerable contribution not only to our medical staff, but also to the CTD-patients in terms of the advantages that MSKUS is non-invasive procedure to visualize easily the early pathological findings concerned with the concept of early diagnosis and early treatment. The impressive algorism for RA diagnosis and treatment by using MSKUS was published from OMERACT-US group in recent years[1)]. However high-frequent probe delineates images so clear that some pit-falls naturally revealed during examination. The fact that Japanese MSKUS committee have already published initiatively about the MSKUS pit-falls was finally led to the remarkable attention from other countries[2)3)]. Here in this session, I wanna introduce the MSKUS technique focused on small joints including the pit-falls of US-images and latest evidence for beginners with your vigorous discussion. *1) D'Agostino MA. Ann Rheum Dis:2016;0:1-7 2) Ikeda K, Misaki K et al. Mod Rheumatol. 2016;26 (1):9-14 3) Bruyn GA et al. Mod Rheumatol. 2016;26 (1):1-2*

LS28-2

The advanced scanning technique and pitfall of large joint ultrasonography in rheumatoid arthritis

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Conflict of interest: Yes

The usefulness of ultrasonography especially in the differential diagnosis has increased greatly, but the diagnosis cannot be confirmed only by ultrasonographic findings. In the shoulder, rheumatoid arthritis may cause intra-articular synovitis, but the frequency of typical intra-articular synovitis is not so high. Bursitis, which can be the typical findings of polymyalgia rheumatica, may be found in patients with rotator cuff tears, as well as in patients with rheumatoid arthritis. In addition, gouty arthritis and calcium pyrophosphate crystal deposition disease may cause inflammation in the shoulder, and it is necessary to pay attention to the presence of crystal components in the surrounding tissue and synovial fluid. In the elbow, the presence or absence of enthesitis on the lateral and medial epicondyles of the humerus and the ulnar head is useful in differentiating spondyloarthritis. Since the range of the hip joint that can be seen by the ultrasound is limited, it is mainly to check the presence of joint fluid. In addition, the presence or absence of bursitis around the greater trochanter is a useful finding when diagnosing polymyalgia rheumatica, but it may be seen in patients with osteoarthritis. The knee joint is a joint with a high incidence of osteoarthritis, it is always necessary to identify whether or not it is a symptom caused by osteoarthritis even in patients with rheumatoid arthritis or psoriatic arthritis. In addition, the enthesitis of quadriceps tendon and patella tendon is useful for the diagnosis of spondyloarthritis. Imaging of hyaline cartilage of the femur may be useful for differentiating gouty arthritis or calcium pyrophosphate crystal deposition disease. It is necessary to pay attention to these points, and to evaluate not only intra-articular lesions but also around the joints. In this lecture, we use typical imaging and we will also explain the scanning tequnique, pathological findings and pitfalls encountered in daily clinical practice.

LS29-1

Treatment of elderly rheumatoid arthritis patients aiming at extending healthy life expectancy

Tsuyoshi Watanabe
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Conflict of interest: None

The number of elderly RA patients is increasing due to the Biologics agents and T2T treatment strategy. The average age of RA patients at our hospital is 75.5 years old. Elderly people are characterized by the combination of geriatric syndromes such as multiple illnesses and dementia, so rheumatologists are required to deal with various problems associated with aging as well as RA disease management. There are currently no recommendations or guidelines specifically for elderly RA. In addition to RA treatment as an inflammatory disease, treatment as a musculoskeletal disease such as locomotive syndrome, sarcopenia, and physical frailty is becoming increasingly important for extending healthy life expectancy. Some cases will not be able to achieve a good recovery without total management through multidisciplinary multidisciplinary collaboration that integrates exercise therapy, drug therapy, and surgical therapy. Elderly RA patients with major joint destruction that require surgical treatment often use biologics agents. The rehabilitation ward and the acute ward should be used alternately to continue drug treatment even during long-term hospitalization. Elderly RA patients often have osteoporosis and low muscle mass (LMM). and in our hospital, osteoporosis was associated with 58% and LMM with 52%. In RA patients treated with osteoporosis medication containing vitamin D, an increase in muscle mass has been observed. The Criteria of the Asian Sarcopenia Working Group (AWGS) was revised in 2019. Protein and Vitamin D intake with sufficient energy intake are efficient to prevent sarcopenia. A combination of resistance exercise and aerobic exercise is desirable. However, it is necessary to give careful consideration to the resistance exercise because RA patients usually have joint disorder. I would like to present some experience cases related to healthy life expectancy.

LS29-2

Aiming for high-level treatment of rheumatoid arthritis with Golimumab - Impossible? Make it Possible! -

Taichi Hayashi[1,2,3]
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Conflict of interest: Yes

The concept of "Difficult to Treat RA (DT-RA)" has been proposed. What does this mean? And what is the solution? In this lecture, we will discuss DT-RA and introduce patient-centered treatment of RA and the usefulness of Golimumab. In RA practice, remission has been achieved in many cases due to the target drugs and the practice of Treat to Target

(T2T). On the other hand, even in the registry constructed by specialists, the remission maintenance rate has peaked at 50-60% for DAS and 30-40% for SDAI and Boolean. The origin of this gap is DT-RA, which is attributed to complications such as infections, malignancy, depression, adverse events, adherence, and treatment delays. Although these are difficult to solve due to evidence, we would like to show from our clinical experience that each remission can be increased by at least 20% by adopting the concept of "Narrative". There are safety and communication issues at the root of DT-RA. The latter can be solved with the Shared Decision Making (SDM) methodology. If the patient can make the right decision and choices, adherence problems and treatment delays will not occur, and sometimes financial problems will be resolved. Here, "Patient Report Outcome (PRO)" is useful as a common language for SDM, and is also an important indicator when aiming for remission maintenance and deep remission, so I would like to recommend appropriate evaluation and clinical application. On the other hand, early tight control is important for safety issues. High disease activity increases complications and the need for corticosteroids increases safety concerns. In cases where safety has already been compromised, we are faced with a shortage of therapeutic drugs, which can be supplemented by strategic practice. In my practice, the use rate of PSL has dropped to 10%, and the reduction of infectious diseases means that this is possible. Golimumab is an anti-TNF antibody with low immunogenicity, and in our center, mainly in cases where TNF inhibitors are taboo, such as cases without MTX and TNF-IR, by April 2019 227 cases have been introduced. Surprisingly, the Kaplan-Meier survival curve also showed a 60% / 6-year continuation rate even in cases without MTX (n = 119). This result shows that Golimumab can play a role in the treatment of MTX intolerant cases that are prone to DT-RA. Golimumab is highly useful, but if you are satisfied with its features, you will not be able to maintain stable results over the long term. Here, we will review the actual clinical tips along with the actual use of Golimumab at our facility.

LS30-1

Management of comorbidities in patients with rheumatoid arthritis: Look before you leap

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Conflict of interest: Yes

Proper management of comorbidities and prevention of adverse drug reactions are prerequisite for the success of treatment of patients with rheumatoid arthritis (RA). Incidence and prevalence of comorbidities are relatively high in patients with RA, and each comorbidity and RA have significant influence to each other, which is called multi-morbidity. A spate of reports on comorbidities in patients with RA has been published. In a multi-national, cross-sectional COMORA study, prevalence of comorbidities was as follows: depression 15%, bronchial asthma 6.6%, cardiovascular disease 6%, malignancy 4.5%, and COPD 3.5%. An observational study using a Japanese insurance database demonstrated that risk for hospitalized infection, cardiovascular disease, and facture was higher in patients with RA compared to non-RA individuals with hazard ratios of 1.74 (1.52-1.99), 1.38 (1.04-1.85), and 1.88 (1.54-2.31), respectively. Analysis of IORRA database revealed incidence of comorbidities requiring hospitalization as 8.15 (7.4-8.95)/100 patient-years. Rheumatologists should recognize that patients with RA have high incidence and prevalence of comorbidity and that the risk increases with age. Comorbidities that should be checked before starting to treat RA include chronic or on-treatment infectious disease, vaccination (especially for *Pneumococci* and *Varicella Zoster Virus*), dental treatment, cardiovascular disease, respiratory disease, peptic ulcer, diverticulosis, renal disease, osteoporosis/fracture, cognitive impairment, and malignancy. Medical interview and evaluation of these comorbidities will enable us to provide proper management of patients with RA. In this seminar, I would like to discuss how to look before we leap based on recent evidence in clinical settings.

LS30-2

Complications and comorbidities of rheumatoid arthritis and their management

Atsushi Kawakami
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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an inflammatory disease that involves the synovial joint as the head of the lesion, but it also frequently affects extra-articular tissues. Severe RA may be accompanied by vasculitis (rheumatoid vasculitis: rheumatoid vasculitis). In Japan, extra-articular manifestations including vasculitis are referred to as RA with malignant rheumatoid arthritis and are designated intractable diseases. (0.6% of RA: from the designated intractable disease HP). Many of the extra-articular lesions in this malignant rheumatoid arthritis (rheumatoid vasculitis) are caused by small vessel vasculitis, and are typically represented by interstitial pneumonia, polyneuritis (polyneuritis multiplex), and skin ulcers. An analysis from the insurance database also revealed that the proportion of comorbidities such as infections, cardiovascular diseases, and bone fractures was higher in RA than in non-RA, and that management for comorbidities are also supposed to be crucial. Airway lesions are frequently seen as extra-articular complications of RA, and expression of citrullinated protein in the small airways in ACPA-positive RA, detection of ACPA in bronchoalveolar lavage fluid and intensive inflammatory cell infiltration have been reported compared with ACPA-negative RA. Analysis of DMARDs-naïve very-early RA in our cohort detected consolidation by HRCT, especially in the ACPA-positive group. Bronchiectasis is also important as an airway lesion in RA, and it has been reported that RA complicated with bronchiectasis is associated with an increased risk of infection due to the use of bDMARDs. It is also important to respond to infections, cardiovascular diseases, and bone fractures that are significantly higher in RA as analyzed from the insurance database described above, and in the presence of these comorbidities, it becomes difficult to perform T2T in RA in clinical practice. Osteoporosis is a major risk factor for fracture and RA patients tends to be accompanied by osteoporosis. "Presence of RA" is incorporated in FRAX, an assessment tool for further development of fracture. In addition, in Japan, aging (super-aging) is progressing, and the aging of RA patients is also becoming clear. The accompanying sarcopenia and frail have also become important in the clinical practice of RA, and there are reports of the association in the subset of RA patients that are likely to be accompanied by sarcopenia and/or frail. Although RA treatment has been greatly improved with the advance of DMARDs, we are going to discuss the importance of management of complications and comorbidities in patients with RA.

LS31-1

Significance of quality of life in SLE treatment

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Conflict of interest: Yes

For systemic lupus erythematosus (SLE), unlike rheumatoid arthritis (RA), innovative new drugs have not been developed. However, the prognosis has been markedly improved by the improved use of conventional therapeutic drugs and the advances in supportive treatment including infection control. In Japan, the 5-year survival rate reportedly exceeds 95% in specialized centers. Nevertheless, physicians who actually treat patients often face various problems with quality of life (QOL), which cannot be measured in terms of prognosis. Meanwhile, SLE itself is associated with a wide range of symptoms and, additionally, causes diverse organ involvement. The frequently used drugs, such as high-dose steroids, also induce adverse reactions that greatly affect daily living. Because such diverse aspects need to be simultaneously considered, understanding the QOL of SLE patients is not always easy. Furthermore, such difficulty in assessing their QOL makes it difficult for treating physicians to determine the level of patient satisfaction with treatment. This is the ground that is likely to cause differences between the patient reported outcome (PRO) and assessment by physicians. The PRO is a new assessment tool, in which the methodology has been established in recent years. It has also been attracting attention in the field of RA, and a number of studies have been conducted. This tool appears to be far more important for SLE than for RA, and studies have been conducted to develop the use of PRO in the treatment of SLE. Although the common assessment tools used for RA and other diseases, such as SF-36, have been also actually used in clinical trials on SLE,

recent trials have shown that the state of SLE may not be accurately assessed with such common assessment tools. Thus, various SLE-specific tools for PRO measurement that enable more accurate understanding of the conditions of SLE patients have been proposed, including LupusPRO and LIT etc. Each assessment tool has its own advantages and disadvantages. On the assumption that these tools will be used in actual clinical practice, studies seem to be needed in the future to consolidate them into a few assessment tools that should be used. In addition, if assessment tools using PRO are actually advanced further, how to use them in actual clinical practice will be a future issue.

LS31-2

The treatment of lupus nephritis and patient stress

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Conflict of interest: Yes

In the case of rheumatoid arthritis (RA), since there is a subjective symptom of pain that should be avoided as much as possible, it is generally welcomed that treatment is enhanced and pain is reduced. Visual analog scale (VAS) by a patient is a major component of disease activity evaluation, and calculation of DAS28, SDAI, and CDAI requires patient's VAS. In this case, the VAS can also be regarded as the degree of patient satisfaction with the current treatment. On the other hand, systemic lupus erythematosus (SLE) does not often evaluate disease activity including the satisfaction of patients, and there is only item of "fatigue" in BILAG, SLAM, and ELCAM. It is not clear from the various scales of SLE whether patients are satisfied with the current treatment. Therefore, it should be noted that intensifying treatment and suppressing disease are not always welcome. For example, there are treatment guidelines for lupus nephritis, which is frequent in SLE, and it is necessary to use steroids and immunosuppressants. If steroids are used in large quantities, urine protein decreases, but it is possible that the moon-face appearance will worsen and patient satisfaction will be decreasing. The appearance of biologics and low molecular compounds produce new anxiety in the case of RA such as necessary of self-injection or economic burden, and they have not been evaluated by current methods. Similarly, patients with SLE receive anxiety (i.e. pregnancy, bone fractures, carcinogenesis) to medications, but this is rarely evaluated in daily practice. Here, we explain the standard treatments for lupus nephritis, imagine the patient's stress due to the treatments, and consider the evaluation method for patient's assessment to the disease and medications. SDAI: Simplified Disease Activity Index CDAI: Clinical Disease Activity Index BILAG: The British Isles Lupus Assessment Group SLAM: The Systemic Lupus Activity Measure ELCAM: The European Consensus Lupus Activity Measurement

LS32-1

Reconsidering pathogenic involvement of TNFalpha in patients with rheumatoid arthritis

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Conflict of interest: Yes

Recent therapies for rheumatoid arthritis (RA) were dramatically progressed continuously, we need to diagnose earlier, and intensive therapy aimed to clinical remission and its maintenance are strongly recommended especially in active RA. A lot of biologics targeting inflammatory cytokines (TNFα and IL-6), T cells-co stimulator and JAK are available in Japan. TNF inhibitors are clearly the pioneer for evolution of therapy in RA, we can use five kinds of TNF inhibitors nowadays. Also, TNF inhibitors are available in other autoimmune and auto-inflammatory diseases, help to understand mechanistic effectiveness of those drugs. Drug free and drug holidays are achievable, and appearance of bio similar, we reasonably select as a first biologic therapy due to the cost effectiveness. But which patients are fit to use, and which TNF inhibitors are ideal? To understand this, we need to know the each character of biologics, as well as fundamental mechanisms of the pathogenic involvement of TNFα in patients with RA. TNFα are strongly linked to inflammatory memory in fibroblast, which lead to synovium proliferation, induction of inflammatory cytokines including IL-6 and chemokines, differentiation of osteoclast, maintenance and recruitment of inflammatory macrophages. Those mechanisms induce and maintain arthritis. In addition, several important mechanisms are unveiled by human-TNFα transgenic models, such as induction of ACPA in mid-arthritis course, female predominance of earlier and severe arthritis, involvement of cardiovascular and lung diseases, and epigenetic profiling of fibroblasts, which clearly linked to the pathogenesis of RA. In this seminar, we discuss and summarize the updated pathogenic involvement of TNFα in RA. In addition, we also discuss about the link between TNFα and new biomarker such as citrullinated ITIH4 proteins in serum, and hypo sialic autoantibodies via immunocomplexes in patients with RA, and reconsider the significance of TNF inhibition in RA

LS32-2

Positioning of TNF inhibitors in current clinical practice for rheumatoid arthritis

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Conflict of interest: Yes

Sixteen years have passed since the first TNF inhibitor (TNFi) for rheumatoid arthritis (RA) was approved in Japan in 2003. TNFis have not only brought a paradigm shift to treatment for RA due to their breakthrough therapeutic effects, enabling the maintenance of QOL through suppression of joint destruction, but also triggered conceptual changes in both diagnostics and therapeutics of RA, including the revised ACR / EULAR 2010 classification criteria and the "treat-to-target (T2T)" strategy. Supported by successful global evidences, TNFis have been established as the standard therapy for patients with inadequate response to MTX (MTX-IR), leading to the development and launch of new TNF is with designated molecular structure and other various molecular targeted drugs with different mode of action. On the other hand, TNFis have made many rheumatologists realize that RA is a systemic immune disease and that the treatment of RA is just an immunosuppressive therapy. In Japan, the post-marketing surveillances confirmed that life-threatening serious infections such as tuberculosis, Pneumocystis pneumonia, and de novo hepatitis, correspondingly link to treatment for RA. Japan's rheumatology should be proud of the early establishment of prophylactic protocols ahead of the world based on the results. Furthermore, TNFis are the first anti-rheumatic drugs that challenged the drug holiday, and clinical researches from Japan has played a significant role in this area. Adalimumab is often used in the control group in recent clinical trials of other new molecular targeted drugs as a representative of TNFis, the current standard therapy. In the near future, novel drug that surpasses TNFis will be expected. To date, we have acquired many effective therapeutics for RA. Moreover, the therapeutic options still keep on expanding. Thus, we would like to reconsider the position of TNFis in current clinical practice for RA in this seminar.

LS33-1

Management of Large Vessel Vasculitis

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Conflict of interest: Yes

Currently primary systemic vasculitides are categorized by the size of blood vessels involved as determined at the 2012 International Chapel Hill Consensus Conference. In this nomenclature of vasculitides, primary large vessel vasculitides (LVV) include two diseases; Giant Cell Arteritis (GCA) and Takayasu Arteritis (TAK). GCA is a disease of elderly mainly involving cranial arteries, whereas TAK occurs in young women predominantly involving aorta and its first branches. Although glucocorticoids dramatically changed a landscape of therapy in both diseases, glucocorticoids monotherapy is often insufficient and frequently leads to undesirable long-term side effects. Various immunosuppressive agents were advocated in order to lessen glucocorticoids toxicity, however, evidence of their use in LVV has been extremely limited. In rheumatology, particularly in rheumatoid arthritis, multiple biologics and targeted synthetic disease modifying anti-rheumatic drugs (tsDMARDs) have been developed and been in use

with great success since late 1990s. Unfortunately initial clinical trials of tumor necrosis factor alpha inhibitors (TNF alpha inhibitor) were unfruitful in GCA. In 2017 GiACTA trial broke through the barrier of fruitless clinical trials in LVV, where tocilizumab proved efficacy for maintaining remission in patients with GCA when used with the tapering course of prednisone for 6 months. TAKT trial followed this milestone and tocilizumab was approved for GCA and TAK in August 2017. In this new era of biologics use in LVV, clinicians should be aware of long-term glucocorticoids toxicity and try to minimize glucocorticoids use in LVV. Here in this session, up to date strategies for managing LVV will be discussed.

LS33-2

Impact of targeting IL-6 in the treatment of large vessel vasculitis

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Conflict of interest: Yes

The pathogenesis of large vessel vasculitis (LVV) such as Takayasu arteritis (TAK) and giant cell arteritis (GCA) consists of the immune abnormalities including the interaction between vascular dendritic cells, macrophages and T cells. It is reported that genetic polymorphisms in the immune-modulating cytokine genes such as *IL6* and *IL12B* are associated with the onset of LVV. Although survival of LVV patients has improved with conventional treatments such as immunosuppressants and glucocorticoids, these drugs are limited by inefficacy and intolerance in some patients. Therefore, innovative therapeutic approaches need to be developed. Large randomized controlled clinical trials of anti-IL-6 receptor antibody tocilizumab (TCZ) (TAKT for TAK and GiACTA for GCA) showed the efficacy and tolerability of TCZ as a novel biologic agent for the treatment of LVV. However, little is known about immunological features of LVV and pathological immune cell subsets targeted by IL-6 blockade. We analyzed the relationship between the phenotype of peripheral immune cells with clinical manifestations and responsiveness to the treatment in patients with LVV. The data indicated that immunophenotypic features in LVV patients are characterized by increase of activated Th17 cells and $CD27^{-}IgD^{-}$ effector B cells and decrease of activated Treg cells. TCZ reduced Th17 cells and effector B cells and increased Treg cells, indicating that IL-6 blockade may correct the impaired balance of Th17 and Treg and B cell differentiation in patients with LVV. TCZ has a potential, not only for the suppression of disease activity, but also for the prevention of the exacerbation of disease activity and steroid sparing effect. In this seminar, we highlight recent advances that pertain to this topic and the impact of targeting IL-6 in the treatment of LVV.

LS34

Behçet's disease, update on pathophysiology and treatment

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Conflict of interest: Yes

Behçet's disease (BD) is a systemic condition characterized by oral aphthae and genital ulcers, as well as ocular and skin manifestations. Although the mechanism of the disease is not fully understood, BD is thought to consist of a combination of autoinflammatory and autoimmune dysfunctions, inclining more towards the autoinflammatory spectrum of disorders. Neutrophils, Th17 cells, γδT cells, NK cells, monocytes, and macrophages have a role in various processes in BD. Activation of innate sensors leads in turn to the activation of inflammasomes, which serve as a platform for IL-1β processing and release. In this respect, BD is very similar to another autoinflammatory disease, Familial Mediterranean Fever, as seen in the activation of the inflammasome by molecular mechanisms and its inhibition by colchicine. Genetic variants at *IL12A*, *IL10*, *STAT4*, *RIPK2*, *IRF8,* and *CEBPB-PTPN1*, which have been reported in previous GWAS for BD are in high linkage disequilibrium and have consistent effect direction with patients with recurrent aphthous stomatitis. This coincidence raises the possibility of a similar mechanism leading to clinical presentation with mouth ulcers in both conditions, yet emphasizes the importance of HLA alleles in BD. Anti-TNFα therapy is efficient in almost all severe and refractory BD manifestations. Oral ulcers do not increase mortality, but cause pain; difficulty in eating, drinking, and talking; and decreased participation in routine daily activities and quality of life. Recently, apremilast, an orally available small-molecule phosphodiesterase 4 inhibitor, resulted in a more significant reduction in the number of oral ulcers than placebo in patients with oral ulcers associated with BD. Further prospective studies are warranted to define the place of anti-TNF agents, apremilast, and other coming new agents in BD.

LS35

Perspectives and roles of rheumatologists in pulmonary hypertension practice

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Conflict of interest: Yes

Although connective tissue disease (CTD) can affect various organs, pulmonary hypertension (PH) is one of the most devastating organ involvements. Among subgroups in clinical classifications of PH, not only pulmonary arterial pulmonary hypertension (PAH), but also pulmonary veno-occlusive disease, left heart disease, chronic lung disease, chronic pulmonary thromboembolism can be seen in CTD-PH. In the past, PH carried a very worse prognosis, but in recent years, selective pulmonary vasodilators have been developed. After verification of efficacy and safety in clinical trials for all forms of PAH including CTD-PAH, 11 drugs have been approved for PAH in Japan. It is shown that symptoms, hemodynamics, and prognosis of PAH have been improved. As a result, better outcome has been yielded and knowledge has been accumulated in practice of CTD-PAH. It became clear that characteristics of CTD-PAH is diverse and unique, and perspectives and roles in rheumatologists are quite different from the one in PH expert cardiologists who struggled with high pulmonary arterial pressure. In fact, although idiopathic PAH has worse hemodynamics at diagnosis than CTD-PAH, there is a reality that long-term prognosis is worse in CTD-PAH, and more optimization of treatment is required. The main roles of rheumatologists in PAH medical practice are summarized below. (1) Diagnosis: To make a diagnosis of an underlying disease as a member of a multi-disciplinary PH team when PH is confirmed at a PH expert center. (2) Systemic evaluation: To evaluate comorbid lesions such as lungs or heart systematically that can be affected by medication. (3) Risk assessment: To conduct a PAH risk assessment in line with the actual condition of CTD. (4) Therapeutic strategy: To consider the indication of initial combination therapy but also to select cases that allow the start of monotherapy. (5) Management: To evaluate the improvement of PAH during follow-up, and to perform management that does not deteriorate oxygenation in total after treatment. On the other hand, issues such as very little evidence limited to CTD-PAH and lack of guidelines for management of overlapping multiple subgroups in clinical classifications are also highlighted. In this lecture, I will discuss from a viewpoint unique to a rheumatologist and introduce the evidence of CTD-PAH under treatment of Riociguat.

LS36

The current therapy for osteoporosis

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Conflict of interest: Yes

The objective of treatment for osteoporosis is to prevent a fragility fracture, and it is desirable to choose the drug based on the evidence of the fracture prevention. The evidence that can prevent all skeletal sites such as vertebral, non-vertebral, and hip has beed proved in alendronate, risedronate, zoledronic acid, denosumab and romosozumab. Because the risks of the hip fracture gradually increase after 70 years old in the postmenopausal women, in this case we have to the choose of five drugs mentioned above. In the case of comparatively young postmenopausal osteoporosis women, we should choose amino-bisphosphonatees, SERMs, elcecalcitol, denosumab, teriparatides, romosozumab which has been established the evidence of the most frequent vertebral fracture reduction effect. When principally, we suggest anabolic therapy first, followed by potent antiresorptive therapy. The common practice of switching to teriparatide only

after patients have an inadequate response to antiresorptives is not the optimal utilization of anabolic treatment. On the other hand, it is shown that further increase of bone mineral density is obtained when we use romosozumab following an oral bisphosphonates. The American Society for Bone and Mineral Research (ASBMR) and the United States National Osteoporosis Foundation (NOF) formed a working group to develop principles of goal-directed treatment and identify gaps that need to be filled to implement this approach. With goal-directed treatment, a treatment goal would first be established and choice of treatment determined by the probability of achieving that goal. Goals of treatment would be freedom from fracture, a T-score>-2.5, which is above the NOF threshold for initiating treatment, or achievement of an estimated risk level below the threshold for initiating treatment.

LS37

New perspectives on treatment of rheumatoid arthritis by JAK inhibitors

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Conflict of interest: Yes

Rheumatoid arthritis is a systemic autoimmune disease characterized by inflammation and joint destruction that causes significant morbidity 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 are classified as targeted synthetic DMARDs. 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.

Evening Seminar

ES1-1

Basic research in immunology and its clinical applications

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Conflict of interest: Yes

Immune systems have evolved to protect us against attach from the foreign pathogens, consisting of two sophisticated systems, the innate and adaptive immunity. The innate immune systems are succession of simple and immediate responses, which are activated by the recognition of microbial constituents or molecular patterns. On the other hand, the adaptive immune systems rely on the antigen-specificity generated by receptor rearrangement in T and B lymphocytes. The immune system must function to achieve the balance between host defense and damage, of which defects result in immune deficiency, allergy, autoimmune and autoinflammatory diseases. Over the course of decades, cumulative pioneering studies have clarified the mechanism of the systems, and the resulting findings have been applied for the diagnosis/treatment of immunological disorders such as rheumatoid arthritis. In this seminar, I will present such overviews, including pathogenic and therapeutic implications of abatacept.

ES1-2

State-of-the-art progress in T cell-targeting treatment for rheumatoid arthritis

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Conflict of interest: Yes

The combined use of conventional synthetic DMARDs such as methotrexate and biological DMARDs as well as the application of the treat-to-target strategy has revolutionized the treatment of rheumatoid arthritis (RA), and clinical remission or low disease activity are now realistic targets. Sustained disease control in turn leads to good long-term outcomes without any clinical flare of the disease, progressive joint destruction or functional impairment, but requires patient adherence and ensured safety. Among multiple biological DMARDs, abatacept is a characteristic one which prevents T cell activation by inhibiting costimulatory signals, and its safety and effectiveness have been established in several clinical studies. Moreover, the AMPLE clinical trial in RA patients with inadequate response to MTX, showed similar efficacy of abatacept and adalimumab. We also reported that efficacy for remission induction of abatacept was comparable to that of biological DMARDs targeting TNF or IL-6 in observational cohorts of the FIRST registry using sophisticated statistical methods are often used to reduce the selection bias both propensity score matching and IPTW method. Tolerable safety results were obtained by the post-marketing surveillance in 28-week observation of 3985 patients with RA in Japan. It is noteworthy that aging was not picked up as a risk factor for serious adverse events and infections in patients treated with abatacept, different from biological DMARDs targeting TNF or IL-6. In the FIRST registry, abatacept revealed high long-term retention rate in elderly RA patients classified as 65-74 years old or older than 75 years. Taken together, abatacept has potential as remission induction and long-term maintenance therapy in patients with RA.

ES2-1

The current situation and treatment issues for WoCBA (Women of Child-Bearing Age) Patients-The Promotion of preconception care-

Shigeru Saito
President University of Toyama, Toyama University

Conflict of interest: Yes

In recent years, with the development of biological products, women with RA who had given up on childbearing are starting to achieve remission and think positively about pregnancy and childbirth. As 35% of patients with RA are aged 20-39 years, so approximately 175,000 women

have a chance of getting pregnant and giving birth. Since the low birthrate in Japan is a serious problem, it is important that patients with RA achieve remission and are guided through pregnancy and delivery to increase the birth rate. Although data sharing between internists, orthopedists, and obstetricians before pregnancy is needed, only approximately 50% of pregnancies in women with RA are planned according to our study supported by Health and Labor Sciences Research Grants, the Health, Labor and Welfare Ministry in Japan. As many pregnant women with RA are treated for infertility, such as ovulation induction (5.7%), in vitro fertilization (13.6%), and microinsemination (7.9%), collaboration with fertility clinics is also necessary. When we compared the number of births by women with RA with the expected number from vital statistics using data from a multicenter database (NinJa); the number of births by women with RA was only 42.2% of the expected value (i.e., they are hesitant to get pregnant). We encourage the doctors of patients with RA to inform them that they can get pregnant after remission. Preconception care improves maternal and child health outcome, so it is recommended to promote preconceptional care with rheumatologists, obstetricians and patient. Seventy percentage of cases were complicated with obstetnics/Gynecologic problems such as infertility, rearrent miscarriage, menstrual abnormalities and cervical dysplasia. As regulatory T cells increase during pregnancy, RA symptoms resolve in many cases. Anti-TNF-α antibodies are used to treat implantation failure (a type of infertility) and recurrent miscarriages or stillbirths in Europe and the USA, and the risks of infertility, miscarriage, and stillbirth are reduced after anti-TNF-α antibody therapy. The risk of teratogenicity caused by the anti-TNF-α antibody has also been denied. Anti-TNF-α antibodies, prednisolone (up to 15 mg/day), and azathioprine are safe to use during pregnancy. Cyclosporine and tacrolimus are also allowed during pregnancy under certain circumstances. I hope that many RA patients will give birth after preconception care.

ES2-2

Considering for the current situation and issues of pre-conception care in daily practice for the WoCBA Patients with Rheumatoid Arthritis

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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. These advances are also very helpful for WoCBA (Women of Child-Bearing Age) patients. Many RA patients in WoCBA tended to avoid to become pregnacy before. Recently, RA with remission or low disease activity could hope to become mothers. However, it is necessary to pay much attention when deciding a treatment strategy for a WoCBA patient because of various characteristics they are associated with. A treatment strategy for a WoCBA patient should be decided individually for each of the three pregnancy phases (preconception, during pregnancy, after pregnancy). Preconception care should be practiced not only for women planning to become pregnant, but also for all WoCBA RA patients before pregnancy. I want to be able to plan pregnancy in a better state in anticipation of future life events such as pregnancy, breastfeeding, and childcare. This talk will present typical characteristics and necessary considerations in WoCBA 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.”

ES3-1

Treatment optimization of Spondyloarthritis based on the joint symptom and extra-articular manifestations

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Conflict of interest: None

Spondyloarthritis (SpA) is a term for diseases characterized by the central feature of enthesitis and includes ankylosing spondylitis and psoriatic arthritis that can cause secondary arthritis. Unlike rheumatoid arthritis, autoantibodies are not detected in SpA. Articular symptoms manifest themselves in the form of peripheral arthritis and axial arthritis as well as in extra-articular symptoms occurring in organs other than joints manifest in the eyes, skin and intestines. SpA is a systemic inflammatory disease that may also be associated with cardiovascular disease, obesity and metabolic syndrome, etc. In the field of psoriasis, where research is making remarkable advances, the subsequent prognosis has also been reported to be influenced by the impact of systemic inflammation and cardiovascular complications have also been found to play a significant role in the prognosis. While several cytokines have been identified in SpA, tumor necrosis factor (TNF) plays a central role. As a pioneer biologic therapy for SpA, TNF inhibitors reveal a broad range of evidence of articular and extra-articular symptoms and its complications and TNF inhibitors are ranked as a first-line therapy in Japanese and overseas treatment guidelines. In SpA, the manifestation site and the severity of the symptoms vary from patient to patient making it necessary to determine which lesions and complications require aggressive treatment while working with the patient to select treatment options. In this lecture, the evidence necessary to optimize treatment for individual patients and the treatment options will be organized and presented followed by a discussion with participants based on their actual clinical experiences.

ES3-2

Roles of imaging in understanding pathophysiology and improving management of spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis (SpA) encompasses a number of diseases which share common articular pathophysiology and is seen as a spectrum between axial and peripheral SpA. Ankylosing spondylitis/radiographic axial SpA is the most typical entity for the axial SpA, whereas psoriatic arthritis (PsA) is the most prevalent disease classified as the peripheral SpA. In SpA, inflammation initially occurs at various entheseal sites and frequently extends to the surrounding soft tissues and the bone. These inflammatory lesions are clinically recognized as peripheral arthritis, spondyloarthritis, enthesitis, and/or dactylitis and result in the characteristic mixture of osteolytic and osteoproliferative bone changes. Imaging such as ultrasound and magnetic resonance imaging (MRI) illustrates these articular features characteristic to SpA and helps with understanding pathophysiologies, making diagnosis, and managing the disease. Enthesitis in SpA develops under genetic and environmental backgrounds and involves various types of cells related to innate-/acquired-immunity or inflammation and various cytokines. TNF is a cytokine which has multiple effects on immune reaction and inflammatory cascade and thus plays important roles in the pathogenesis of above-mentioned articular lesions of SpA. In addition to suppressing inflammation, TNF inhibitors have been reported to inhibits structural destructions in SpA. This has been mostly shown for peripheral osteolytic lesions, but recent evidence suggests that TNF inhibitors also inhibits osteoproliferative lesions. On the other hand, extra-articular organ involvement such as gut and eye is also important in SpA, for which TNF inhibitors has broad evidence. A wholistic approach, taking into account various organ involvement, patient-reported outcome, and risks of adverse events, is necessary in the management of SpA.

ES4

Rheumatoid Arthritis Treatment Strategy Considered from ultrasound examination and MMP-3

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Conflict of interest: None

Matrix metalloproteinases (MMPs) are produced from synovial cells and chondrocytes stimulated by TNFα, interleukin, TGFβ, etc. produced from inflammatory cells present in synovial fluid. The produced MMPs are involved in the destruction of bone and cartilage through the degrada-

tion of extracellular matrix such as proteoglycan and collagen. Among them, MMP-3 is considered to be a key enzyme for cartilage destruction because it activates other MMPs as well as being involved in the degradation of extracellular matrix. Currently, it is widely used as a useful serum marker that indicates the disease activity of rheumatoid arthritis. Ultrasound examination is more sensitive than physical examinations and blood tests, and it can detect synovitis in the joint area and judge the state of individual arthritis in more detail. Even in patients with clinical remission, residual synovitis may be visualized, and it can be judged that there is a risk of progressive destruction and relapse. When MMP3 is high, we consider the possibility of disease activity, high synovitis, and major joint disease. However, it is necessary to interpret the values taking into account the presence or absence of steroid use and renal dysfunction. When MMP3 is normal or low, the condition is stable and synovitis is thought to have calmed down. However, the possibility of suffering from small joints, especially wrist joints, cannot be denied. When it is difficult to interpret the obtained MMP3 value, it is easy to judge the disease state and deepen understanding by complementing with ultrasound examination. By knowing the characteristics of both MMP3 which can understand more systemic disease states, and ultrasound examination which can understand the disease states of individual joints including small joints in detail, and using them, it is possible to conduct higher-quality rheumatic treatment. In this program, I will introduce the importance and utilization of both examinations, and I will do my best to provide useful information for daily medical care from tomorrow.

ES5-1

Interstitial lung disease with polymyositis and dermatomyositis

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Conflict of interest: Yes

PM / DM is a disease in which muscle strength is reduced due to inflammation of skeletal muscle. In recent decade, many autoantibodies have been discovered by Japanese researchers, and the strong association between autoantibodies and clinical symptoms has become a hot topic. Conventionally, it has been known that PM / DM frequently accompanies interstitial lung lesions (ILD). Many are responsive to steroids, but it has been reported that some cases relapse with steroid alone. Therefore, the combination of steroids and immunosuppressive drugs has been used. The immunosuppressive drugs are mainly tacrolimus and cyclosporine. In the 2000s, it became known that ILD, which progresses rapidly in some DMs, was merged, and steroid resistance was considered to be extremely bad. Many cases die from respiratory failure within 6 months. This rapid progression type ILD was found to be associated with DM with almost no muscular symptoms, and the combination of steroid and one immunosuppressant could not suppress the progression. These DMs were named as amyopathic DM, and it was found that anti-MDA5 antibody was positive. In addition, the severity of ILD was found to correlate with the levels of serum ferritin. In Japan, anti-ARS antibodies can be measured in general clinics, and not only collagen disease internal medicine but also pulmonologist have come to measure autoantibodies. As a result, it has been found that some anti-ARS antibody positive patients have poor muscle symptoms but only ILD progresses. These appear to be free of typical DM eruptions, unlike the amyopathic DM described above. When anti-ARS antibody cannot be measured, this case was treated as idiopathic interstitial pneumonia (IIP). And combined treatment with steroids and immunosuppressive drugs. On the day, I will explain in detail the actual treatment method of ILD based on autoantibodies.

ES5-2

Trends in the treatment of lupus nephritis

Tomonori Ishii
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Conflict of interest: Yes

Lupus nephritis is the most frequent visceral lesion in systemic lupus erythematosus (SLE) and is a primary organ lesion directly linked to SLE prognosis. Because of its importance, many clinical studies have been conducted on lupus nephritis, and this lesion also has the most abundant evidence related to its treatment. The basic framework for treatment of lupus was established in the 2000s. Treatment with administration of mycophenolate mofetil (MMF) or cyclophosphamide (a central immunosuppressive agent), in addition to steroid administration, generally produces excellent results for both renal and life prognoses. However, in some cases, it is difficult to control the inflammation associated with nephritis. Many researchers are interested in reducing the steroid dosage, while preventing a relapse. Steroid drugs exert a vast range of effects, especially when administered over prolonged periods of time because almost all cells express steroid receptors. Steroids exert immunosuppressive effects, which may be related to their high efficacy and rapid onset of effects; however, these effects also increase the risk of infectious diseases. Steroids have the most evident risk of infection compared to other biologics. Additionally, many steroid-related side effects have a significant impact on quality of life, particularly in patients with diabetes and osteoporosis. Many clinical studies have shown an increased damage associated with steroid administration in patients with diseases shown in the Systemic Lupus International Collaborating Clinics Damage Index. Reducing steroid doses may similarly reduce steroid-related side effects, but may increase the incidence of disease relapse. In clinical practice, it is important to determine the relationship between side effects and steroid-sparing related relapse. In recent years, hydroxychloroquine, MMF, and belimumab, which have recently been approved for use in Japan, and conversely, tacrolimus, which is rarely used in the United States and Europe, are increasingly used to prevent relapse. Future clinical research in Japan, such as on how to best use these formulations, is necessary.

ES6-1

Cumulative and Updated Evidence of IL-6 from Basic Research

Kazuhiko Yamamoto
RIKEN Center for Integrative Medical Sciences, Japan

Conflict of interest: None

Interleukin (IL)-6 has an ability to control the survival, proliferation, and differentiation of cells and can direct both pro-inflammatory and anti-inflammatory outcomes in infection, autoimmunity, and cancer. In inflammation, IL-6 controls leucocyte recruitment, determines the activity and maintenance of the inflammatory infiltrate, and drives various innate and adaptive immune responses. There are 3 forms of receptor signaling, classical IL-6 receptor signaling, IL-6 trans-signaling, and recently reported IL-6 trans-presentation. Membrane-bound IL-6R and soluble IL-6R are associated with the classical signaling and trans-signaling pathways, respectively. In general, classical IL-6 signaling is responsible for the anti-inflammatory properties of IL-6 and trans-signaling is responsible for the pro-inflammatory actions of IL-6. Membrane-associated IL-6R is present in a small number of cell types, such as leucocyte subsets, hepatocytes, and specialized epithelia, particularly in the gut. Therefore, IL-6 trans-signaling widen the types of cells that elicit IL-6 activities, for example, fibroblasts, endothelial cells, and smooth muscle cells. IL-6 production has been reported to be dysregulated in chronic inflammatory diseases such as rheumatoid arthritis (RA), several different inflammatory diseases, and Castleman disease, along with malignant cells of cancers. Therefore, anti-IL-6 receptor (anti-IL-6R) therapy is now used worldwide in various rheumatic diseases, Interestingly, unlike TNF inhibitors, tocilizumab monotherapy was superior to methotrexate for reducing the signs, symptoms and radiographic progression of RA, suggesting unique features of anti-IL-6 therapy. Further, tocilizumab was approved for the treatment of patients with giant cell arteritis (GCA) by FDA and EMA and has been approved in Japan for the treatment of Takayasu arteritis. Tocilizumab was also approved for the treatment of AOSD in Japan in 2019.

ES6-2

Cumulative and Updated Evidence of IL-6 Signaling Inhibition from RA

Tsutomu Takeuchi
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Conflict of interest: Yes

For the treatment of rheumatoid arthritis (RA) patients, appropriate disease modifying anti-rheumatic drugs (DMARDs) can inhibit inflammation and improve clinical outcome. Currently, physicians aim to achieve clinical remission or at least low disease activity, according to recommendation or guideline using the listed DMARDs such as methotrexate, TNF and IL-6 receptor antibodies. RA is a heterogeneous disease, and there are many individual differences in genetic background, environmental factors, joint symptoms and immune response, and treatment response also varies individually. So far, we have demonstrated not only clinical research data, but also comprehensive molecular and cellular data using blood samples (i. g; the relationship between bone and cartilage destruction and IL-6 concentration, and so on). While it is required to accurately evaluate various RA conditions and treat patients appropriately in clinical practice, recent our research suggested the serum cytokine and several subsets of peripheral cells were coming closer to healthy individuals in RA patients treated with different bDMARDs. However, when we look at the much more precisely for the transciptome, proteome, and immunophenotype in individual patient, those signatures are different with different DMARDs, and the level of these molecular signatures are not comparable to those of healthy individuals, even if they have achieved clinical remission. The characteristics of molecular remission clarified in this study might not only lead to the elucidation of unmet pathological mechanisms, but also might be an important step towards the realization of RA precision medicine and new drug discovery. In this evening symposium, we would like to highlight the significance of IL-6 inhibition based on our tocilizumab data.

ES7-1

Advance and challenges of RA treatment - more patients' better life-

Hiroaki Dobashi
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Conflict of interest: Yes

Rheumatoid Arthritis (RA) treatment has progressed dramatically and RA patients' quality of life have improved remarkably. The spread of treatment strategies such as T2T and Tight Control and the launch of biological DMARDs (bDAMARDs) had greatly contributed to the treatment for RA. As a result, an increasing number of patients have high expectations for the treatment. To meet these patients' expectations, we have to properly use MTX, csDMARDs, bDMARDs, and JAK inhibitor to each patient. As a guideline of proper use of medicines, EULAR Recommendation 2019 had announced at EULAR 2019 Madrid Spain. I would like to talk about the details in this lecture. As RA treatment advances, molecular target drugs that are low molecular weight compounds (JAK inhibitor) are being actively developed likewise high molecular bDMARDs. The JAK1/2 inhibitor Baricitinib has also been available in Japan since 2017. At present three JAK inhibitors (Tofacitinib, Baricitinib, and Peficitinib) are currently available for RA. (December 2019) JAK inhibitors are known to suppress multiple cytokine signaling and bring about high clinical effects. Baricitinib has four major phase 3 international studies (RA BEGIN, RA BUILD, RA BEAM, and RA BEACON). Its effect through clinical trial has been proved, but the evidence through clinical practice is unknown. So I expect the accumulation of it. On the other hand, in terms of safety, JAK inhibitor has a side effect profile different from bDAMRDs, and it goes without saying that management of Herpes zoster is required In this lecture, I will show you the Baricitinib's usefulness and challenges for RA treatment in order to "make more patients better".

ES7-2

Mode of action of JAK inhibitors in rheumatoid arthritis

Akio Morinobu
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Conflict of interest: Yes

It has been 7 years since the first JAK inhibitor (JAKi) came to be used in clinics. Now we have 3 JAKi available as tsDMARDs, with a few possibly approved in the near future. The three JAKi possess different selectivity on JAKs, which may lead to different clinical effects. I will discuss the modes of actions of JAK inhibitors in this seminar. JAKs are tyrosine kinases within cells. When a type I or type II cytokine binds with its receptors, JAKs are activated to in turn activate STAT molecules, and activated STATs translocate to the nucleus to work as a transcription factor. JAKi is an oral drug with low molecular weight and inhibits the kinase activity of JAKs. The importance of type I or type II cytokines in synovitis has been well documented. Because JAKi inhibits signaling of multiple cytokines which belongs to type I and II cytokine families, the mechanisms of immunosuppression should be different from biologics which blocks a specific cytokine. At cellular levels, JAKi have anti-rheumatic effects on various type of cells, including synovial fibroblast, macrophages, and lymphocytes. Interestingly, even the outcomes of stimulation by TNFa, LPS, or CD3 are also blocked by JAKi. This is because these stimulations induce endogenous type I or type II cytokines such as IFNa or LIF, and JAKi shut down of the autocrine loops of these cytokines. There are 4 JAKs and each JAKi has slightly different selectivity for JAKs. Baricitinib inhibits JAK1 and JAK2, but not JAK3 and Tyk2. Clinically, Baricitinib improves patient reported outcomes such as pain VAS scale and fatigueness, as well as disease activity. There is arguments that GM-CSF may be associated with pain in arthritis model mice, and also that depression and fatigueness is closely related with type I IFN, suggesting that Baircitinib may reduce patient pain and fatiguness by inhibiting these cytokines, which are not the direct targets of previous bDMARDs. The characteristics of JAKi is that they inhibit actions of multiple cytokines compared to the bDMARDs which specifically inhibits single cytokine. At the same time these natures of JAKi is also ascribed to their adverse actions such as herpes zoster, hyperlipidemia and so on. The rheumatologist should well know these characteristics of JAKi for its best clinical use.

ES8

Positioning and characteristic of interstitial lung disease associated with connective tissue diseases

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Conflict of interest: Yes

Interstitial lung disease is one of important organ involvements which determine the prognosis of the patients with connective tissue diseases (CTDs). Based on the ATS/ERS classification of diffuse parenchymal lung diseases (DPLDs), interstitial lung diseases (ILD) associated with CTDs are categorized into "DPLDs of known causes" and sequestered from "idiopathic interstitial pneumonia (IIP)" or "granulomatous DPLD". Even CTD-ILD is in this group altogether, it should be subclassified by the underlying diseases since each disease has different pathogenesis, pattern of histopathology and treatment approaches of its own. Furthermore, the concept of interstitial pneumonia with autoimmune features (IPAF), which is an entity proposed to identify patients with DPLDs and features suggestive of CTDs, but not meeting established classification criteria for CTDs, is also recognized. In the clinic, history taking especially associated with CTDs, physical examination including joints and skin and laboratory tests with autoantibody profile are necessary for the differentiation of CTDs from other DPLDs. It is of note that imaging and histopathology do not help for the differentiation. In some cases, ILD is followed by CTD-associated symptom afterwards, which makes difficult to recognize as CTD-ILD at the initiation of the disease. Important characteristic of CTD-ILD is inflammation in the pathogenesis, thus some reversibility of the disease process might be expected. On the other hand, biopsy, including cyrobiopsy or surgical lung biopsy, play an important role for the prediction of the prognosis and/or assessment of the effectiveness of treatment for IIP. However, these significance in CTD-PAH are still unclear. In this session, positioning and characteristic of CTD-ILD in DPLD will be presented and perspective will be discussed.

ES9

Basic Seminar for Spondyloarthritis 2020

Tetsuya Tomita[1], Masahiro Yamamura[2], Manabu Fujimoto[3], Shigeyoshi Tsuji[4]
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Conflict of interest: Yes

Spondyloarthritis (SpA) is a disease group primarily characterized by enthesitis and classified into peripheral SpA or axial SpA depending on the area mainly affected. The representative disease is psoriatic arthritis (PsA) for peripheral SpA and ankylosing spondylitis (AS) for axial SpA. SpA also includes other diseases, such as non-radiographic axial SpA (nr-axSpA), which have common clinical features including bone and joint symptoms, as well as various extra-articular symptoms such as uveitis, psoriasis, inflammatory bowel disease, cardiovascular disease etc. Since rheumatoid arthritis and many other diseases also present similar symptoms, early differential diagnosis of SpA diseases is clinically important while at the same time often difficult in actual clinical practice. This seminar will cover etiological and pathological differences of SpA diseases, important considerations upon diagnosis and clinical management of these diseases, as well as related latest findings from the perspectives of rheumatology, orthopedics, and dermatology.

ES10

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

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

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Conflict of interest: Yes

*Limiting the intended attendees of physicians to 54, this seminar shall be conducted in **a workshop format including discussions and role-play**. *Co-sponsored by The Asahi Shimbun Company and The 64th Annual General Assembly and Scientific Meeting of the JCR. Supported by The RA Patient Association of Japan CONVERSATIONS in MOTION (CIM) is a communication technique program designed for physicians to improve physician-patient communications in the time-pressured reality of office visit. CIM has been developed collaboratively by linguistic and communication experts and rheumatologists in and out of Japan, the effectiveness of each technique in CIM has been scientifically verified. CIM is comprised of four modules: Module I: Shared decision making (SDM); Module II: Empathy and Trust; Module III: Practice efficiency; and Module IV: Medication adherence. This seminar shall focus on Module 1. SDM represents an evolution from informed choice, and it is a concept that physician/patient bi-directionally share information and make a decision. In treatment of RA, the importance of SDM has also been emphasized in Treat-to-Target approaches and the EULAR recommendations. SDM consists of the following six steps: 1) The physician invites the patient to participate in the decision making regarding the treatment; 2) The physician presents treatment options; 3) The physician provides information on benefits and risks; 4) The physician assists the patient in evaluating options based on their goals, concerns and preferences; 5) The physician facilitates the decision making process; 6) The physician continues to assist patients to follow through on their decision. Three critical techniques in this process are “setting expectations”, “weighing pros/cons”, and “eliciting patient preferences”. In this workshop, group discussions will be held on selected points followed by some role-play, so that participants can learn SDM methods that may be put to use immediately in daily clinical practice.

ES11-1

Hand surgery in RA patients under various drug controls

Hiroyasu Ikegami
Department of Orthopaedic Surgery, Toho University

Conflict of interest: None

In Japan, 20 years and 16 years elapsed from the approval of MTX and biologic agents for the treatment of RA. These drugs, which has been initially used as a final tool, become to be used from early disease period according to the concept of early diagnosis, early treatment, and T2T, is one of the standard treatment. The powerful anti-inflammatory effect of these drugs would be able to calm down the synovitis more efficiently, then severe limb deformity and large bone defect, which were well common in the past, have been less. Tight control with methotrexate and biologics leads to remission and low disease activity in the majority of patients, and it seems that there has been a big change in patient needs and the indications even in surgical treatment. Therefore, this time, we made two part consisting of a floor participation type case examination using Answer Pad and a special lecture with the theme of Hand surgery in RA patients under various drug controls. In case examination, we present some cases of thumb, fingers and wrist joints, and we would like to discuss with participants how we face patients at the stage of remission, what needs to be addressed, and how to treat with them. For the special lecture, Dr. Natsuko Nakagawa will give a lecture on Hand Surgery i in patients with rheumatoid arthritis treated with biological DMARDs. We would like to make this workshop useful for clinical practice of all participants and to make it possible to contribute to realization of higher treatment target of RA patients.

ES11-2

Strategy of RA hand surgery for the patients with tight controlled disease activity by biologic agents

Natsuko Nakagawa
Department of Orthopaedic Surgery, Hyogo Prefectural Kakogawa Medical Center

Conflict of interest: None

The treatment of rheumatoid arthritis (RA) has remarkably progressed. Tight control of RA disease activity makes it possible to inhibit the progression of the joint destruction. For this reason, small joint surgeries are assumed to increase in number, which is why RA hand surgery has become more important and been considered than ever. If chronic swelling of the synovium of finger joints does not respond to any conservative treatment, synovectomy should be attempted before bone changes occur, since surgical synovectomy for rheumatoid finger joints has anti-inflammatory effects. We find some patients suffering from active arthritis even with good RA control. For these patients, synovectomy, which directly approach the synovitis inside the affected joint, has been considered to be effective. It is important to preserve the joint. In addition, especially for the wrist joint, synovectomy will be able to prevent extensor tendon rupture. Even under tight control, RA joint destruction proceed in some cases. Therefore, in these cases, it is essential to consider and decide appropriate surgical indication, and also surgical timing is important. For typical RA hand deformity, surgical intervention must be planned according to the pathological cause of the deformity. For wrist surgery, it is important to plan the favourable surgical treatment depending on both the presence of structural change and the degree of joint destruction. For RA patients of finger deformities with only slight joint destruction and dislocation, joint-preserving surgery will be useful. For destructive joint cases surgical intervention is also often necessary. Joint arthrodesis is indicated for unstable joints with poor activity of daily living. This procedure provides pain relief and stabilization. In the future, the number of small joint surgeries is predicted to increase, and RA hand surgery must be planned and carried out under tight control with medication. On the other hand, we should take special caution against infection since RA patients often use immunosuppressive drugs. Even in this era, we find some patients suffering from severe finger deformity despite good RA control. For these patients, surgical intervention and rehabilitation are considered to be effective. Nevertheless, there are still unsolved problems of RA hand. In the near future, it is important for RA surgeon to have ‘aggressive attitude’ toward restoration of rheumatoid hands and fingers, along with drug and

surgical treatment.

ES12

An old and new disease "Hereditary angioedema"~ Important knowledge for rheumatologists

Takahiko Horiuchi
Director, Professor and Chair of the Department of Internal Medicine, Kyusyu University Beppu Hospital

Conflict of interest: Yes

Hereditary angioedema (HAE) is an old disease, which was first reported in 1888 in the US. Recently, there has been amazing progress in HAE research. HAE is an old and new disease. Now, the new findings related to HAE has become the need-to-know knowledge for rheumatologists. In this seminar, I would like to present first the conventional understandings of HAE, and then introduce the most recent research progress. In addition, the need-to-know knowledge of HAE is presented. HAE is a rare hereditary disease with clinical features of sudden and transient edema in the entire body including the face, tongue, extremities, intestine and larynx. As HAE can cause airway obstruction and severe abdominal pain, HAE should not be overlooked by physicians. The symptoms of HAE sometimes resemble those of rheumatic diseases. Moreover, HAE is occasionally complicated by autoimmune disorders. Bradykinin generated by C1-INH deficiency increases vascular permeability and leads to edema attack in HAE. In Japan, we established a Non-Profit Organization, called the Center for Research, Education, And Treatment of angioEdema (CREATE) in 2011 and performed the management of an HAE patient registry, genetic analysis and a patient association of HAE. The data accumulated by CREATE since its foundation will be presented. In addition to the conventional findings, there has been a profound progress in HAE research. First, the pathogenesis of HAE was newly clarified. In 2000, HAE with normal C1-INH was reported. A number of causative gene mutations have been demonstrated, which has shed light on the detailed mechanisms of action of acute edema of HAE. Second, new treatment modalities of HAE are appearing. In these several years, a number of drugs with novel mechanisms of action has been developed. In addition to the conventional purified C1-INH, an inhibitor of bradykinin receptor B2 (icatibant) was launched in Japan in November 2018. Other oral and injectable drugs targeted for bradykinin are under clinical trials or in market in other nations. Bradykinin is one of the most important inflammatory mediators and the strongest pain-inducing agent. Now, the mechanisms of generation, destruction and the know-how of regulation of bradykinin are being clarified owing to the recent HAE research. Finally, I would like to discuss the possible role of bradykinin in the pathogenesis of rheumatic diseases.

ES13-1

Achieving Remission in RA: Elevating expectations for new treatment

Tsutomu Takeuchi
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: Yes

The advent of biologics (bDMARDs) has triggered a paradigm shift in the treatment of rheumatoid arthritis, which has allowed us to aim for clinical, structural, and functional remission. Furthermore, the widespread use of "Treat to Target (T2T)" strategy, which seeks to optimize the treatment to achieve the treatment target of clinical remission in order to improve the long-term quality of life in patients with rheumatoid arthritis, has greatly transformed the treatment of rheumatoid arthritis, which had been lagging in terms of standardization. The recent emergence of oral Janus kinase (JAK) inhibitors (tsDMARDs) has widen the range of treatment options for achieving the treatment target. However, treatment targets are not easy to achieve in routine clinical settings. Indeed, the results from a Japanese cohort study show that clinical remission can be achieved in approximately half of the patients, and there has been no increase in the proportion over the last few years. In addition, joint destruction progresses rapidly particularly during the early stages of disease, and joint deformity occurs within a few years after the onset of bone erosion. Therefore, rapid induction of clinical remission is important to inhibit progression of joint destruction during these stages. In this seminar, we will affirm the significance of clinical remission in the treatment of rheumatoid arthritis and discuss treatment strategies to achieve clinical remission earlier and with higher probability based on the latest clinical study results.

ES13-2

New Possibilities of RA Treatment

Hideto Kameda
Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine

Conflict of interest: Yes

The emergence of biological products targeting inflammatory cytokines led to remarkable advances in the treatment of rheumatoid arthritis. Furthermore, as oral Janus kinase (JAK) inhibitors were recently approved in Japan as well, there is no major difference in available drugs and algorithms for treatment of rheumatoid arthritis between Japan and overseas. In 2016 update of EULAR recommendations, the use of biologics or JAK inhibitors is recommended for patients with a diagnosis of rheumatoid arthritis who have no improvement within three months or attainment of the targeted state within six months after starting treatment with methotrexate or other conventional synthetic disease-modifying antirheumatic drugs or who cannot continue the treatment because of adverse events. It also states that biologics and JAK inhibitors should be combined with methotrexate wherever possible, but if impossible, interleukin-6 inhibitors and JAK inhibitors should be preferred. Thus, while we have many options and established algorithms for the treatment of rheumatoid arthritis, there are some patients who cannot achieve their treatment goal or continue treatment for safety or tolerability reasons. Therefore, therapeutic drugs with high efficacy and safety profile have been demanded. In this lecture, we would like to discuss the clinical significance and position of treatment of rheumatoid arthritis based on the latest evidence.

ES14-1

Considering combination treatment for rheumatoid arthritis treatment

Takeshi Mochizuki
Kamagaya General Hospital

Conflict of interest: Yes

In Japan, rheumatoid arthritis treatment has been successful in pharmacotherapy for more than 15 years after the appearance of biological disease-modifying anti-rheumatic drugs (DMARDs); however, many patients do not benefit from their effectiveness. There are various factors affecting the treatment success, such as complications, economics, and anxiety. The therapeutic goals cannot be achieved despite the use of biological DMARDs or JAK inhibitors. Rheumatoid arthritis treatment requires four pillars, including pharmacotherapy, surgical treatment, rehabilitation, and care. Surgical treatment has been reported to improve pain and function and contribute to the control of disease activity. In rehabilitation, successful joint therapy and functional improvement are expected after exercise therapy and use of orthoses. The physical functions of patients with rheumatoid arthritis are affected not only by disease activity, joint destruction, and complications but also by muscle mass, nutrition, and degenerative diseases. There are many patients, especially those with rheumatoid arthritis, have locomotive syndrome and sarcopenia, and rheumatoid arthritis itself might be a risk factor for physical function deterioration. Improving physical function can be faced with a lot of challenges. What can you do to overcome them? If physical function can be maintained by drug therapy along with surgical treatment and rehabilitation, treatment results can be improved further. Therefore, I would like to consider combination treatment for rheumatoid arthritis.

ES14-2

Clinical effectiveness of abatacept in daily clinical practice -Data from RCT and TBCR-

Nobunori Takahashi
Department of Orthopedic Surgery, Nagoya University Hospital

Conflict of interest: Yes

Abatacept (ABA) has been applied to rheumatoid arthritis (RA) since 2011 in Japan. In the early years, clinical effectiveness of ABA was considered to be mild and slow. However, ABA demonstrated quite similar efficacy in the AMPLE study, a head-to-head comparison between ABA and adalimumab, within patients with equivalent characteristics. ABA became one of the first-biologics considered to be used in the MTX-IR patients in recent years. More and more elderly patients have been treated in the clinical practice in Japan. The balance between effectiveness and safety is more important in the elderly. Elderly patients often have renal dysfunction and pulmonary comorbidity which would be the reasons not being able to use sufficient dose of methotrexate (MTX). In the patients with sufficient concomitant MTX, all biologics would demonstrate their signature effectiveness. However, non-TNF agents would be the optimal treatment option in the patients with no or low dose of MTX. We demonstrated the effectiveness of ABA was similar between patients with and without MTX treatment using propensity score matching. Management of infection risk is one of the most important point when we treat the elderly patients. Previous study demonstrated that >65 years RA patients had higher incidence rate of hospitalized infection disease. We should consider >65 years patients as the elderly and high infection risk group. In Japanese PMS data, incidence rate of serious infection in elderly patients (>65 years) was similar to that in younger patients. Results of Early AMPLE study was demonstrated in 2020 EULAR congress. Early AMPLE was a head-to-head comparison study between ABA and ADA in ACPA/RF double positive, early disease duration, and MTX-IR RA patients. Achievement rate of ACR50 was significantly higher in ABA group. ABA may be a good treatment option in sero-positve early RA patients as well as elderly patients in daily clinical practice.

Workshop

W1-1

Monotherapy with Upadacitinib in MTX-naïve Patients with Rheumatoid Arthritis: Results at 48 Weeks from the SELECT-EARLY Study

Tsutomu Takeuchi[1], Ronald Van Vollenhoven[2], Aileen L Pangan[3], Alan Friedman[3], Su Chen[3], Maureen Rischmueller[4], Ricardo Blanco[5], Ricardo M Xavier[6], Vibeke Strand[7]
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Conflict of interest: Yes

[Objective] Assess safety and efficacy of upadacitinib (UPA) monotherapy through 48 weeks (wks) in methotrexate (MTX)-naïve patients (pts). [Methods] Pts were randomized to UPA 7.5 (Japan only)/15/30mg or MTX. Pts were rescued from Wk12-24 and at Wk26 if they met the rescue criteria. Efficacy data are reported based on initial randomized treatment for the overall and Japan pts. AEs/100 PY are summarized up to Aug 16 2018. [Results] 945 pts, including 138 pts from Japan, were treated. At Wk48, ACR50 was achieved by 63% and 68% of pts on UPA15 and 30 vs 43% on MTX (Japan: UPA7.5, 76%; UPA15, 85%; UPA30, 86%; MTX, 43%). DAS28 (CRP)<2.6 was 49/53% for overall pts on UPA15/30 vs 29% on MTX (Japan: UPA7.5, 71%; UPA15, 78%; UPA30, 75%; MTX, 39%). At Wk48, ΔmTSS were significantly less on UPA15 and UPA30 vs MTX while UPA7.5 was not significant vs MTX. In general, the safety profile of UPA15/30 was similar to MTX, except for total AEs and herpes zoster, which were higher with UPA15/30. 11 deaths due to varied causes were reported with monotherapy. [Conclusions] UPA15/30 continued to show significant improvements in RA signs and symptoms and inhibition of structural damage vs MTX through 48 wks, including among pts from Japan. The safety profile remained consistent with other studies of UPA in RA.

W1-2

Upadacitinib as Monotherapy in Patients with Rheumatoid Arthritis: Results at 48 weeks from the SELECT-MONOTHERAPY Study

Yoshiya Tanaka[1], Josef S Smolen[2], Paul Emery[3], William Rigby[4], Juan Ignacio Vargas[5], Nemanja Damjanov[6], Manish Jain[7], Yunxia Sui[8], Jeffrey Enejosa[8], Aileen L Pangan[8], Heidi S Camp[8], Stanley B Cohen[9]
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Conflict of interest: Yes

[Objective] Assess safety and efficacy of upadacitinib (UPA) monotherapy up to 48 weeks (wks) in patients (pts) with an inadequate response to methotrexate (MTX). [Methods] Pts on stable MTX were randomized to either continue MTX (cMTX) or switch to once-daily UPA15 or 30mg for 14 wks. From Wk14, pts randomized to cMTX were switched to UPA15 or 30. Efficacy data are reported as observed for the overall and Japanese pts. Adverse events (AEs)/100 PYs are summarized up to May 25 2018. [Results] 648 pts, including 65 pts from Japan, were randomized. Cumulative exposures to UPA15/30 were 336.0/337.1 PYs. At Wk48, ACR20 was achieved by 87% of pts continuing UPA15 as well as UPA30 (Japan: UPA15, 90%; UPA30, 84%). DAS28 (CRP)≤3.2 was achieved by 72/80% for pts continuing on UPA15/30 and 85/95% of Japanese pts. Overall, TEAEs/100PYs were numerically higher in the UPA30 vs 15 arm for herpes zoster and hepatic disorders and were comparable for serious infections and malignancies excluding NMSC. Adjudicated VTEs were

observed only on UPA15 (DVT: 2 pts; PE: 2 pts; all pts had at least one risk factor for VTE). [Conclusions] UPA 15/30 resulted in similar improvements in signs and symptoms through 48 wks, including among pts from Japan. The overall benefit-risk profile of both UPA doses was favorable.

W1-3

The long-term safety and efficacy of upadacitinib (UPA) in Japanese patients (pts) with rheumatoid arthritis (RA) and an inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs): 84-week results from SELECT-SUNRISE

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Conflict of interest: Yes

[Objective] Long-term safety and efficacy of UPA in Japanese pts with active RA and inadequate response to csDMARDs. [Methods] All pts who completed the 12-week double-blind period entered the blinded extension, in which they continued with UPA 7.5, 15, or 30 mg once daily (QD), or were switched from placebo to UPA 7.5, 15, or 30 mg QD per the prespecified randomization assignments. Efficacy and safety were assessed over 84 wks. [Results] Of 197 pts randomized, 152 (77.2%) completed Wk 84. ACR20 response rates at 84 wks were 95.5%, 90.5%, and 93.5% for pts continuing UPA 7.5, 15, and 30 mg, respectively, and similar for pts who switched to UPA. Favorable response rates were also seen for more stringent endpoints. AE rates per 100 patient-years were 352.9, 366.1, and 464.3 in the 7.5 mg, 15 mg, and 30 mg groups, respectively, and rates of serious AEs were 16.2, 20.8, and 20.4. Rates of infection (142.5 and 151.9 vs 191.8), opportunistic infection (0.8 and 3.2 vs 8.3), serious infection (4.6 and 6.4 vs 12.0), and herpes zoster (8.5 and 13.6 vs 20.4) were lower with UPA 7.5 and 15 mg vs 30 mg. [Conclusions] In Japanese pts with RA, efficacy with UPA remained favorable over 84 wks. No new safety signals were identified and the overall safety was consistent with previous reports.

W1-4

Efficacy and Safety of Upadacitinib in the SELECT-AXIS 1 Randomized Controlled Phase 2/3 Clinical Study of Patients With Active Ankylosing Spondylitis: Findings in Overall and Japanese Population

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Conflict of interest: Yes

[Objective] Upadacitinib (UPA), a JAK1 inhibitor, is being investigated for the treatment of ankylosing spondylitis (AS). [Methods] Eligible patients (pts) who fulfilled modified New York criteria, were bDMARD naïve, and had an inadequate response/intolerance to NSAIDs were randomized 1:1 to UPA 15 mg once daily or placebo (PBO). [Results] Of 187 pts, 13 were from Japan (UPA, n=6; PBO, n=7). In the overall group, significantly more UPA (48/93 [52%]) vs PBO (24/94 [26%]; P=0.0003) pts achieved the primary endpoint ASAS40 at week 14; in Japan, 2/6 (33%) vs 0/7 (0%). Japanese data were consistent with multiplicity-controlled secondary endpoints significant for the overall group (all P<0.01): ASAS PR (overall UPA vs PBO, 19% vs 1%; [Japan, 17% vs 0%]), BASDAI50 (45% vs 23%; [33% vs 29%]), and change from baseline in ASDAS (-1.5 vs -0.5; [-0.9 vs -0.2]), BASFI (-2.3 vs -1.3; [-1.2 vs -0.5]) and SPARCC MRI spine (-6.9 vs -0.2; [-5.0 vs 2.0]). AEs were reported in 58 (62%) UPA vs 52 (55%) PBO pts overall; 4 (67%, including 1 esophageal candidiasis case that resolved) and 3 (43%) in Japan. No serious infections, malignancy, thromboembolic events, MACE, herpes zoster, or deaths occurred. [Conclusions] UPA 15 mg was efficacious and well tolerated in pts with active AS including in Japanese pts.

W1-5

Examination of patient background for herpes zoster (hz) causedby JAK inhibitor

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Conflict of interest: None

[Objective] In Japan, JAK inhibitors (JAK) for RA have been approved since 2013. The onset of HZ is a problem. We examined the background of HZ. [Methods] 151cases JAK from December 2013 to November 2019. The incidence of HZ and patient background were examined. In addition, we conducted a survey on the awareness of HZ in 400 patients. The subjects (1) outpatient (2) non MTX/Bio RA (3) on MTX RA (4) Bio/JAK RA. [Results] The background of 20 patients who developed HZ was average 65.3 years / 20 cases, only JAK 5 cases, PSL combination 12 cases, MTX combination 14 cases. 3 cases of trigeminal zoster were hospitalized in 2 cases, 15 cases were re-administered, and 3 cases were discontinued. The period from the start of administration to the onset of HZ was 36 to 1751 days (average 515 days). onset within 2 years accounted for 75%. In the awareness survey, HZ Awareness was 90% or higher in all groups, but Recognition for early visits was low (1) 46% (2) 51% (3) 61% (4) 85%. [Conclusions] JAK are high risk factors for HZ, especially in the Japanese. Moreover, despite the high level of awareness of HZ among patients, the degree of recognition for the importance of early treatment is quite low, so it is often difficult to treat. reaffirmed the importance of frequent guidance and created a pamphlet

W1-6

Efficacy and Safety of E6011, an Anti-Fractalkine Monoclonal Antibody, in Rheumatoid Arthritis Patients with Inadequate Response to Methotrexate: Results of a Randomized, Double-blind, Placebo-controlled Phase 2 study

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Conflict of interest: Yes

[Objective] We evaluated the efficacy and safety of E6011, a novel humanized anti-FKN monoclonal antibody, in a Phase 2, double-blind, placebo-controlled study in RA patients inadequately responding to methotrexate (MTX-IR). [Methods] Active RA patients with MTX-IR were randomly assigned to E6011 100, 200, 400/200 mg or placebo in a 1:2:2:2 ratio. Patients received study drug at Weeks 0, 1, 2, and then every 2 weeks. After the 24-week double-blind period, patients received an open-label E6011 until Week 102. [Results] A total of 190 patients (28: 100 mg, 54: 200 mg, 54: 400/200 mg, 54: placebo) were enrolled, and 169 patients completed the 24-week double-blind period. While a statistically significant difference from placebo was not found in the ACR20 response at Week 12 (39.3%, 48.1%, 46.3%, and 37.0% in 100, 200, 400/200 mg and placebo), it was attained at Week 24 in the 200 and 400/200 mg doses with statistical significance (39.3%, 53.7%, 57.4%, and 35.2% in 100, 200, 400/200 mg and placebo). E6011 was well tolerated for 24 weeks. We will also report the long-term (up to Week104) safety data at presentation. [Conclusion] E6011 provided efficacy and tolerability in RA patients with

MTX-IR. This study suggest that a novel approach to target FKN pathway could be beneficial for RA.

W2-1

SAFETY PROFILE OF Upadacitinib IN RHEUMATOID ARTHRITIS: INTEGRATED ANALYSIS FROM THE SELECT PHASE 3 CLINICAL PROGRAM

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Conflict of interest: Yes

Objectives: Assess the safety of UPA as monotherapy (mono) and as combination therapy with csDMARDs in pts with moderately to severely active RA from the safety data of the Phase 3 program. **Methods:** Treatment-emergent adverse events from 5 pivotal, randomized, double-blind, controlled Phase 3 trials of UPA 15 mg [5 trials] or 30 mg QD [4 trials] were analyzed by integrated short-term (ST, 12/14 week, PBO; n [%]), studies with long-term [LT] active comparator and integrated LT (all Phase 3; E/100PY) analyses sets. **Results:** Across the Phase 3, 3834 pts received ≧ UPA 15 mg (n=2630) or 30 mg QD (n=1204). Serious infection (SIEs) frequencies were higher on both UPA doses vs PBO and vs MTX, but similar on UPA 15 mg vs adalimumab (ADA). Herpes zoster (HZ) frequencies were higher on both UPA doses vs PBO, and vs MTX, ADA. LT MACE rates were similar on UPA 15 mg and ADA and on UPA 15 mg and MTX mono, but higher on UPA 30 mg mono. Adjudicated VTEs occurred at comparable frequencies on UPA vs PBO and at comparable rates on UPA vs active comparators. Malignancy excluding NMSC rates were similar on UPA vs MTX, UPA 15 mg vs ADA, and 15 vs 30 mg. **Conclusion:** These data support that UPA has an acceptable safety profile iwith moderately to severely active RA.

W2-2

Safety profile of upadacitinib (UPA) in Japanese patients (pts) with rheumatoid arthritis (RA)

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Conflict of interest: Yes

Objectives To assess long-term safety of UPA in Japanese pts with RA from the UPA development program. **Methods** Japanese pts were included from three studies: the Phase 2b/3 SELECT-SUNRISE study and the Phase 3 SELECT-EARLY and SELECT-MONOTHERAPY studies. Results in Japanese pts were compared with the global population in UPA Phase 2 and 3 studies (twice-daily [BID] dosing in Phase 2; once-daily [QD] dosing in Phase 3). **Results** Overall, 121, 126, and 124 Japanese pts received UPA 7.5, 15, and 30 mg, respectively, and 2883 and 1375 pts (global population) received UPA 6 mg BID/15 mg QD and 12 mg BID/30 mg QD. In Japanese pts, the exposure-adjusted incidence rate (EAIR) of serious AEs was higher in the UPA 30 mg group vs the 7.5 and 15 mg groups (21.2 vs 11.5 and 12.2 n/100 PY, respectively). Similar results were seen for AEs leading to discontinuation. The EAIR of herpes zoster was higher in Japanese pts (7.8, 12.4, and 16.7 n/100 PY in the 7.5, 15, and 30 mg groups, respectively) compared with the global population (3.7 and 7.0 n/100 PY in the 6 mg BID/15 mg QD and 12 mg BID/30 mg QD groups, respectively). **Conclusions** No new safety signals were identified with UPA in Japanese pts. Herpes zoster occurred at higher rates in Japanese pts receiving UPA versus the global population.

W2-3

Incidence and risk factors for herpes zoster (HZ) in Japanese and global rheumatoid arthritis (RA) populations receiving upadacitinib (UPA)

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Conflict of interest: Yes

Objectives To evaluate the incidence and HZ risk factors in Japanese and global RA populations receiving UPA. **Methods** Rates of HZ in Japanese pts were assessed from three studies: Phase 2b/3 SELECT-SUNRISE and Phase 3 SELECT-EARLY and SELECT-MONOTHERAPY. Results in Japanese pts were compared with the global pts in UPA Phase 2 and 3 studies (twice-daily [BID] dosing in Phase 2; once-daily [QD] dosing in Phase 3). **Results** Overall, 121, 126, and 124 Japanese pts who received UPA 7.5, 15, and 30 mg QD and 2883 and 1375 pts who received UPA 6 mg BID/15 mg QD and 12 mg BID/30 mg QD were included. Exposure-adjusted incidence rates (n/100 PY) of any HZ/serious HZ were 7.8/1.5, 12.4/0.9, and 16.7/3.8 in the 7.5, 15, and 30 mg QD groups, while rates in the global 6 mg BID/15 mg QD and 12 mg BID/30 mg QD groups were 3.7/0.2 and 7.0/0.8. Age ≧65 years and history of HZ were significant risk factors for HZ in both the Japanese and global populations. Asian region was also a risk factor for HZ in the global population. **Conclusions** Incidence of HZ was higher in Japanese RA pts versus global pts. Age ≧65 years and history of HZ were risk factor for HZ during UPA treatment in both Japanese and global RA populations.

W2-4

Clinical features and treatment of patients with rheumatoid arthritis (RA) who complicated with malignant tumors from Ninja 2018

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Conflict of interest: None

[Objective] To investigate the clinical features and treatment of RA patients with malignant tumors. [Methods] A patient information was collected using NinJa 2018 from national consisting of 59 facilities in Japan. We investigated disease activity, physical function and treatment for the patients who complicated with malignant tumors. [Results] Fifty thousand and four hundred forty patient's information were collected in NinJa 2018. In these patients, 236 newly malignant tumors was occurred (74 men (31%)), the mean age at diagnosis of malignant tumor and DAS28-CRP was 73.3 ± 9.4y and 2.41 ± 1.09. In 15204 cases without malignant tumors (3036 men (20%)), average age and DAS28-CRP was 66.4 ± 12.8 y and 2.25 ± 0.99. In patients with malignant tumors, the tendency of more common in men, more aging ($p < 0.0001$), and higher disease activity ($p = 0.03$) were seen. The most common malignant tumor was lung cancer (38), followed by malignant lymphomas (34) and gastric cancers (33). In lung cancer, 18 patients had a history of smoking. 66 patients used bDMARDs, but 33 patients discontinued because of malignancy. [Conclusions] This result suggested RA patients complicated with malignant tumors tended to have high disease activity. We need to establish RA treatment for the patients with malignant tumors.

W2-5

Treatment of rheumatoid arthritis associated with other iatrogenic immunedeficiency-associated lymphoproliferative disorders

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Conflict of interest: None

[Objective] The choice of treatment for rheumatoid arthritis (RA) with other iatrogenic immunodeficiency-associated lymphoproliferative disorders (OIIA-LPDs) remain unresolved. Here we present the current status of treatment of RA complicated with OIIA-LPDs. [Methods] RA cases with OIIA-LPDs were retrospectively extracted from medical records and examined for their treatment and prognosis. [Results] Forty-two RA patients with OIIA-LPDs had received 39 methotrexate (MTX) and 7 tacrolimus. Nine of them died. Four cases died of LPDs. Eleven patients had inactive RA during chemotherapy including Rituximab (RTX). Six patients had relapsed RA after on average 32 months of chemotherapy. In all 8 cases treated with RTX alone, RA control was well. RA relapsed in 18 of 21 cases with MTX withdrawal -LPDs remission. RA relapsed on average 6.1 months after MTX discontination, of which 9 cases within 3 months. Many were treated with steroids. Three patients with TCZ, two patient with ABT, and one patient with ETN were treated for relapse of RA, and LPDs have not recurred for more than 1 year. [Conclusions] RA patients treated with chemotherapy containing RTX for OIIA-LPDs tended to have low disease activity over the long term. Large-scale study is necessary in the future.

W2-6

The trends of conventional synthetic DMARDs in Japanese patients with RA by NinJa 2018 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 15440 Japanese RA patients registered with NinJa2018, 11310 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 NinJa2018. [Results] The single use of csDMARD were used 4267 patients medicated MTX, 838patients with SSZ (5.4%), 515patients with TAC (3.3%), 318 patients with BUC (2.1%), 224patients with IGU (1.5%), respectively. The combined therapies of csDMARD were used 806patients medicated MTX+SSZ (5.2%), 493patients with MTX+TAC (3.2%), 440patients with MTX+IGU (2.8%), 333patients with MTX+BUC (2.1%), 192patients with SSZ+BUC (1.5%), 113patients with MTX+SSZ+BUC (0.7%), 440patients with MTX+SSZ+IGU (1.5%), respectively. [Conclusions] The 63.8% of all patients registered with NinJa2018 were medicated csDMARDs therapy. The anchor drug, MTX was most currently used in RA. Iguratimod were widely used in combination therapies with other csDMARDs.

W3-1

Comparison of continuation rate of each biologic agent for Takayasu arteritis

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Conflict of interest: None

[Objective] We compare the continuation rate of each Bio as an index of effectiveness and safety in clinical practice. [Methods] TAK patients who visited our hospital between 1998 and 2019 and who met the ACR classification criteria of 1990 and were receiving Bio were included. We collected the information on clinical courses retrospectively from medical records and analyzed the difference in the continuation rate between IL-6Ri and TNFi and the reason for discontinuation. [Results] There were 21 TAK patients who met the criteria. The prednisolone dose at the time of the introduction of the first Bio was a median of 12.5 mg/day, and an immunosuppressant was used in 13 cases. The median time from initial treatment to the introduction of the first Bio was 31 months. TNFi was discontinued in all 9 patients, and IL-6Ri was continued in 14 of 19 patients. The cumulative continuation rate was significantly higher in IL-6Ri than that in TNFi (72.9% vs. 33.3% at 1 year, P = 0.0295) [Conclusions] IL-6Ri has a higher continuation rate, suggesting that it may be more useful in clinical practice.

W3-3

Clinical features of patients with Takayasu arteritis with pulmonary artery involvement

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Conflict of interest: None

[Background] Pulmonary artery involvement (PAI) in Takayasu arteritis (TAK) is related with severe complications, but its backgrounds have not been fully clarified. [Objectives] To investigate backgrounds and clinical features of TAK with PAI. [Methods] We retrospectively investigated 166 consecutive patients with TAK who were treated in Kyoto University Hospital from 1997 to 2018. We compared clinical features of TAK with PAI and TAK without PAI. TAK was diagnosed according to ACR classification criteria (1990) or Japanese diagnostic criteria (2008). PAI was identified using enhanced CT, MRI, or lung scintigraphy. [Results] PAI was complicated in 14.6% (n=24) of total TAK patients. Dyspnea (25% vs. 8.6%, p=0.043), pulmonary hypertension (PH) (29% vs. 0.7%, p<0.001) and ischemic heart disease (IHD) (29% vs. 9.3%, p=0.018) were significantly more frequent, and stenosis of renal arteries (0% vs. 17%, p=0.007) was significantly less frequent in TAK with PAI than in TAK without PAI. [Conclusions] PAI did not coincident with renal artery involvements, suggesting the presence of subgroups with different vascular distribution patterns. PH and IHD should be screened in TAK with PAI.

W3-4

Percutaneous transluminal renal angioplasty for renal artery stenosis-induced renovascular hypertension in patients with childhood-onset Takayasu arteritis: Four case reports

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Conflict of interest: None

Objective: We investigated the role of percutaneous transluminal renal angioplasty for renal artery stenosis-induced renovascular hypertension in patients with childhood-onset Takayasu arteritis (cTAK). Methods: We retrospectively investigated 4 patients with cTAK who underwent PTRA for renal artery stenosis-induced RVHT between 1990 and 2019. Results: Baseline characteristics evaluated included sex (male: female, 3:1), median age at diagnosis (88 [6-151] months), median interval between onset of cTAK and PTRA (9 [5-13] months), and post-PTRA follow-up (147 [5-228] months). Reversible occipital leukoencephalopathy occurred in 2 patients before performing posterior reversible encephalopathy syndrome. Laterality of renal artery stenosis was as follows: right (2), left (1), and bilateral (1). All patients improved clinically. Antihypertensive drug doses were reduced immediately after PTRA in 3 patients with unilateral lesions. Antihypertensive drug dose reduction was possible after the 2nd PTRA in the patient with bilateral disease. In one patient, PTRA was complicated by a femoral artery pseudoaneurysm. No patient showed post-PTRA renal artery restenosis during follow-up. Conclusions: PTRA effectively treats renal artery stenosis-induced RVHT in cTAK if complications are avoided.

W3-5

A pediatric patient with Takayasu arteritis (TAK) treated by intravenous tocilizumab (TCZ) followed by subcutaneous administration

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Conflict of interest: None

[Introduction] TCZ is used for a treatment to refractory TAK. However, TCZ should be used for patients of 12 years old or older, and be used subcutaneous (s.c.) as a general rule of Japanese public health insurance. [Case] An 8 year-old girl developed persistent fever with inflammatory reaction over 2 weeks. Prednisolone (PSL) was effective; however fever was relapsed during tapering of PSL. Then diagnosis of TAK (Type 1) was made with ultrasonographic imaging followed by 18FDG-PET. TCZ was started because of refractory to therapy combining monthly intravenous cyclophosphamide, PSL and azathioprine at the age of 8. (Bodyweight was 19kg). Initial dose of TCZ was instituted 8mg/kg/2weeks div according to protocol of systemic juvenile idiopathic arthritis, and TCZ was effective for maintenance and reduction PSL dose. TCZ administration was changed safely from 8mg/kg/2weeks div to 162 mg/1week s.c. at the age of 11. (BW was 37kg) [Discussion] TCZ therapy is needed even for pediatric patient with refractory TAK. However, 162mg/week s.c. can be overdose for most of pediatric patient. Therefore, intravenous therapy of which can be modified according to the patient's BW should be also considered for pediatric TAK patient for the reduction adverse event resulting from overdose of TCZ.

W3-6

A refractory case of Takayasu arteritis complicated with pseudo-aneurysm while treating with glucocorticoids, tocilizumab and immunosuppressive agents

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Conflict of interest: None

A 19-year-old woman developed hoarseness. Computed tomography (CT) revealed expanded ascending aorta and aneurysms. She was suspected of Takayasu arteritis and underwent total aortic arch replacement. Inflammatory cells were found in the aortic wall in pathological findings. We administered prednisolone (PSL), tacrolimus (TAC) and tocilizumab. She developed pain of the left side of the neck. CT revealed two pseudo-aneurysms in the left common carotid artery and ascending aorta. She underwent stent deployment and ascending aorta replacement. TAC was replaced with methotrexate (MTX). While CRP had been within the normal range, she presented pain of the left upper extremity. Pseudo-aneurysm of sinus of Valsalva was detected in CT. She had also tricuspid valve insufficiency. She underwent Bentall procedure and tricuspid valvuloplasty. Pathological findings showed the necrosis of medial elastic lamina and aggregate of lymphocytes in adventitia. We increased the dosages of PSL and MTX, and then we were tapering PSL. 18-fluoro-2-deoxyglucose positron emission tomography (FDG-PET) revealed no positive findings. There was a possibility of the existence of disease activity without elevation of CRP. And regular FDG-PET may be useful in detecting the disease activity.

W4-1

Examination of cases with extended tocilizumab administration interval for giant cell arteritis in our hospital

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Conflict of interest: None

[Objective] We report 6 cases that have extended the TCZ administration interval in our hospital. [Methods] Among GCA cases that can be collected from medical records at our hospital and related hospitals as of November 2019, a total of 6 cases with a TCZ administration interval extended to 2 weeks or more The prednisolone dose, relapse, and adverse events were investigated for the first 4 cases that were introduced and 2 cases that were relapsed and TCZ was introduced in order to strengthen treatment. [Results] The age at the time of TCZ introduction was 78.2 years, the mean PSL dose / day was 37.5 mg / day in the first case, and 4.0 mg / day in the relapsed case. As of November 2019, the average observation period after extension of the TCZ interval is 8 months, with 4 cases admission TCZ biweekly intervals and 2 cases every 3 weeks. In all cases, prednisolone and immunosuppressants are off, and no cases of relapse or serious adverse events were observed. [Conclusions] TCZ was able to suppress disease activity in all cases and it was possible to extend the interval. However, evaluation of disease activity is a future research subject because it is necessary to evaluate by image diagnosis.

W4-3

Proposal of a method for diagnosis by vascular echo using 3DCTA as a signpost as an optimization of Cranial type imaging diagnosis of giant cell arteritis

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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 compared clinical and serological characteristics and imaging findings and biopsy findings in 20 cases diagnosed with GCA between 2012 and 2018 in our hospital. [Results]: There were 18 cases with Cranial lesions, with a PMR of 50%. The first symptoms were headache symptoms, 15% were blind to one eye. Head and neck CTA patients were 77.8%, and the positive rate of findings was 78.6% for CTA. The highest rate of CTA findings and other imaging tests was 63.3%. Based on these results, we first perform vascular echo, followed by CTA and MRI / A, PETCT for negative cases, and biopsy if negative. By constructing an image in 3DCTA, the running of the temporal artery and stenotic lesion are visualized, and a blood flow map is created by performing blood vessel echo again and feeding it back as a signpost of blood vessel echo. [Conclusions]: We propose a diagnostic method that creates a blood flow map by combining vascular echo and 3DCTA as an optimization of diagnostic imaging for practicing early diagnosis and treatment initiation to eradicate blindness and stroke patients associated with GCA.

W4-4

Temporal artery biopsy in the diagnosis of giant cell arteritis requires only one side if the serum CRP level is 10 mg/dl or more

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Conflict of interest: None

[Objective] Temporal artery biopsy (TAB) is the gold standard for the diagnosis of giant cell arteritis (GCA). Since the rate of bilateral TAB (b-TAB) positive only on one side is reported to be 5-20%, one-sided TAB alone may miss the diagnosis. We investigated the background of GCA positive only on one side. [Methods] All GCA cases on which b-TAB was performed from April 1, 2011 to July 31, 2019 were extracted retrospectively. Patient characteristics and clinical data just before TAB were extracted from medical records and compared between the bilateral positive group (BPG) and the unilateral positive group (UPG) statistically. [Results] Forty seven GCA patients were identified (median age 75 years, 32 women). Of these, 31 were BPG and 6 were UPG. Fever, intra-cranial symptoms, abnormal findings in the temporal arteries, shoulder girdle pain, imaging, laboratory data (ESR, CRP, albumin, blood count, liver en-

zymes, MMP-3) were examined. Among these, the median of serum CRP level (mg/dl) of each group was 10.6 and 6.5 (median test: p=0.031). In prediction of the BPG, the cut-off value of serum CRP value with a specificity of 100 % was 9.3 (AUC 0.726). [Conclusions] When the serum CRP level was 10 mg/dl or more, the diagnostic accuracy could be maintained with unilateral TAB alone.

W4-5

A case of elderly-onset large vessel vasculitis diagnosed and followed by Diffusion weighted Whole body imaging with Background Suppression (DWIBS)

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Conflict of interest: None

[Case presentation] A 73-year-old woman was referred to our hospital due to persistent low-grade unknown fever for two months. Standard blood examination and nonenhanced CT scan failed to reach a diagnosis. There were no associated symptoms without 5kg weight loss. Initial laboratory findings as follows: WBC: 5400/μl, CRP: 12.3mg/dl, PR3-ANCA: 0.1U/ml, MPO-ANCA: 0.3U/ml, ferritin: 333ng/ml, sIL2-R: 828U/ml. Both blood and urine cultures were negative. There were no remarkable findings on transthoracic echocardiogram. Ultrasonography and contrast-enhanced CT scan revealed only arteriosclerosis of aorta. Diffusion weighted Whole body imaging with Background Suppression (DWIBS) revealed high signal intensity in the wall of thoracoabdominal aorta. Therefore, she was diagnosed as large vessel vasculitis (LVV). 40 mg of prednisolone (PRD) and low dose aspirin were started. The fever disappeared immediately. The serum CRP levels were *decreased* rapidly. After 23 days of therapy, the lesions detected on DWIBS was completely disappeared. [Discussion] In this case, ultrasonography and contrast-enhanced CT scan cannot distinguish vasculitic lesions from arteriosclerotic legions. DWIBS seems to be effective especially for elderly-onset LVV patients associated with arteriosclerosis.

W4-6

A case of giant cell arteritis treated with tocilizumab complicated with recurrent aortic dissections

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Conflict of interest: None

Case: a 68-year-old female with fever and headache Medical History: In September 2017, she visited our hospital complaining of fever and headache. CRP and ESR were elevated, and contrast-enhanced CT scan revealed circumferential wall thickness from the descending aorta to the abdominal aorta. Temporal artery biopsy showed a finding of vasculitis and the patient was diagnosed as GCA. In October 2017, steroid was started and the response was good. Steroid was decreased with additional MTX. Contrast-enhanced MRI the wall thickness of abdominal aorta improved. In October 2018, it relapsed with PSL 7mg. The symptoms improved with steroid and added subcutaneous TCZ. In June 2019, a Stanford type B aortic dissection developed and the patient was transferred to Nippon Medical School Hospital and treated conservatively. On August 20, a Stanford type A aortic dissection developed and artificial blood vessel replacement was performed. Pathological specimens of the aorta showed elastic fiber destruction and rupture with inflammation. Clinical Significance: we report a rare case of recurrent aortic dissection with GCA. Imaging evaluation of the activity of large vessel vasculitis is not easy and TCZ may make it more difficult by making CRP negative.

W5-1

Analysis of the discrepancy between disease activity between patients and doctors, and determination of relevant factors of SLE

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Conflict of interest: None

Objective: Lately, gaps in the evaluation of rheumatoid arthritis (RA) disease activity (DA) between patients and doctors have been pointed out; yet, there are few reports about systemic lupus erythematosus (SLE). This study aims to seek if the gaps exited in SLE and viable basis behind them. **Methods**: 318 SLE outpatient questionnaires at our hospital (Jan 2018 - Sep 2019) were collected. The correlation between Physician's Global Assessment (PGA, 10cm scale) and Patient Global Visual Analogue Scale (PG-VAS), and between the difference of PGA minus pVAS (Δ(PGA-pVAS)) and 24 items of SLE Disease Activity Index (SLEDAI) or 38 items of SLE symptom checklist (SSC) were studied. **Results**: PGA significantly and positively correlated with pVAS ($p<.0001$, R^2: 0.09). Leukopenia and anti-DNA antibody significantly and positively correlated with Δ(PGA-pVAS). Alopecia, mucosal ulcer, leukocyturia, and all of the SSC items significantly and negatively correlated with Δ(PGA-pVAS). **Conclusions**: Due to unusual laboratory results, doctors had lower DA scores, while patients had lower DA scores due to subjective assessment. Assent of the basis of the gaps will help improve the quality of medical care and patient life.

W5-2

The effects of disease activity, organ damage and treatment at the time of diagnosis on the quality of life with young patients with SLE

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Conflict of interest: None

[Objective] To clarify the effects of disease activity, organ damage and treatment at the time of diagnosis on the quality of life (QOL) in young SLE patinets. [Methods] We collected SF12v2®, the disease activity, damaged organs and initial treatment at the time of diagnosis from the young patients who enrolled in the PLASURE-J study. Statistic analysis were performed to estimate the relationship between SF12v2 and other factors. [Results] 73 patients (65 women, 8 men) were analyed. The median age and quartile are 27 years (21.5, 31). SF12v2® component summary scores (median, quartile) are 49.6 (40.5, 55.5), 48.6 (41.7, 55.0), 41.8 (31.5, 49.1), respactively. Patients with high disease activity had significantly lower PCS scores, while MCS / RCS scores were not necessarily associated with disease activity. In terms of symptoms, PCS scores were higher in

patients with blood cell disorders and skin symptoms. The RCS score decreased significantly in patients treated with steroid and cyclophosphamide pulse therapy, while the MCS score was significantly higher in patients treated with hydroxychloroquine (HCQ) than in non-treated patients. [Conclusion] More large cohort study is needed to cralify the factors that could affect QOL with young SLE patiets in early stage after diagnosis.

W5-3

Validation of the Japanese SLE Symptom check list in Japanese patients

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Conflict of interest: None

[Objective] Lately, Patient Reported Outcome (PRO) was proposedfor the evaluation and improvement of QOL in systemic lupus erythematosus (SLE) patients. One of the PRO evaluation tools, SLE Symptom Checklist (SSC) is a simple tool that evaluates the severity of 38 types of symptoms from patient interviews with 0 to 4 points, and measures PRO with a total score of 0 to 152. A Japanese version of SSC, J-SSC was created and its usefulness verified in this study. [Methods] 47 SLE patients at Kyoto University Hospital were surveyed by questionnaires using J-SSC, SF-36, LupusPRO, and Patient Global Visual Analog Scale (PG-VAS). [Results] The average score for J-SSC was 37, whichsignificantly correlates with PG-VAS and all areas of SF-36 and LupusPRO healthy area, except for the pregnancy worry. The top three areas with strong correlations are social life function, physical pain, and mental health in SF-36, and health-related quality of life, psychological health, and SLE symptoms in LupusPRO. [Conclusions] J-SSC is excellent in the evaluation of health areas, and is shown to work properly as a disease-specific PRO evaluation tool. The symptoms that worry the patients can be confirmed. Thus J-SSC is a useful tool for assessing the cause of patient's QOL reduction and measures for improvement.

W5-4

The association between the dose of glucocorticoids and emotional health in patients with systemic lupus erythematosus in Lupus Low Disease Activity State: a cross-sectional analysis of a LUpus registry of NAtionwide institutions (LUNA)

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Conflict of interest: None

[Objective] Glucocorticoids (GC) were widely used for treatment of systemic lupus erythematosus (SLE) and were generally known to cause emotional health problems. Association between current GC dose and emotional health status among SLE patients in Lupus Low Disease Activity State (LLDAS). [Methods] Data collection was completed in April 2018 through August 2019. SLE patients aged ≧20 years were enrolled from 8 institutions in Japan. The exposure was daily GC dose. Main outcome was Emotional Health domain (EH) score of Lupus Patient Reported Outcome (LupusPRO). Relationship between daily GC dose and EH score was analyzed using multiple regression analyses, excluding patients with missing data. [Results] Overall, 175 patients were included; 89.7% were female and median age was 47 (IQR 37-61) years. Median SLEDAI was 2 (IQR 0-4), and median daily GC dose was 4.0 (IQR 2-5) mg. Median EH score was 79.2 (IQR 58.3-91.7). β coefficient (every GC 2.5mg) was -5.31 (p=0.03) for daily GC dose and EH score. Multivariate analysis showed that the daily dose of GC was significantly associated with the EH score (β=-5.74 [95%CI -10.54 to -0.93], p=0.02). [Conclusions] The daily GC dose may affect emotional health status even in LLDAS.

W5-5

Impact of low disease activity and remission on quality of life in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] In recent years, the importance of lupus low disease activity (LLDAS) and achievement of remission has been proposed in the treatment of systemic lupus erythematosus (SLE). However, there are few reports on the impact of these achievements on patient's quality of life (QOL). In this study, we analyzed the effect of achieving LLDAS or Clinical Remission on T (CRT), which is one of Definition Of Remission In SLE (DORIS) remissions, on the patient's QOL. [Methods] We surveyed the background of 295 SLE patients who have been commuting to Kyoto University Hospital for more than 3 years from the electronic medical record. The results of the questionnaire survey of 38 items of SLE symptom check list (SSC) and Patient Global Vas (PG-VAS), one of the Patient Reported Outcomes (PRO) evaluation tools, were analyzed. [Results] The achievement rate was 34.9% for LLDAS and 28.8% for CRT. PG-VAS was significantly lower in patients who achieved LLDAS or CRT than those who did not (LLDAS 31.6 vs 38.6, p = 0.0170; CRT 29.4 vs 38.9, p = 0.0019). Although there was no significant difference in the SSC total score, significant improvement was observed in 7 items. [Conclusions] Patients with LLDAS or CRT achieved good PG-VAS and SSC, suggesting the possibility of contributing to QOL improvement.

W5-6

Treat-to-target strategy in patients with systemic lupus erythematosus (SLE) according to Lupus Low Disease Activity State (LLDAS, Franklyn et al, 2016) and DORIS (Definitions Of Remission In SLE, van Vollenhoven et al, 2015)

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Conflict of interest: None

[Objective] Retrospective assessment of 83 SLE patients according to LLDAS and DORIS. [Methods] **LLDAS**: patients with prednisolone (PSL) ≦7.5 mg/day and SLEDAI ≦4. **DORIS**: with PSL ≦5 mg/day and 1) Clinical remission on treatment (ClinROT) or 2) complete remission on treatment (CompROT), and PSL off and 3) clinical remission (ClinR) or 4) complete remission (CompR). [Results] Disease duration was 24.7±8.6 years. Fifty-one (61.4%) had LLDAS at final day, 19 had ClinROT and 21 had CompROT: no ClinR and no CompR. Flares occurred in 67.4% of LLDAS, and in 69.9% of ClinROT and 2 ClinR which were significantly higher than flares of seronegative CompROT (45.7%). Patients with LL-

DAS or remission of more than 50% of observed time had significantly lower maximum PSL, maximum and final SLEDAI, fewer nephropathy, lower SLICC/ACR damage index (SDI) than those with less than 50% of duration. Twenty-one patients with PSL 2.5 mg daily had significantly less flares, lower final SLEDAI and SDI, and longer cumulative LLDAS and remission years than patients maintaining PSL 5~7.5 mg. [Conclusions] Treat-to-target approach in SLE is firstlly to achieve LLDAS with PSL 7.5 mg daily, followed by reduction of PSL to 5 mg and mainteining 2.5 mg. PSL off ClinR and CompR should not be achieved to prevent flares.

W6-1

Effects of hydroxychloroquine administration on LLDAS achievement in systemic lupus erythematosus

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Conflict of interest: None

[Objective] This study aimed to investigate the effect of hydroxychloroquine (HCQ) administration on LLDAS achievement ratio in the treatment of systemic lupus erythematosus (SLE). [Methods] Patients with SLE under the treatment of HCQ during 2015 and 2018 are enrolled. We reviewed retrospectively the LLDAS achievement ratio and the factors influencing achievement every 6 months up to 42 months in patients receiving HCQ. [Results] There were 78 cases (11 males), the age at the start of HCQ was 43 ± 12.9 years, the prednisolone (PSL) dosage was 10 ± 10.1 mg, and 15 had achieved LLDAS since the start of treatment. In the achieved group, PSL dosage after HCQ addition was reduced or maintained. Of the unachieved groups, 10/63 (15.9%) achieved LLDAS in 3 months. CH50 titers increased by 2.9 ± 15.9 U/mL and 4.7 ± 13.5 U/mL, C3 increased by 6.5 ± 16.9 mg/dL and 7 ± 17.4 mg/dL 12 months and 24 months after HCQ, respectively. The anti-dsDNA antibody decreased by 2.5 ± 85.9 IU/mL and 1.0 ± 140.26 IU/mL, and SLEDAI-2K decreased by 2.0 ± 3.17 and 2.0 ± 2.27 respectively. The most common side effects was rash, nausea, diarrhea. [Conclusions] HCQ administration showed increased complement levels and decreased anti-dsDNA antibodies, and contributed to achievement to LLDAS by clinical symptoms improved.

W6-2

The effectiveness of hydroxychloroquine for sparing PSL among the patients with systemic lupus erythematosus: a cross-sectional study of the LUNA registry

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Conflict of interest: None

[Objective] To investigate the glucocorticoid sparing effect of hydroxychloroquine (HCQ) in patients with systemic lupus erythematosus (SLE) using a multicenter SLE registry. [Methods] Among SLE patients who were registered in the LUNA registry and administrated prednisolone (PSL) less than 15 mg/day, those who used HCQ both at baseline and a year later was included in HCQ group and those without HCQ both at baseline and a year later was included in non-HCQ group. The demographic, clinical, and laboratory data were compared between the two groups. [Results] Of the 931 registered SLE patients, 230 (24.7%) used HCQ. The rate of HCQ use significantly varied among facilities ($p < 0.001$). Among the SLE patients who were extracted by the method, the HCQ group included 62 patients, and the non-HCQ group included 265. As to baseline data, although mycophenolate mofetil were used more frequently in HCQ group ($p = 0.012$). During the one year observation period, the reduction of glucocorticoid dose was significantly larger in HCQ group as compared to non-HCQ group (1.81±2.11 vs 1.16±1.93 mg/day, $p = 0.020$). [Conclusions] HCQ can have glucocorticoid sparing effect in the maintenance therapy of SLE in the real world.

W6-3

Effect of HCQ on LLDAS achievement in SLE patients

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Conflict of interest: None

[Objective] To clarify the effect of HCQ treatment on the disease activity in SLE patients. [Methods] All SLE patients with low disease activity started additional HCQ treatment from Jan 2016 were enrolled. Disease activity was evaluated by SLEDAI, CLASI, and LLDAS, and serum complement, anti-DNA antibodies (antiDNA), and cytokines were analyzed before and after HCQ treatment. [Results] 34 of 45 patients achieved LLDAS and 3 patients achieved CR before additional HCQ. Of the 20 patients not achieved LLDAS before HCQ, 28% were in the glucocorticoid dose not achieved (GC) group and 72% were in the SLEDAI not achieved (SLEDAI) group. LLDAS rate in the GC group was 80% at 6 month (6M) and 100% at 12M. The LLDAS rate in the SLEDAI group was 50% at 6M and 82% at 12M and the factors for LLDAS were rash and low complement at 6M, and arthritis and antiDNA at 12M. CR rate in the SLEDAI group (98%) was 14% at 6M and 33% at 12M, and the factors for CR were rash and antiDNA at 6M and low complement at 12M. Serum levels of S100A8, S100A9, TNF-α, IL-6, VEGF and IL-1ra were associated with L-SLEDAI achievement and those patients with past LN were associated with serum levels of IL-8. [Conclusions] Additional HCQ treatment is useful not only in reducing GC but also in controlling SLE disease activity.

W6-4

The efficacy and safety of hydroxychloroquine (HCQ) for SLE, the effect on dose reduction of PSL

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Conflict of interest: None

[Objective] To examine the details of cases to which hydroxychloroquine (HCQ) was administered with systemic lupus erythematosus (SLE). [Methods] Among the patients diagnosed as SLE in 1997 ACR classification criteria, 73 patients who received HCQ were analyzed. They were added during maintenance therapy for SLE. [Results] The average dose of prednisolone in the maintenance therapy was reduced (- 2.31±4.34mg at 1st year (61 cases), and -8.23mg ±13.1mg at 2nd year (39 cases), -9.60±14.2mg at 3rd year (20 cases). The serum complement C3 and C4 were increased (C3: 22.7 ± 16.5 mg/dL at 1st year, 7.65±35.3 mg/dL at 2nd year, 6.83±21.5 at 3rd year. C4: 6.0 ±5.2 mg/dL at 1st year, 1.67 ±8.23 mg/dL at 2nd year, 1.34±5.32 at 3rd year). Among the patients who started HCQ, the disease status of SLE in 5 cases worsened. Seven cases withdrew HCQ for drug rash, 1case withdrew for general malarise,1 case withdrew for HCQ retinopathy, and 1 case withdrew for patient's decision. [Conclusions] The results of this study suggested that, additional adminis-

tration of hydroxychloroquine is expected to reduce predonisolone without flare of the disease activity of SLE. Conflict of interest: No

W6-5

The effect of hydroxychloroquine on reduction of prednisolone for Japanese patients with systemic lupus erythematosus on maintenance therapy of low-dose corticosteroid

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Conflict of interest: None

Objective: We evaluated the additional therapeutic effect of HCQ for Japanese SLE patients receiving low-dose corticosteroid. Methods: We retrospectively evaluated Japanese SLE patients with prednisolone (PSL) 7.5 mg/day or less for at least 6 months up to 2 years without flare, during November 2016 to April 2019 in our hospital. We compared the change of PSL dose, the number of immunosuppressant (IS) use, and flare rate between patients who were newly treated with HCQ and were not treated with HCQ. Result: Among the 134 patients, 30 patients were newly treated with HCQ. The clinical features between two groups were different in mean age (51±17 y.o. / 58 ±14 y.o.), median disease duration (103 [45-169] / 216.5 [135.2-311] months), mean observation period (15.2±5.8 / 21.8±5.0 months), and the ratio of IS use (60.0 vs. 34.6%). Mean PSL dose were 4.88±1.66 mg /4.94±2.03 mg. PSL dose was significantly reduced in patients with HCQ (-1.5mg vs -0.5mg mg/day, $p<0.001$). Each group had one patient who newly started IS, and no one stopped. The flare rate of HCQ group was 10 /100 patients/year, which was double of non-HCQ group (5 /100 patients/year). Couclusion: In Japanese SLE patients with low-dose PSL, HCQ could reduce the daily PSL dose of 1mg/day, however, HCQ increased the flare rate.

W6-6

Prescription ratio of hydroxychloroquine in SLE patients undergoing immunosuppressive treatment and the reason for non-prescription based on patient factors and physician factors

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) is positioned as standard treatment for SLE, but the prescription rate in Japan is unknown and the reason for non-prescription is unclear. The purpose of this study is to examine patient factors and physician factors in non-prescription cases of SLE in our hospital. [Methods] 210 cases which used steroids and/or immunosuppressants at the end of October 2019 were included. We retrospectively compared patient factors and physician factors in two groups of HCQ prescription and non-prescription, and performed logistic regression analysis. [Results] 102 cases (48.6%) were prescribed HCQ, and 109 cases (51.4%) were not. In univariate analysis, age (49.2±15.9 vs. 58.4±14.6), disease duration (11.4±9.8 vs.21.0±10.7), SLEDAI (5.5±4.4 vs.3.2±2.5), PSL dose (13.6±13.2 vs. 4.9±2.8), eGFR (83.9±29.6 vs. 69.8±26.8), and post-graduate years of physicians ≧10 years (34.3% vs. 72.3%) were associated with non-prescription. In multivariate analysis, statistically significant items included PSL dose (mg) [Odds 0.83], disease duration (year) [Odds 1.06], post-graduate years of physicians (≧10 vs. <10) [Odds 2.72]. [Conclusions] Long disease duration and low PSL dose were suggested as patient factors related to non-HCQ prescription, and long post-graduate years as physician factors.

W7-1

Validation of the diagnostic criteria for IgG4-related kidney disease (IgG4-RKD) 2011: a multi-center study by the IgG4-RKD working group of the Japanese Society of Nephrology

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Conflict of interest: None

[Objective] To validate the diagnostic criteria for IgG4-RKD proposed by the IgG4-RKD working group in 2011. [Methods] Among patients diagnosed as having renal injury between April 2012 and May 2019 at the institutions affiliated to the IgG4-RKD working group, we initially selected those whose serum IgG4 values and/or data for immunohistological staining of IgG4 in renal biopsy samples were known, and then further selected those with sufficient clinical information for inclusion in the study. These patients were classified as IgG4-RKD or non-IgG4-RKD based on the diagnostic criteria for IgG4-RKD (2011), and the results were evaluated by expert opinion. [Results] Among 105 included patients, the expert panel diagnosed 55 as true IgG4-RKD and 50 as non-IgG4-RKD (mimickers). Among the former, 40 were classified as IgG4-RKD based on the diagnostic criteria for IgG4-RKD 2011 (sensitivity 72.7%). On the other hand, 45 of the 50 mimickers were classified as non-IgG4-RKD (specificity 90%). Among the 15 patients with true IgG4-RKD who were classified as non-IgG4-RKD, many lacked storiform fibrosis upon renal histology and biopsy-proven IgG4-related extra-renal lesions. [Conclusions] Although the diagnostic criteria for IgG4-RKD (2011) are highly specific, their sensitivity is relatively low.

W7-2

Automatic diagnosis support for IgG4-related disease based on machine learning

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Conflict of interest: None

[Objective] It is necessary for systemic evaluation in the diagnosis of IgG4-related disease (IgG4-RD). Enhanced computed tomography (CT) is usually effective for the screening, but there are patients cannot use it due to renal dysfunction. Therefore, we performed a retrospective analysis whether it is possible to predict the presence of the other organ involvements (OOI) using the physical and laboratory findings at the first visit based on machine learning in the patients with IgG4-RD. [Methods] The subjects were 332 IgG4-RD cases in Sapporo Medical University Hospital (SMU) and 30 IgG4-RD cases in Kanazawa University Hospital (KNU). At the Institute of Medical Science, the University of Tokyo, we built the model by the data set consisted of 42 clinical and laboratory items in the first visit at SMU, and verified to predict the presence of OOI in KNU data set. We finally evaluated its accuracy. R-code was used for statistical analysis software. [Results] The accuracy of lasso regression showed the sensitivity and specificity was 0.853 and 0.663. The AUC (area under the curve) was 0.869. [Conclusions] The machine learning algorithm showed that it may be possible to predict the presence of the OOI in IgG4-RD.

W7-3

Analysis of the CCL8/CCL1-CCR8 axis in LAT Y136F knock in mice as a model of IgG4-related-disease (IgG4-RD)

Fumika Honda[1], Hiroto Tsuboi[1], Yuko Ono[1], Saori Abe[1], Hiroyuki Takahashi[1], Kiyoaki Ito[2], Kazunori Yamada[2], Mitsuhiro Kawano[2], Yuya Kondo[1], Isao Matsumoto[1], Takayuki Sumida[1]
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Conflict of interest: None

[Objective] Recently we have revealed the upregulation of CCL18-CCR8 axis in IgG4-RD. The purpose of this study was to clarify pathogenic roles and therapeutic potential of CCL8/CCL1-CCR8 axis, using the animal model of IgG4-RD (LAT Y136F knock in mice; LAT mice). [Methods] LAT or littermate mice were sacrificed at 6 and 10 weeks of age. 1) Salivary glands (SG) and pancreas were examined by HE and immunofluorescence staining. For SG, the inflammatory lesions were graded by focus score (FS). 2) mRNA expression levels of CCL8, CCL1 and CCR8 in spleen, cervical lymph node, thymus, kidney, pancreas, SG and lacrimal glands were examined by qPCR. [Results] 1) The infiltration of mononuclear cells including $CD4^+$T and $B220^+$B cells was detected in SG and pancreas of LAT mice. The FS of SG was significantly higher in LAT mice than in littermate (FS at 6 and 10 weeks: littermate 0 vs LAT 2.3) ($p<0.05$). 2) mRNA expression levels of CCL8, CCL1 and CCR8 in SG, pancreas and kidney, as well as CCL8 and CCL1 in spleen and thymus were significantly higher in LAT mice than in littermate ($p<0.05$). [Conclusions] LAT mice developed mononuclear cells infiltration and upregulation of CCL8, CCL1 and CCR8 in SG and pancreas. We are plannig to examine the effectiveness of CCR8 blocking therapy for these lesions.

W7-4

Analysis of T/B cells specific gene expression pattern by RNA-Seq in patients with IgG4-related disease

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Conflict of interest: None

[Objective] To clarify T/B cells specific gene expression pattern using RNA-Seq in IgG4-related disease (IgG4-RD). [Methods] Pathologically confirmed submandibular gland (SMG) and PBMC were collected from a treatment naïve patient with definite IgG4-RD, subsequently PanT and $CD19^+$B cells were sorted by MACS. We compared the gene expression of 1) PanT and 2) $CD19^+$B cells by RNA-Seq between SMG and PBMC, and performed pathway analysis for differentially expressed genes (DEGs) using web tool (reactome). [Results] 1) We identified 844 up-regulated and 597 down-regulated DEGs in PanT cells from SMG compared with PBMC. Pathway analysis for up-regulated DEGs in SMG clarified co-stimulation by CD28, PD-1, TCR, cytokines (IL-2, 4, 6, 10, 13) signaling, and Treg development. 2) We identified 1085 up-regulated (including IGHG4) and 783 down-regulated DEGs in $CD19^+$B cells from SMG compared with PBMC. Pathway analysis for up-regulated DEGs in SMG clarified BCR, FCGR, FCERI signaling, and complement activation. [Conclusions] T cells in affected organs of IgG4-RD highly expressed TCR and Th2/Treg cytokines signaling, corresponding with previous reports. B cells in affected organs highly expressed BCR, IgG/IgE receptor, and complement signaling, suggesting a novel pathogenic mechanism of IgG4-RD.

W7-5

Study on PET-CT and detection rate of biopsy site in IgG4-related disease

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Conflict of interest: None

[Objective] In IgG4-related diseases, PET-CT is important for the selection and differentiation of biopsy sites. However, there are no reports on detection rates of SUV and biopsy sites. [Methods] The purpose of this retrospective study was to investigate whether the SUV of PET-CT at the biopsy site was associated with a positive biopsy in 21 patients who underwent PET-CT before treatment for IgG4RD at our hospital and our hospital associated hospitals. The age at diagnosis was 64.5 ± 11.9 years, serum IgG4 was 743.8 ± 584.1 mg/dl, and the biopsy site was 24 sites, and the result was consistent with IgG4RD at 19 sites. [Results] SUV-max at the biopsy site was not related to the biopsy results, but SUV-mean and SUV-max/liver SUV-mean at the biopsy site were significantly higher in the positive group, and the optimal cut-off points were 4.07 and 1.99, respectively. Of the 10 submandibular glands examined at the same site, 9 were positive, and in the negative cases, the SUV-mean and SUV-max lesions were lower than the mean of the SUV-mean lesions. And, the correlation between SUV value and number of the IgG4 organ lesion and exacerbation rate for 1 year was not recognized. [Conclusions] In IgG4-related diseases, PET-CT is effective for selecting the biopsy site.

W7-6

Clinical significance of serum uromodulin in IgG4-related disease

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Conflict of interest: None

[Objective] To clarify the clinical significance of serum Uromodulin (UMOD) in IgG4-related diseases (IgG4-RD). [Methods] Serum UMOD was measured using an Enzyme-Linked ImmunoSorbent Assay (ELISA) kit in the serum of IgG4-RD group (21 cases) which newly diagnosed in our department and in serum of control group (97 cases). Control group (group C) included the cases with chronic glomerulonephritis, diabetes, hypertension, dyslipidemia. Serum UMOD and UMOD/estimated glomerular filtration rate (eGFR) were compared with various clinical parameters. [Results] Serum UMOD was positively correlated with eGFR ($P<0.01$, $r = 0.55$). There was no significant difference in the average age, sex, eGFR calculated from Creatinine between IgG4-RD group and C group (67.3 ± 6.8 years vs 67.7 ± 14.8 years, male 81% vs 68%, 65.5 ± 21.6 vs 63.7 ± 22.6 mL/min/1.73m^2). Serum UMOD was no significant difference between the two groups (175.6 ± 88.1 vs 213.1 ± 98.6 ng/mL, $p = 0.11$), but UMOD/eGFR was significantly lower in IgG4-RD group (2.73 ± 1.3 vs 3.46 ± 1.4, $p = 0.03$). [Conclusions] The UMOD/eGFR ratio was significantly lower in the IgG4-RD group, suggesting that it may be useful for the diagnosis of IgG4-RD in the previous stage before severe renal dysfunction.

W8-1

Influence of Arteriosclerosis on IgG4-Related Periaortitis/Periarteritis

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Conflict of interest: None

[Objective] This study aimed to clarify the relationship of arteriosclerosis with periaortic/periarterial lesions and aneurysmal changes in IgG4-related periaortitis/periarteritis (IgG4-PA). [Methods] We retrospectively investigated the medical data, including the presence of IgG4-PA, arteriosclerotic and aneurysmal changes of the affected lesions, and classic risk factors for arteriosclerosis in 130 patients with IgG4-related disease. The relationship of arteriosclerosis with the PA lesions and aneurysmal changes was analyzed. [Results] Of the 130 patients, 44 were diagnosed with IgG4-PA. The proportions of males and smoking history were significantly higher in the 44 with IgG4-PA than in the 86 without it. Arterial wall calcification and/or mural thrombus in the affected lesions were detected in 86% of the IgG4-PA patients. Five of the 10 patients who newly developed IgG4-PA during the course had had arteriosclerotic changes in the aorta/artery where the PA lesions later appeared. Nine IgG4-PA patients with aneurysmal changes of the affected lesions had a significantly higher incidence of hypertension and mural thrombus than the remaining 35 patients. [Conclusions] The present study suggests that arteriosclerosis may

be related to PA lesions and their aneurysmal changes in IgG4-PA.

W8-2

Risk factors of relapse and clinical features in IgG4-related retroperitoneal fibrosis

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Conflict of interest: None

[Objective] We aim to clarify clinical features and risk factors of relapse in IgG4-related retroperitoneal fibrosis (IgG4-RPF). [Methods] We retrospectively reviewed hospitalized patients with IgG4-RPF between January 2001 and August 2019. Clinical features and treatment progress were collected. [Results] Forty-two patients were included (mean age 70.0±9.0 years old). Mean serum IgG4 and IgG were 563.1±849.6 mg/dL and 2410.9±1543.4 mg/mL, respectively. Thirty-three (78.6%) patients had periarterial lesions and 28 (66.7%) patients had periureteral lesions. Twenty (47.6%) patients had hydronephrosis. Fourteen (33.3%) patients had dacryoadenitis and/or sialadenitis, 13 patients (31.0%) pancreatitis and/or cholangitis, and 1 patient (2.4%) had interstitial nephritis. Thirty-two patients were given prednisolone (≧0.4mg/kg) and 13 patients (40.6%) relapsed. Patients with relapse had significantly higher levels of serum IgG4 (1160.1 vs. 301.0 mg/dL, p=0.026) and lower levels of serum IgA (189.5 vs. 307.5 mg/dL, p=0.0093) at baseline. The most useful cut-off value of serum IgG4 to predict relapse was 337.0 mg/dL, with a sensitivity of 72.7% and a specificity of 71.4% (AUC 0.80). [Conclusions] Baseline serum IgG4 and IgA might be a useful biomarker for predicting relapse of IgG4-RPF.

W8-3

IgG4-related disease complicated by rheumatoid arthritis; a case report

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Conflict of interest: None

[Case] A 63 year-old woman developed upper eyelids swelling 4 years earlier. Blood examination showed IgG4 259 mg/dl and IgG 1589 mg/dl. Enhanced CT revealed bilateral lacrimal glands (LG) swelling and abnormal paravertebral soft tissue. LG biopsy showed IgG4 positive plasma cells (IgG4+PC) (55 /HPF). IgG4-related disease (IgG4-RD) was diagnosed. No other related lesions or arthropathy was detected. Without corticosteroid, these lesions diminished and serum IgG4 level decreased. Three months earlier, arthritis of right knee developed. As osteoarthritis was suspected by X-ray and MRI, high tibial osteotomy was performed. During the operation, synovial proliferation was noticed. Pathology of synovium revealed hyperplasia of synovial lining layer, follicle formation, and neovascularization, with IgG4+PC (70 /HPF, IgG4/CD138 45%). No obstructive phlebitis or fibrosis was detected. Blood examination showed CRP 5.2 mg/dl, RF 87 IU/ml and anti-CCP antibodies 312 U/ml. Rheumatoid arthritis (RA) was diagnosed with improvement by tacrolimus. [Discussion] Although arthropathy could develop in 10% and a few cases with synovitis have been reported in IgG4-RD, no case complicated by RA was reported. RA should be included as one of the differential diagnosis of arthropathy in IgG4-RD.

W8-4

A case of IgG4-related disease with panhypopituitarism

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Conflict of interest: None

[Case] The patient was a 58-year-old man. He was admitted to our department since he had symptoms of general malaise, anorexia, and loss of vision in left eye. Physical examination showed left eyelid drooping, visual field abnormalities, and double vision due to binaural hemi blindness, abductor and oculomotor neuropathies in addition to the enlargement of lacrimal and submandibular glands. Blood test showed a high titer of IgG4 and low levels of anterior pituitary hormones (TSH 0.10 IU/mL, GH 0.6ng/mL, ACTH 3.9 pg/mL, LH <0.2 mIU/mL). Head MRI revealed swelling and enhancement of the pituitary stalk and inflammation of the optic chiasm and bilateral optic tracts. The histological findings of submandibular glands showed storiform fibrosis and marked infiltration of $IgG4^+$plasma cells. Based on these results, he was diagnosed as panhypopituitarism due to IgG4-related disease (IgG4-RD) and started treatment with Prednisolone (PSL). The dose of PSL has been decreasing because of the improvement of his symptoms. [Clinical significance] IgG4-RD is reported to affect pituitary and induce panhypopituitarism due to hypophysitis, suggesting the importance of performing head MRI and evaluating pituitary hormones in patients with IgG4-RD with general malaise and anorexia as this case.

W8-5

A case of IgG4-related disease with lower level of ChE

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Conflict of interest: None

(Case) A 77-year-old woman had been treated for angina and bronchial asthma. She has been aware of submandibular mass for 5 years. Laboratory test revealed high levels in total protein, IgG, IgE and IgG4, so that she was hospitalized for the purpose of examining the cause. Laboratory test additionally revealed lower level of ChE (154 U/L). FDG-PET/CT showed submandibular mass, multiple lymphadenopathy, bronchial thickening and bilateral renal enlargement with high FDG uptake. Biopsy specimen of submandibular gland showed striform fibrosis and IgG4/IgG positive plasma cell ratio of 90%. The patient was diagnosed with IgG4-related disease and PSL 0.6mg/kg was initiated. 2-week after administration, enlarged submandibular gland, bronchial thickening and renal enlargement were improved, and PSL was tapered. ChE level, which correlated with disease activity, dramatically improved. (Conculusion) Several cases of IgG4-related disease demonstrate that ChE level correlated with disease activity. We review IgG4-related disease with lower level of ChE, and report the characteristics.

W8-6

A case of IgG4-related disease complicated with autoimmune autonomic ganglionopathy

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Conflict of interest: None

Background: Autoimmune autonomic ganglionopathy (AAG) is a rare acquired channelopathy that is characterized by pandysautonomia. AAG is sometimes found in association with other autoimmune diseases. Patient: A 61-year-old man was diagnosed with IgG4-RD. He suddenly felt dizzy, so he was taken in the ambulance. He had severe orthostatic hypotension, paridrosis, and constipation. Examinations also suggest that he developed autonomic disorder. Furthermore, serum IgG4 was high, and contrast-enhanced computed tomography revealed that IgG4-related dacryoadenitis, sialoadenitis, pancreatitis, cholecystitis, and bronchitis. Clinical course: We presumed that his autonomic disorder was caused by AAG, so he was treated with intravenous methylprednisolone and subsequently oral prednisolone. His symptoms of both autonomic disorder and IgG4-RD were

improved. Later on, he had a positive autoantibodies to ganglionic nicotinic acetylcholine receptors (gAChR) test result. Discussion: AAG is associated with gAChR. Recently, we became able to measure autoantibodies to gAChR, so patients of AAG may be more than expected. In case patients who have autoimmune diseases including IgG4-RD develop autonomic disorder, we should measure serum autoantibodies to gAChR.

W9-1

Tph reflects the disease activity of sero-positive rheumatoid arthritis with treatment of methotrexate and biologic therapy

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Conflict of interest: None

[Objective] To investigate the peripheral blood mononuclear cell (PBMC) fraction that strongly correlated with the disease activity of rheumatoid arthritis (RA), and to clarify the time-series course by treatment. [Method] For patients with untreated RA who met the ACR / EULAR RA classification criteria we analyzed PBMC fraction by 8-color flow cytometry compared with healthy controls. [Results] The subjects were 53 RA patients (40 sero-positive RA, 13 sero-negative RA) and 33 healthy individuals. The average age was 56.4 (RA), 41.4 (healthy individuals), and the proportion of women was 75% (RA) and 67.7% (healthy individuals). Tph (T peripheral helper) cells correlated with DAS28-CRP at the time of diagnosis, and were significantly increased ($p < 0.01$) in RA patients compared to healthy individuals. In 29/53 cases (54.7%) using methotrexate (MTX) resulted in remission, and Tph was significantly decreased in sero-positive RA after 3, 6, and 12 months ($p < 0.01$). In 7/36 cases (19.4%) of MTX refractory cases, Tph did not decrease but in cases that subsequently introduced TNF-α inhibitors or IL-6 receptor inhibitors, Tph decreased significantly ($p < 0.05$). [Conclusion] Tph reflects the disease activity of sero-positive RA treated in both methotrexate and biologics.

W9-2

Skin lesions as a side effect of Tocilizumab therapy: Transcriptome analysis of peripheral blood shows a risk of paradoxical leukocyte activation and exacerbation of skin ulcer

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Conflict of interest: None

[Objective] Skin lesion as a side effect of Tocilizumab therapy (TCZ-Tx) has not been paid much attention. We experienced several RA cases with development of various skin lesions associated with neutrophil activation after TCZ-Tx and exacerbation of skin ulcer despite the activity of RA was absolutely under control. In this study, we try to detect the changes in transcriptome of peripheral blood after TCZ-Tx. [Methods] Peripheral whole blood at just before and 3M after TCZ-Tx from 10 RA cases without any side effects were subjected to gene ontology enrichment analysis with using next generation sequencing. [Results] After TCZ-Tx, most of up-regulated genes were relevant to leukocyte activation and the genes related to wound healing were suppressed. [Conclusions] Our findings becomes a rationale for the development of skin lesion and exacerbation of skin ulcer after TCZ-Tx. It also helps the increased margination of neutrophils in normal situation, and it becomes a hint for the secret behind the decreased neutrophil counts after TCZ-Tx. Inhibition of a multifunctional cytokine signaling such as IL-6 may cause unexpected side effects, as the cytokine network is very complicated and an exquisite balance presented in immune and homeostatic system is strictly maintained.

W9-3

Effectiveness of abatacept on clinical disease activity and radiographic progression in rheumatoid arthritis patients in daily clinical practice in Japan: Comparisons according to ACPA status

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Conflict of interest: Yes

[Objective] The effect of Abatacept (ABA) in RA patients has been reported to be higher when ACPA status is positive. However, there has been only a few data in clinical practice in Japan. [Method] Participants were RA patients treated with ABA and followed up for at least 52 weeks whose ACPA data was available, from a Japanese multicenter registry system (TBCR). Achievement rate of SDAI-LDA and ΔTSS at 52 weeks were compared between ACPA positive and negative group. [Results] Number of cases was 446/107 (ACPA positive/negative). Mena age was 68.0/67.3 years, MTX using rate was 41.2/50.0%, and bio-naive rate was 28.0/31.8%. The achievement rate of SDAI-LDA was 72.1/56.0% at 52 weeks ($p<0.01$). In multivariate logistic regression analysis, ACPA positive was an independent predictor for achievement of SDAI-LDA (OR: 2.3, 95% CI: 1.2-4.4). Mean ΔTSS at 52 weeks was 1.7/1.2 and the achievement rate of radiographic remission ($\Delta TSS \leqq 0.5$) was 66.2/62.1%. No significant difference in radiographic progression was observed between group. [Conclusions] The ACPA positive group demonstrated significantly higher SDAI-LDA achievement rate but similar ΔTSS. Considering the known data that ACPA positive is the risk of progression of joint destruction, the current results would be considered as reasonable.

W9-4

The efficacy of abatacept in patients with anti-CCP antibody-positive rheumatoid arthritis

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Conflict of interest: None

[Objective] To examine the difference in the efficacy of abatacept (ABT) between anti-CCP antibody (ACPA) negative and positive groups in patients with rheumatoid arthritis (RA). [Methods] We analyzed a retrospective observational study of 121 patients who treated with ABT at our hospital for more than 1 year. We evaluated the patient background at the initiation of ABT and the disease activity at 12, 24, 52 weeks after ABT initiation in the ACPA negative and positive. [Results] There were 18 patients in ACPA negative and 103 patients in ACPA positive. There was no significant difference in age, disease duration, DAS28-CRP, HAQ-DI, or MMP-3 at ABT initiation, but CRP was significantly higher in ACPA positive than negative (ACPA negative: 1.6±2.4 mg/dL, ACPA positive: 2.4±2.3 mg/dL, $p<0.05$). In addition, there was no significant difference in DAS28-CRP, HAQ-DI, ΔHAQ-DI, CRP and MMP-3 between ACPA negative and positive at 12, 24, 52 weeks after ABT introduction. ΔDAS28-CRP was significantly lower in ACPA positive than ACPA negative at all times (12 weeks: -0.8±0.9 vs -1.5±1.0, $p<0.05$, 24 weeks: -1.1±1.0 vs -1.8±1.0, $p<0.005$, 52 weeks: -1.2±1.0 vs -2.0±1.0, $p<0.01$). [Conclusions] These results suggested that the efficacy of ABT is higher in ACPA positive than ACPA negative.

W9-5

Ultrasonographic evaluation of Baricitinib and TNF antagonist therapy in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] To evaluate the clinical efficacy of Baricitinib (BAR) and TNF antagonist (TNF) therapy in patients with rheumatoid arthritis (RA) using ultrasonography (US). [Methods] We used BAR and TNF treated 9 and 33 RA patients more than 12 weeks. We evaluated the improvement of gray scale (GS) and power doppler (PD) score from baseline to week 24.

[Results] In the patients receiving BAR (n=9) and TNF (n = 33), the mean age was 53.3 vs 55.0 years old (p=0.771), disease duration was 5.0 vs 5.1 years (p=0.425), the mean MTX dose was 10.7 vs 10.8 mg/w (p=0.949), the rate of ACPA positive was 100% vs 85% (p=0.213), DAS28-ESR was 3.83 vs 4.78 (p=0.010), GS score was 15.1 vs 17.3 (p=0.701) and PD score was 10.0 vs 9.0 (p=0.712). The respective changes in GS and PD score after 4 weeks were as follows: GS: -5.4 vs -3.9 (p=0.477) and PD: -4.0 vs -1.3 (p=0.140). The respective changes in GS and PD score after 12 weeks were as follows: GS: -7.7 vs -5.2 (p=0.365) and PD: -5.6 vs -2.6 (p=0.085). The respective changes in GS and PD score after 24 weeks were as follows: GS: -7.4 vs -7.9 (p=0.789) and PD: -6.9 vs -4.7 (p=0.231). [Conclusion] The present study provides evidence supporting the BAR and TNF therapy improved not only the disease activity not also the inflammatory synovitis.

W9-6

Half dose reduction of MTX in patient with RA who achieved deep clinical remission

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Conflict of interest: None

[Objective] To determine whether dose redaction of MTX in RA patient who achieved clinical remission is possible without relapse. [methods] Patients had to have been receiving stable dose of MTX and in remission as defined by DAS28-CRP at least 12 weeks were included in this study. MRIs of dominant hands at baseline were obtained and scored using the RAMRIS system. MTX dose was reduced by half from baseline. Clinical disease activity was evaluated from baseline to week 52. [Result] Fifteen patients were enrolled in this study. The mean (±SD) age, disease duration, MTX dose before including study and DAS28-CRP at baseline was 66.6±9.8y, 6.4±4.0y, 8.5±2.9mg/w and 1.35±0.26. Eleven patients were seropositive. Low grade subclinical MRI inflammation was detected in all patients. The median (range) synovitis, bone edema and bone erosion sore were 2 (0-7), 0 (0-4) and 7 (1-22). There was a significant correlation between DAS28-CRP and synovitis score at baseline ($r=0.64$, $p<0.05$). RAMRIS bone erosion score of patient experienced disease flare tends to be higher and not RAMRIS synovitis but total RAMRIS score was significantly higher in these patients (18.3 vs. 8.0 $p < 0.05$) [Conclusion] MRI evaluation was useful for prediction of successful dose reduction of MTX within deep clinical remission.

W10-1

Anti-drug Antibodies, Efficacy, Safety and Impact of Concomitant Methotrexate in Ixekizumab-treated Patients with Psoriatic Arthritis: Phase 3, Randomized, Double-Blind, Placebo-controlled Studies (SPIRIT-P1 and SPIRIT-P2)

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Conflict of interest: Yes

Objectives: To evaluate if anti-drug antibody (ADA) development was affected by concomitant MTX or affected efficacy/safety. **Methods:** 52-week Phase 3 studies in patients (pts) with PsA (SPIRIT-P1, biologic-naïve; SPIRIT-P2, TNFi-experienced) were analyzed. Pts received placebo or 80 mg ixekizumab (IXE) every 2 weeks (Wks; Q2W) or 4 Wks (Q4W) after 160-mg loading dose. **Results:** A total 445 pts (5 Japanese) were analyzed. ADA+ rates were comparable in the Q4W group between MTX use (10% with; 12% without), as also seen in the Q2W group. The proportion of pts in SPIRIT-P1 achieving ACR20 at Wk 52 in the Q4W group was 50% of ADA+ pts and 64% of ADA-; in the Q2W group, 55% of ADA+/67% of ADA-. The proportion of pts in SPIRIT-P2 achieving it in the Q4W was 92% of ADA+/57% of ADA-; in the Q2W, 50% of ADA+/51% of ADA-. There was no temporal relationship between the development of ADA and ACR20 across studies. No association between the development of ADA and allergic reactions/hypersensitivity events or injection site reactions was established. **Conclusion:** The presence of ADA was relatively small and was not clinically relevant, since it did not affect efficacy or safety of IXE in PsA pts. Concomitant MTX did not appear to have a meaningful effect on ADA development.

W10-2

Ixekizumab efficacy in psoriatic arthritis patients with severe disease; a Phase 3 randomized, double-blind, placebo-controlled study (SPIRIT-P1, 24-week data)

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Conflict of interest: Yes

Objectives: To evaluate ixekizumab (IXE) efficacy in psoriatic arthritis (PsA) patients (pts) with severe disease. **Methods:** Using modified composite psoriatic disease activity index (mCPDAI), "severe" pts (total score >7 and peripheral arthritis score ≧3) were classified from biologic-naïve active PsA pts in SPIRIT-P1, and analyses were post-hoc. In the study, pts were randomized to placebo (PBO), or IXE 80 mg once every 4 weeks (Q4W) or Q2W including 160 mg loading dose, or adalimumab (ADA; active reference). Treatment comparisons were made using logistic model (significance level < 0.05). Non-responder imputation was used for missing data. **Results:** Of 417 pts, 204 were categorized as severe. Mean mCPDAI (range) at baseline was 8.1 (3-14) in overall population; 9.7 (8-14) in severe population. In both, pts characteristics were generally similar across treatments. In overall population, significantly more pts achieved the primary ACR20 response at Wk24 in Q4W (58%, $p<0.001$), Q2W (62%, $p<0.001$), ADA (57%, $p<0.001$), compared with PBO (30%). In severe population, significantly more pts also achieved the ACR20 in Q4W (63%, $p<0.001$), Q2W (60%, $p<0.001$), ADA (54%, $p=0.006$), compared with PBO (25%). **Conclusion:** IXE treatment showed joint symptom improvement in PsA pts with severe disease.

W10-3

Early diagnosis of arthritis preceding-psoriatic arthritis

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Conflict of interest: None

[Objective] Psoriatic arthritis (PsA) requires early diagnosis and treatment. However, the early diagnosis of PsA, especially arthritis-preceding PsA, is difficult. Factors contributing to early diagnosis of arthritis-preceding PsA were analyzed. [Methods] Of the psoriasis patients who visited our hospital in 2001-19, the patients who met CASPAR criteria were analyzed for clinical features, laboratory findings, and imaging as PsA. [Results] Among 1511 patients with psoriasis, there were 153 cases of PsA (10.1%). The sensitivity of the CASPAR criteria in the first visit was only 37.5%. The findings with high sensitivity in PsA were RF negative, dactylitis, and osteogenesis, but the arthritis-preceding PsA had only 8% of dactylitis. For DIP joint, thoracolumbar, sacroiliac, and entheses lesions, the sensitivity at the first visit was the same as at the time of diagnosis. X-ray findings such as diaphyseal periosteitis, taftal erosions, and capsular calcification contributed to early diagnosis, and the sensitivity of MRI, ultrasound, bone scintigraphy, and PET-CT were all high sensitivity. [Conclusions] Arthritis-preceding PsA lacks specific tests and findings, and early diagnosis based on current classification criteria is not always easy. New classification criteria are required.

W10-4

Effectiveness of IL-17 inhibitors revealed by Minimal Disease Activity (MDA) achievement of Psoriatic Arthritis patients

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Conflict of interest: None

[Objectives] We investigate the effectiveness of IL-17 inhibitors which were introduced to the Psoriatic Arthritis (PsA) patients in our institution. [Methods] We examined 19 patients who were diagnosed as PsA and to whom IL-17 inhibitors were initiated. We analyzed DAS28-CRP as the evaluation of arthritis, PASI as that of rash, and Minimal Disease Activity (MDA) achievement as that of overall disease activity. [Results] Of all cases to which IL-17 inhibitors were introduced, half were biologics naïve (naive group), and the least were switched from TNF-α inhibitors (switch group). As for arthritis, DAS28-CRP has significantly improved at fourth weeks in naïve group. It has also improved at twentieth weeks in switched group. As for rash, 60% of all cases have achieved PASI90 at twentieth weeks in both naïve and switch groups. As for MDA, 60% have also achieved MDA at twentieth weeks in both naïve and switch groups. In the switch group, all cases to which IL-17 inhibitors were initiated for either arthritis or rash have achieved MDA, however, 22% cases which were introduced for both arthritis and rash have not achieved. [Conclusion] In PsA patients, IL-17 inhibitors have improved disease activity and effective for both biologics naïve and switched from TNF-α inhibitors.

W10-5

Comparison of the efficacy of biologics in patients with psoriatic arthritis in the real world

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Conflict of interest: Yes

[Objective] Recently each biologic has shown efficacy in psoriatic arthritis (PsA), but comparison among biologics about treatment efficacy in the real world has not been reported well enough. In this study, we compared with treatment efficacy between biologics in PsA in our hospital. [Methods] Participants were the patients who started biologics in our hospital and received the same biologics for at least more than six months. We divided these patients into anti-TNF inhibitor (TNFi) and IL-17 inhibitor (IL-17i) groups and compared with the response to each symptom at 0, 6, 12M. [Results] TNFi group (n=35) was significant higher rate of the first biologics than IL-17i group (n=22) (85.7% vs. 27.3%) and higher of physician VAS (20 vs. 10, p=0.04), but other factors were balanced. PASI and DASCRP significantly improved in both groups. ASDAS significantly improved in TNFi group. TNFi group was superior for DASCRP CR and ASDAS inactive achievement at 6 months. TNFi group significantly improved in dactylitis (p=0.02) and IL-17i group in nail (p=0.003). [Conclusions] Efficacy of both biologics for skin lesion was equally impressive, but TNFi group for joint symptoms was superior to IL-17i group. A large-scale analysis with matched patient-characters will be expected.

W10-6

Investigation of Clinical Features in Patients with Psoriatic Arthritis

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Conflict of interest: None

[Objective] It is known to cause psoriatic arthritis (PsA) in 15-30% of patients with psoriasis (PsO). The appearance of joint symptoms is reported that to cause psoriasis lesions on the scalp, nails and Intergluteal/perianal. The object purpose of this study is to investigate the cause of joint symptoms. [Methods] 205 patients (PsA: 118, PsO: 87) participated in the study. Site of psoriatis (scalp, nails and buttocks Intergluteal/perianal), severity of psoriasis (PASI score), BMI, DAS28-CRP, Biologic (BIO) usage rate, MTX usage rate, and PASE score were examined. [Results] As a result of univariate analysis, DAS28-CRP, BIO usage rate, MTX usage rate and PASE were significantly higher in PsA group. Psoriatic lesions on the scalp, nails and buttocks was not significantly different in the onset of PsA (PsA group: 66.9%, PsO group: 69.0%, p = 0.88). PASE score was a significant risk factor in multivariate analysis with PsA as the objective variable. [Conclusions] The PsA group had significantly higher BIO usage rate (p = 0.015) and MTX usage rate (p <0.001) than the PsO group. A significant association was observed PASE score and PsA (OR1.06, 95% CI: 1.01-1.11, p = 0.01). There was no significant association between site of psoriatis (scalp, nails and Intergluteal/perianal) and PsA.

W11-1

A case of thrombotic thrombocytopenic purpura secondary to systematic lupus erythematosus

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Conflict of interest: None

A 23-year-old woman visited the hospital because of left abdominal pain and was diagnosed of the left ureteral calculus. A few days later she visited the hospital and her laboratory tests indicated hemolytic anemia with red cell fragmentation, platelet depletion, uric protein, uric blood, CRP elevation. She was admitted to the hospital. Examination of her plasma showed ADAMTS13 deficiency but no ADAMTS13 inhibition. Also anti-nuclear antibody, anti-ds-DNA antibody and hypocomplementemia were detected. She was administered fresh frozen plasma (FFP) for two days, but not improved. She moved to our hospital. A tentative diagnosis of thrombotic thrombocytopenic purpura (TTP) secondary to systematic lupus erythematosus was made because of no response from FFP transfusion. Plasma exchange therapy and methylprednisolone 1g pulse started immediately. Also intravenous cyclophosphamide (IVCY) pulse and hydroxychloroquine were added. Momently, it proved that IgG antibody bound to ADAMTS13 was detected from her serum. The case is rare that had reduced ADAMTS13 activity but showed no ADAMTS13 inhibition. The previous study reported antibodies that bound to ADAMTS13, but did not neutralize protease activity. In this case the antibodies is detected, so this case is highly suggestive.

W11-2

Eight cases analysis of pulmonary arterial hypertension associated with connective tissue disease treated with immunosuppressive drugs

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Conflict of interest: None

[Objective] The purpose of this study is to evaluate the efficacy of immunosuppressive therapy in patients with pulmonary arterial hypertension associated with connective tissue disease (CTD-PAH), other than the pulmonary vasodilators. [Methods] This study included 8 CTD-PAH patients who treated with immunosuppressive drugs. We compared underly-

ing disease, age, sex, disease duration, complications, laboratory findings, treatment content and response. [Results] There were 7 females and 1male, mean age was 45 years. Underlying disease were 3 patients with mixed connective tissue disease, 2 with systemic lupus erythematosus and Sjogren's syndrome (SjS), 1 with systemic sclerosis and SjS overlap. All patients received corticosteroids, and 3 patients received immunosuppressant. Period and dose were depending on the complications. Pulmonary vasodilator was used for all patients. In the right heart catheter, mean pulmonary artery pressure (mPAP) decreased from 33mmHg to 21mmHg on the average, after treatment. [Conclusions] These results suggest that the immunosuppressive therapy including corticosteroids may be effective for CTD-PAH. However, these drugs may cause severe adverse events, careful consideration was required. In the future, long-term efficacy needs to be examined.

W11-3

Clinical presentation of renal involvement in sarcoidosis patients

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Conflict of interest: None

[Objective] We aimed to examine clinical presentation of renal involvement in sarcoidosis patients (RS). [Methods] Five sarcoidosis patients received renal biopsy were identified. We collected patients back ground, histopathological findings and clinical outcome. [Results] The median age was 66 years. Four patients was female, median of eGFR (IQR) was 19 ml/min/1.73m^2 (18, 27), urine protein/creatinine ratio was 0.88 g/gCr (0.40, 0.93). Hypercalcemia was three patients. Mean level of serum calcium with the patients of hypercalcemia was 11.9 mg/dL, and median serum ACE, lysozyme, and sIL-2R was 32.5 U/L (26, 73), 30.2μg/mL (24, 35), 4385 U/mL (3276, 5077) respectively, and these were higher than the 12 patients without renal involvement (NRS). Histopathological findings were followed: granulomatous tubulointerstitial nephritis (TIN) in three patients, and TIN without granuloma in two patients. Several proximal tubular cells had hypereosinophilic protein-reabsorption granules. [Conclusions] Serum lysozyme level was higher in RS patients than in NRS. It is reported that high concentrations of lysozyme can damage proximal tubular cells. We must keep in mind sarcoidosis with higher level of lysozyme may have renal involvement, and try to provide early diagnosis to prevent renal function impairment.

W11-4

Successful therapy with anti-TNF-alfa agent with corticosteroid in patients with refractory cardiac sarcoidosis: a report of three cases

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Conflict of interest: None

α (Objective) Cardiac sarcoidosis (CS) accounts for 5% of all sarcoid patients and carries poor prognosis. Treatment of CS remains challenging. Recently, FDG-PET (PET) was found to be useful to measure the activity of CS. We reported three cases of CS refractory to standard therapies, wherein serial PET investigations demonstrated successful treatment with anti-TNFα agent. (Clinical courses) Among 3 female cases of CS, cardiac findings showed decreased left ventricular ejection fraction in case 1 and 2, thinning of the interventricular septum in case 1, temporal atrioventricular block in case 2, hypokinesis of anterior wall of left ventricle in case 3. Bilateral hilar and mediastinal lymphadenopathies were seen in all cases and uveitis and skin rash were demonstrated in case 3 and in case 2 and 3, respectively. They were initially treated with 30 mg of daily prednisolne and weekly methotrexate without reaching complete remission confirmed by PET. Therefore we added anti-TNFα agents in all cases. Serial PET investigations demonstrated marked improvement of CS as well as other sarcoid manifestations in all cases and no cardiac deterioration was noted with anti-TNFα agents. (Conclusion) Anti-TNFα agents were effective and safe in patients with CS refractory to standard therapies.

W11-5

Clinical study of 2 cases of recurrent Adult-onset still's disease (AOSD) with rapid reduction glucocorticoids therapy (RRGCT)

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Conflict of interest: None

[Case1] 24 y.o. female, diagnosed AOSD and treated, had fever and eruptions two weeks before admission. After started SMX-TMP, she had fever and eruptions again. [physical exam] 38.1degree. She had eruptions around eyes. pharynges pain, and arthritis. [blood test] CRP0.37mg/dl, Ferritin1293mg/dl, IL-18>5000pg/ml. GPT319IU/dl [clinical course] from physical and blood test, diagnosed AOSD relapse, treated with PSL120mg/day RRGCT, all symptoms and blood tests were normalized. After that maintained remission with TCZ. [case 2] 74y.o. female was diagnosed and treated AOSD with RRGCT two years ago. She came to my clinic because she was bitted by itch mite 2 weeks ago and eruptions were spreading. [physical exam] 37.3degrees, eruptions in both palmers, forehands, and knees. [blood test] CRP2.01mg/dl, Ferritin5060mg/dl, IL-18>5000pg/ml. GOT331IU/dl. [clinical course] From physical and blood test, diagnosed AOSD relapse, treated with PSL120mg/day RRGCT all symptoms and blood tests were normalized. After that maintained remission with TCZ. [clinical meaning] The treatment of AOSD must be different from that of Connective vascular diseases. They must take the PSL enough as much as they improved the symptoms and exams. After remission, TCZ was used for maintenance.

W11-6

Clinical Features and Course of Adult-onset Still's Disease by Phenotype

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Conflict of interest: None

[Objective] The clinical course of adult-onset Still's disease (AOSD) is classified into monocyclic (M), polycyclic (P), and chronic arthritic (C) patterns. This study investigated the clinical features and treatment of each phenotype. [Methods] We retrospectively extracted diagnosed AOSD cases classified in each group using the Yamaguchi criteria. We analyzed symptoms, examinations, and treatment by group. [Results] The study enrolled 31 patients [24 (77%) females; median age at onset 33 years; median treatment duration 4 years]. There were 13 (42%) group M, 11 (35%) P, and 7 (23%) C. Sore throat was the only factor that differed significantly (P=0.02). The median maximum C-reactive protein (CRP) and maximum ferritin levels in groups M, P, and C were 21.59, 16.04, & 8.48 (mg/dL) and 9566, 7873, & 8925 (ng/mL), respectively; none differed significantly (CRP, P=0.13; ferritin, P=0.71). The median duration of steroid use was 17.5, 65.5, & 201 months, respectively, and differed significantly (P=0.04). [Conclusions] Sore throat may be associated with AOSD phenotypes and each phenotype may be associated with prolonged steroid treatment.

W12-1

Development of molecular targeted small compounds using reconstituted NLRP3 inflammasome in a cell-free system

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Conflict of interest: None

[Objective] The NLRP3 inflammasome is an intracellular pathogen recognizing pattern recognition receptor consisting of NLRP3, an adapter ASC, and caspase-1. The formation of inflammasomes activates IL-1βand induces inflammation. Since own metabolites also activates inflammasome that the type 2 diabetes and Alzheimer's disease etc. are so called inflammasomopathy. Gain-of-function mutations of NLRP3 cause autoinflammatory diseases. Currently, no small compound that directly inhibit the interaction between NLRP3 and ASC has been reported. Then, we developed reconstituted NLRP3 inflammasome in a cell-free system to screen NLRP3 inflammasome targeted small compound. [Methods] We screened core chemical library, and cell-based assay using human PBMCs. Inflammasome activation in vivo was evaluated using IL-1β based dual operating luciferase (IDOL) mice. Clinical evaluation was assessed using human PBMCs from a patient with Muckle-Wells syndrome (MWS). [Results] We identified KN3014, targeting the interaction between NLRP3 and pyrin domain of ASC. The KN3014 reduced luminescence from IDOL mouse, The KN3014 reduced auto-secretion of IL-1β from PBMCs from a patient with MWS. [Conclusions] The KN3014 could be an attractive candidate for treatment of not only MWS.

W12-2

Barcitinib inhibited uric acid-mediated inflammasome activation in IL-6 primed innate immune cells

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Conflict of interest: None

[Objective] The aim of the present study was to investigate the mechanism of MSU crystal-induced autoinflammatory processes in the innate immune system. [Methods] Human neutrophils were stimulated with MSU in the presence or absence of IL-6 priming to determine NLRP3 inflammasome activation and subsequent cleaved caspase-1 induction or IL-1β production. Cellular supernatants were analysed for IL-1β or caspase-1 by ELISA. [Results] IL-6 or MSU stimulation alone did not result in the efficient IL-1b production from human neutrophils. However, MSU stimulation induced marked IL-1β production from IL-6-primed neutrophils. Pretreatment with baricitinib, which blocks IL-6 receptor signalling, prevented MSU-induced cleaved caspase-1 or IL-1b induction in IL-6-primed neutrophils. Baricitinib inhibited IL-6-induced pro-IL-1β mRNA expression and NLRP3 protein expression in neutrophils. [Conclusions] Priming of human neutrophils with IL-6 promotes uric acid-mediated IL-1β secretion in the absence of microbial stimulation. These results suggest that an endogenous cytokine, IL-6, is involved in MSU-mediated NLRP3 inflammasome activation and subsequent IL-1β production from innate immune cells and has a crucial role in MSU crystal-induced synovial inflammation.

W12-3

Hydroxychloroquine inhibits IL-1b production from amyloid-stimulated human neutrophils

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) is used for the treatment of rheumatic diseases. We tested the hypothesis that HCQ affects the NLRP3 inflammasome, which is involved in autoinflammation. [Methods] Human neutrophils were stimulated with serum amyloid A (SAA) in vitro and measured for IL-1β and caspase-1 (p20) secretion by ELISA. In addition, Pro-IL-1β mRNA expression was quantified by real-time PCR. [Results] SAA stimulation induced IL-1β production, NF-κB activation, pro-IL-1β mRNA expression, and NLRP3 protein expression in human neutrophils. HCQ pretreatment significantly inhibited the SAA-induced IL-1β production in human neutrophils but did not affect the SAA-induced NF-κB activation, pro-IL-1β mRNA expression, and NLRP3 protein expression. Furthermore, SAA stimulation induced cleaved caspase-1 (p20) secretion from human neutrophils, and this release was suppressed by HCQ pretreatment. [Conclusions] Treatment with HCQ was associated with impaired production of IL-1β in SAA-stimulated human neutrophils without affecting the priming process of the NLRP3 inflammasome such as pro-IL-1β or NLRP3 induction. These findings suggest that HCQ affects the NLRP3 activation process, resulting in the impaired IL-1β production in human neutrophils, as representative innate immune cells.

W12-5

The triggering factors with patients of familial Mediterranean fever

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Conflict of interest: None

[Objective] In familial Mediterranean fever (FMF), patients have some factors considered as trigger for the febrile attacks. Our aim was to examine the relationship between FMF attacks and these triggers by investigating their clinical and genetic characteristics. [Methods] We analyzed clinical features and genetic mutations about 372 patients clinically diagnosed as having FMF. [Results] Of the 372 patients, 180 (49.4%) experienced the febrile attacks relating to some triggers. The most common triggering factors were tiredness (32.3%) and emotional stress (32.3%). On the other hand, menstruation (39.7%) was the most common trigger for female patients. They indicated significantly higher frequencies of peritonitis (74.7%) and endometriosis (36.6%) compared with those in patients whose attacks were independent of menstruation. They also showed younger age of disease onset (21.7 years). Although not significant, the frequency of patients carrying mutation in exon 10 tended to be higher in menstruation-triggering patients. [Conclusions] Half of FMF patients were aware of their triggering factors for the attacks. These information might be useful for preventing their febrile attacks. Menstruation was the most common factor which induces febrile attacks in female FMF patients.

W13-1

Consideration of appropriate b/tsDMARDs use regarding with anti-CCP antibodies titer in patient with rheumatoid arthritis

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Conflict of interest: None

[Objective] In order to evaluate clinical effectiveness of b/tsDMARDs in rheumatoid arthritis (RA) patient according to anti-CCP antibodies titer value (ACPA), and discuss more suitable use of b/tsDMARsD. [Methods] Patient who were thrown b/tsDMARD were classified according to ACPA; namely more than 100U/L (H), 4.5 to 99 (M), and less than 4.5 (L). Improve of 28-joints disease activity score (DAS28) at one year after initiation, and success ratio at three years, defined as discontinuation after clinical remission or sustained low disease activity or clinical remission (S-R),

were calculated in accordance with mode of action of b/tsDMARD, and compared statistically with Mann-Whitney U-test and chi square test. [Results] Patients with THF inhibitor, IL-6 inhibitor, abatacept (ABT), and JAK inhibitor counted 22, 17, 26, and 20 in H, 29, 13, 14, 12 in M, and 39, 10, 6, 8 in H, respectively. In H and M group, DAS28 improvement demonstrated significantly more effective with ABT than with the other mode of action drugs, while demonstrated significantly less mprovement reversely in L group. S-R demonstrated no significant differences between any groups. [Conclusions] Clinical efficacy of drug alters with mode of action in according to ACPA in RA patients as long as time span in one year.

W13-2

Can periarticular osteophyte formation predict the incidence of total knee arthroplasty in patients with rheumatoid arthritis?

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Conflict of interest: None

[Objective] To determine the influence of periarticular osteophyte formation on the incidence of total knee arthroplasty (TKA) in patients with rheumatoid arthritis (RA). [Methods] A total of 130 symptomatic (tender and/or swollen) knee joints in 80 patients at initiation of biologics were retrospectively studied. The median follow-up period was 12.1 years. The cumulative incidence of TKA was compared by osteophyte formation or not [OP (+/-)]. [Results] Of all subjects, 44 (34%) had osteophyte formation. According to Kaplan-Meier estimates, the cumulative incidence of TKA for the OP (+) group was significantly lower than that for the OP (-) group in the Larsen grade III, IV, V group (38% vs. 74%, respectively, at 10 years, P = 0.010), whereas there was no significant difference between the OP (+) and (-) groups in the Larsen grade 0, I, II group (9% vs. 10%, respectively, at 10 years, P = 0.774). Multivariate analysis using the Cox proportional hazards model revealed that osteophyte formation (HR: 0.39, 95% CI: 0.19, 0.79) and older age at baseline (HR: 1.04 per 1 year, 95% CI: 1.01, 1.08) independently predicted TKA in the Larsen grade III, IV, V group. [Conclusions] Periarticular osteophyte formation can predict the incidence of TKA in RA knee joints with advanced destruction.

W13-3

Ingenuity for total joint arthroplasty for elderly RA patients with biologics agent and long hospital stay with rehabilitation ward

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Conflict of interest: None

[Objective] We show the good result of total joint arthroplasty for elderly RA patients with Bio, who required long-term hospitalization using the rehabilitation ward. [Patients and method] We performed 5 THA, 8 TKA and 2 TEA from 2016 to 2019. 7 patients were treated with Bio: Golimumab 2, Certolizumab 1, Abatacept 4. Average age was 74.7 years old. MTX and PSL usage rates were 71.4% and 28.6%. The patients changed the wards every 4 weeks for continuation of Bio treatment. [Result] Delayed wound healing were observed in 2 cases using steroids. Deep SSI was not seen. The length of hospital stays was 46.2 (28-116) days. They discharged with no severe trouble. [Representative case] 78 y.o. woman. Abatacept was used due to high disease activity of RA. She couldn't stand and walk due to severe knee contracture at administration. Bilateral TKA was performed and she migrated between rehabilitation and acute ward for abatacept injection. She stayed 4 months and discharged with walker. [Conclusion] The combined use of rehabilitation and acute ward seemed to be useful to achieve an optimized result of total joint arthroplasty for elderly RA patients with Bio.

W13-5

Does medication for RA increase risks of SSI and postoperative death? -systematic review and meta-analysis-

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Conflict of interest: Yes

[Objective] We conducted systematic review and meta-analysis on the clinical questions if bDMARD and oral steroid increase SSI and/or postoperative death. [Methods] A systematic review was performed on articles indexed in the Cochrane Library, PubMed, and Ichushi from 2013 to 2018. Then we added the articles used for the previous meta-analysis and ones published from Jan. to Aug. 2019. The search aimed to identify studies describing SSI or postoperative death in patients with RA treated with or without bDMARDs or oral steroid. [Results] We found 149 articles through specific searches of PubMed and Web of Science, and hand searching. After inclusion and exclusion by full-text review, 29 articles were used for systematic review, 19 for meta-analysis of SSI and 4 for meta-analysis of postoperative death. The use of bDMARDs still appeared to increase the rate of SSI slightly. The risk of postoperative death was inconclusive. Oral steroid apparently increased the risk of SSI, and an article showed the increase of risk of postoperative death. [Conclusions] bDMARDs slightly increase the relative risk of SSI after orthopedic surgery. Oral steroid also increases the risk of SSI and postoperative death. Both drugs should be used with appropriate caution.

W14-1

Characterization of remission in patients with rheumatoid arthritis treated with upadacitinib or comparators

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Conflict of interest: Yes

Objectives: Upadacitinib (UPA), a JAK1-selective inhibitor, was associated with high remission (REM) rates in phase 3 studies for RA patients (pts). To determine the response to UPA on REM and component assessments, we assessed the proportions of pts achieving REM using multiple REM definitions. **Methods:** Three phase 3 studies included; MTX naïve (SELECT EARLY, n=945), MTX-IR (SELECT COMPARE, n=1629) and bDMARD-IR (SELECT BEYOND, n=498). The proportion of pts achieving REM at Week (wk) 12 by 4 definitions (DAS28-CRP<2.6; CDAI ≦2.8; SDAI ≦3.3 and Boolean) were determined. For each definition of REM, the mean change in each of the respective component scores was also assessed. **Results:** At 12 wks, in EARLY and COMPARE, a significantly greater proportion of pts receiving UPA achieved REM by all 4 definitions vs MTX, PBO or ADA. In BEYOND, a significantly greater proportion of pts receiving UPA 30mg achieved all REM definitions vs PBO within the first 12 wks, with significantly greater proportions on UPA 15mg achieving DAS28-CRP<2.6 and Boolean REM. **Conclusion:** All disease activity components of each REM definition were significantly improved in pts receiving UPA compared to MTX or PBO, and all Boolean

components were significantly improved in pts receiving UPA 15mg compared to ADA.

W14-2

Comparison of Persistency and complication of Molecule-targeting Therapeutic Agents for Rheumatoid Arthritis in ages

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Conflict of interest: None

[Objective] To analysis of persistency rate and complication rate according to aging in NDB data [Methods] Using NDB big data, we compare the ressitency rate of each drug by Caplan-Meier mtehod and analyzed complication rate of PCP, TB/NTM, and Herpes zoster in ageing. [Results] TOF shows the highest persistency rate follwed by TCZ, ABT. Persistency rate is decreasing with ageing by comparing four age group. ABT showed higher persistency rate compared with other drugs in higher aged group. Herpes zoster is highest in TOF, and this is more apparent in older ages. [Conclusions] ABT and GLM showed higher persitency rate in aged group indicating favorably used in aged patients.

W14-3

Comparison of biologics tolerability and discontinuation reasons between Bio-naïve and Bio-switched 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 biologics tolerability between Bio-naïve and switched RA patients. [Methods] 4314 treatment courses (2737 Bio-naïve and 1577 switched, female 82.5%, age 57.4y, DAS28-CRP 4.0, combined MTX 62.5% and PSL 43.0%, treated number; ETN 856, TCZ 851, IFX 724, ABT 663, ADA 536, GLM 458, and CZP 226) were included in this multi-center, retrospective study. Data was adjusted by potent confounders (age, sex, disease duration, combined MTX and PSL, biologics started date and switched number) with a Cox proportional hazards model and evaluated at 36 months. [Results] Drug inefficacy rate (%) were as follows. Bio-naive group (ABT 11.1, GLM 14.1, TCZ 14.6, ADA 17.4, IFX 20.9, ETN 22.6, CZP 22.8; Cox P<0.001) and Bio-switched group (TCZ 21.1, ABT 30.9, ETN 33.1, GLM 37.4, ADA 44.8, CZP 46.1, IFX 47.1; Cox P<0.001). Overall retention rates (%) excluding non-toxic events and remission were as follows. Bio-naïve group (ABT 84.8, TCZ 77.0, GLM 75.5, ADA 71.8, CZP 68.0, ETN 65.3, IFX 65.3; Cox P<0.001) and Bio-switched group (TCZ 67.0, ETN 64.1, ABT 62.4, GLM 54.5, CZP 49.3, IFX 46.4, ADA 44.3; Cox P<0.001). [Conclusions] Remarkable difference was observed in inefficacy rate and tolerability between the biologics, and also between Bio-naïve and switched cases.

W14-4

Anti-IL-6 receptor antibody ameliorates disease activity of rheumatoid arthritis patients with knee joint involvement -Answer cohort study-

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Conflict of interest: None

[Objective] It remains unclear which biologics are effective in the patients with rheumatoid arthritis (RA) who have large joint involvement. [Methods] We analyzed retrospectively 786 RA patients who visited our hospitals in 2003 to 2019 and were treated with anti-IL-6 receptor antibody (aIL-6) or TNF-inhibitor (TNFi). We divided the patients into 2 groups with or without knee joint involvement for further analysis. We investigated the CDAI levels at baseline and 12 weeks after the initiation of biologics. [Results] Interestingly, the patients who had knee joint involvement with aIL-6 significantly ameliorated ΔCDAI (15.0±10.8) compared to those with TNFi (11.4±10.3) at 12 weeks. Baseline clinical characteristics were similar between the two groups. By contrast, in the RA patients who had no swelling of knee joint, there was no ΔCDAI improvement between aIL-6 group (5.5±7.4) and TNFi group (6.7±8.9). [Conclusions] Thus, these findings suggest that anti-IL-6 receptor antibody was more effective in the RA patients with knee joint involvement compared to TNF- inhibitor.

W14-6

Efficacy of sarilumab in rheumatoid arthritis (RA) patients with or without MTX and bio-naïve or bio-switch

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Conflict of interest: None

[Objective] Sarilumab is a new drug, therefore, the examination of the therapeutic effect for each patient's background is insufficient. [Methods] In 25 patients who had been treated with salilumab for more than 24 weeks, the therapeutic effect, joint echo image, continuation rate, and safety in patients with or without MTX and bio-naïve or bio-switch were examined. [Results] 20 of 25 patients were female, average age was 65.6 years, average disease duration was 4.4 years. The continuation rate of 24 weeks was 89.2%, the DAS28-ESR was significantly decreased from 5.4 to 2.2, and the CDAI was significantly decreased from 24.3 to 6.2. Regardless of the background, DAS28-ESR / CDAI showed significant improvement after 24 weeks compared with MTX-/+ and naïve / switch cases. In joint echo, a significant improvement was observed in gray scale and power doppler. Three patients were discontinued due to adverse events or inadequate effects, but could continue in patients with mild cytopenia. [Conclusions] In patients who had been treated with sarilumab for more than 24 weeks, regardless of whether MTX was combined or not, and naïve / switch cases, the clinical treatment effect, joint ultrasound improvement effect, continuation rate and safety were high.

W15-1

Exploration of the mechanism (s) of proteinase activation in osteoarthritic cartilage

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Conflict of interest: None

Introduction: Although the involvement of proteinases in cartilage degeneration in OA is widely recognized, mechanisms underlying activation of proteinases is not known well. Objective: To further understand the mechanism (s) for cartilage loss in OA focusing on the role of plasmin activity. Methods: Cartilages were obtained from 17 end-stage OA knees at macroscopically preserved areas (Pres) and degenerated areas (Deg). Proteins were extracted and concentrations of major proteinases were determined by Luminex. Plasmin activity was also determined. Primary cultured chondrocytes were treated with rhTGF-β1, and gene expression was analyzed by qPCR. Results: The concentrations of uPA and MMP-13 were more elevated in Deg than in Pres, while those of MMPs-1, 2, 3 were not. Plasmin activity was also more enhanced in Deg. In cultured chondrocytes, the expression of uPA was significantly increased by rhTGF-β1. Conclusion: Plasmin may be critically involved in cartilage degradation in OA cartilage because the enzyme has a capacity to activate MMPs. Plasmin also has a capacity to activate latent TGF-β1, which may further increase plasmin activity by enhancing uPA expression in chondrocytes. This positive feedback mechanism might be critically involved in the loss of cartilage matrix in OA.

W15-2

Muscle atrophy in hip osteoarthritis

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Conflict of interest: None

[Objective] The aim of this study is to evulate the muscle atrophy in hip osteoarthritis. [Methods] A total of 10 unilateral hip osteoarthritis were included in this study. We measured the cross-sectional muscle volume in gluteus medius, gluteus minimus, tensor fascia lata, and iliopsoas muscle using three dimentional magnetic resonanse imaging. The muscle volume was compared between the osteoarthritis and contralateral side. [Results] Guluteus medius and iliopsoas muscle were significantly reduced in the osteoarthritis side. [Conclusions] Muscle atrophy was seen in guluteus medius and iliopsoas muscle in hip osteoarthritis.

W15-3

Mechanical loading may cause release of pathogenic proteins from degenerated cartilage in OA and RA knee joints

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Conflict of interest: Yes

[Objective] To investigate whether proteins which may cause synovial changes are released from degenerated cartilage by mechanical loading. [Methods] Cartilage tissues were obtained from 7 OA and 6 RA knees at prosthetic surgery at both macroscopically preserved and degenerated areas. Control cartilages were obtained at dissection from 9 donors who had no known history of joint problems. A cartilage tissue was placed in PBS and 1MPs of load, which was close to that given to cartilage during level walking, was given to the tissue repeatedly. After 60 times of loading, PBS was recovered and representative samples were subjected to cytokine array and iTRAQ (Isobaric Tag for Relative and Absolute Quantitation) analyses. [Results] In the cytokine array analysis of a sample from a degenerated OA cartilage, the factors such as Macrophage migration inhibitory factor and Plasminogen activator inhibitor-1 were found to be released abundantly upon loading. In the iTRAQ analysis, 99 proteins were identified to be released from degenerated OA more than 2-fold in amounts compared to the control, which included Angiogenin and Hepatocyte growth factor-like protein. [Conclusions] Several factors which might cause synovial pathologies could be released from degenerated cartilage by mechanical loading.

W15-4

Femoral shaft bowing is influenced by ageing but tibial articular configuration is not influenced by ageing

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Conflict of interest: None

[Objective] Factors that influence varus angle and posterior slope angle of the tibial articular surface (VTA and PTS) and that influence lateral and anterior bowing angles of the femoral shaft (LFS and AFS) were clarified. [Methods] Six parameters (age, height, weight, %YAM, BAP and TRACP-5b) were assessed in 124 knees in 109 patients with medial osteoarthritis. VTA, PTS, LFS and AFS were measured on radiographs. Correlation between four angles and six parameters was analyzed. [Results] The average of six parameters and four angles were 75.2 years, 151.7cm, 60.6kg, 76.4%, 15.1μg/L, 425.9mU/dL, 10.1°, 1.6°, 7.7°, 9.4°, respectively. The correlation coefficient between AFS and LFS and six parameters were 0.15, -0.20, -0.15, -0.20, 0.02, 0.18 and 0.23, -0.25, -0.18, -0.25, 0.20, 0.28, respectively. Positive correlation was found between age, BAP and TRACP-5b and LFS. Negative correlation was found between height and %YAM and LFS. Negative correlation was found between %YAM and AFS. The femoral shaft bowing is influenced by ageing, physique and bone metabolism. No correlation was found between any parameter and VTA or PTS. [Conclusions] Configuration of the femoral shaft changes with ageing. The tibial articular surface configuration is not influenced by ageing.

W15-5

Examination of rat surgical model for hip osteoarthritis

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Conflict of interest: None

[Purpose] In this study, we examined whether an OA model of the hip joint can be created by surgical treatment from the viewpoint of local X-ray and histological evaluation of the hip joint. [Method] Six-week-old male SD rats (n=10) were used, and the right hip joint was expanded by the posterior approach. The group in which the circular ligament was excised after the joint capsule incision was designated as the instability group (n=10). The left hip joint was treated as a control group (n=10). X-ray evaluation and histological evaluation of the hip joint were performed at 1, 2, 4, 8, and 12 weeks after the model was created. The X-ray evaluation was scored using the K-L classification, and the histological evaluation was scored using the OARSI score. And their scores were compared with MIA group. [result] In the X-ray evaluation of the Instability group, cranial collapse of the bone head was observed from the second week after the model was created. In histological evaluation, peeling of the synovial surface layer and cartilage degeneration were observed from the same period. Both progressed over time. [Discussion] In this verification, it was demonstrated that the OA model can be created for surgical treatment as well as the hip joint.

W16-1

Outcome of joint-preserving surgery for rheumatoid forefoot deformity

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Conflict of interest: None

Objective; To investigate the post-operation outcomes, complications and risk factors of joint-preserving surgery combined with metatarsal shortening osteotomy for RA forefoot deformity. Methods; From 2011 to 2018, 14 patients and 16 feet (all women) who underwent joint-preserving surgery for RA forefoot deformity were included. Survey items were 1. Patient background: age, disease duration, DMARDs, Steinblocker classification, disease activity, bone density. 2. Surgidal outcoms: Hallux valgus angle before and after surgery, 1st 2nd metatarsal angle, 1st 5th metatarsal angle, Hardy classification, Japanease society for surgery RA and foot (JSSF) scale, 3. Complications. Results; The mean age was 62.2 ± 11.9 years. RA disease duration was 18.3 ± 8.3. The JSSF scale improved from 52.2 (20-77) to 85.3 (71-96) postoperative a year. Postoperative complications occurred in 6/16 cases; wound healing delayed 4 feet, bone fusion prolongation 2 feet, footpad poor blood flow 1 foot, symptomatic deep vein thrombosis 1 foot, hallux valgus 3 feet, hallux varus with a foot. Conclusions; The outcomes of joint-preserving surgery were excellent, but there were relative many complications such as postoperative wound healing delay. Thus, the future issue is how to eliminate complications.

W16-2

Short-term clinical results of scarf osteotomy for hallux valgus deformity in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To elucidate short-term clinical results of scarf osteotomy for rheumatoid hallux valgus deformities. [Methods] We performed scarf osteotomy for hallux valgus deformity on 23 patients (25 feet) with rheumatoid arthritis and followed them up for at least 6 months. We retrospectively examined preoperative and 6-month postoperative X-rays of the foot, JSSF hallux and lesser scales and SAFE-Q. Early recurrence was defined as HVA of 20 degrees or higher in 6-month postoperative weight-bearing X-rays of the foot. [Results] Preoperative mean HVA of 45.3 degrees was improved to 7.9 degrees postoperatively ($p<0.001$). JSSF scales and SAFE-Q were also improved postoperatively. Early recurrence was observed in 5 feet. T-1MT and NC overlap in lateral views of preoperative weight-bearing X-rays of the foot were slightly higher in recurrence group, indicating that pes planovalgus provokes postoperative recurrence of hallux valgus. Although the HVAs of recurrent cases were 20 to 27 degrees which were within the range of mild hallux valgus deformity, postoperative JSSF scales and SAFE-Q of recurrence group were lower than those of no recurrence group. [Conclusions] Midfoot and hindfoot malalignment is a risk factor for recurrence after scarf osteotomy for rheumatoid hallux valgus.

W16-3

Results after hallux valgus surgery using the Mitchell method in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We compared the results of patients with rheumatoid arthritis (RA) after hallus valgus (HV) surgery using the Mitchell method compared with patients with non-RA. [Methods] Of the 385 cases of HV surgery (517 feet) performed between 2007 and 2018, the subjects were 53 cases (87 feet) operated for 1 year after surgery. HV angle, first metatarsal (M1/2) angle, M1/5 angle and calcaneal pitch (CP) angle were measured before and after surgery, and the postoperative results was compared. [Results] RA patients were 10 cases 17 feet (9 women, average age 65.8 years), and non-RA patients were 53 cases 70 feet (50 women, average age 64.7 years). In RA patients, pre- and post-operative radiographic changes average HV angle from 38.8° to 13.4°, M1/2 angle from 17.2° to 7.4°, M1/5 angle from 35.2° to 25.9°, and CP angle from 13.6° to 12.2°. In non-RA patients, HV angle improved from 40.6° to 11.9°, M1/2 angle from 17.2° to 8.7°, M1/5 angle from 36.6° to 28.5°, and CP angle from 14.0° to 15.2°. There was no significant difference between the two groups, and it was not observed in the X-ray evaluation after one year. [Conclusions] There was no significant difference in postoperative results of hallux valgus by Mitchell method in patients with rheumatoid arthritis.

W16-4

Clinical outcome after the first metatarsophalangeal joint arthrodesis adjusting the sagittal alignment in response to individual cases

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Conflict of interest: None

[Objective] The optimal fused dorsiflexion angle at the first MTP joint is suggested to be within a range of 20 to 40 degrees. However, in a case with decreased inclination of the first metatarsal like RA patients with flatfoot deformity, the application of uniform dorsiflexion angle is considered to be inappropriate. We evaluated our method of MTP joint arthrodesis adjusting the sagittal alignment in response to individual situations. [Methods] A total of 31 cases in 27 patients were included in this study. The flat pad was placed on the sole to simulate weight bearing during surgery, and the great toe was aligned in sagittal plane with 2 to 3 mm of plantar clearance beneath the toe. Osteotomies were done at the metatarsal head and base of proximal phalanx vertically to the pad. [Results] The first metatarsal declination angles were more disperse in RA patients compared to non-RA patients. At the most recent follow-up, the toe to floor distance of the hallux in static standing posture was 2.5 mm in average with range of 0 to 10 mm. There was no complication and revision due to the misalignment of the fused MTP joint. [Conclusion] Good clinical outcome was achieved by the first MTP joint arthrodesis using a dependent dorsiflexion angle on individual cases.

W16-5

Postoperative Differences In The Height Of The Second Metatarsal Head Relative To The First Is Associated With The Recurrence Of Callosities After Forefoot Surgery In Patients With Rheumatoid Arthritis

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Conflict of interest: None

Objective Proximal rotational closing-wedge osteotomies of the first metatarsal bone has yielded good outcomes in our hospital since 2010. The aim of this study was to assess the association between the difference in the post-operative height of the first and second metatarsal heads after forefoot surgery and the recurrence of callosities in patients with RA. Methods We evaluated 134 RA patients (164 feet) who underwent this procedure between 2012 and 2015. The presence of second metatarsal plantar callosities was investigated, and the association between the mean post-operative height of the second metatarsal head relative to the first and the presence of plantar callosities were analyzed using the *t*-test. Results The mean post-operative height of the second metatarsal head relative to the first for patients with plantar callosities (6.3mm±2.0, n=20, 25 feet) was significantly higher than that for those without plantar callosities (2.8mm±1.8, n=114, 139 feet) ($P<0.01$). The difference at which plantar callosities started to appear was 4.5mm, with AUC of 0.88, a sensitivity of 84%, and a specificity of 84.9%. Conclusions We should aim to keep

post-operative height of the second metatarsal head relative to the first within 4.5mm in order to prevent the recurrence of callosities.

W16-6

Three dimensional CT based study comparing the ankle morphology and CT values between patients with osteoarthritis and rheumatoid arthritis

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Conflict of interest: None

[Objective] In total ankle arthroplasty (TAA), aseptic loosening is the most common cause of revision surgery. Previous study showed osteoarthritis (OA) patients had longer anteroposterior length of distal tibia than healthy controls, which increases the risk of cortical bone support failure. The bone mineralized density (BMD) around implants also affects their stability. The aim of study is to clarify the difference of bone morphology and BMD between OA and rheumatoid arthritis (RA) patients. [Methods] Fifteen OA patients and 15 RA patients were included. On three dimensional CT scans, virtual osteotomy planes on tibia and talus under various angle and thickness were obtained. The anteroposterior length of tibial osteotomy plane (AP) and the CT value of tibial and talar osteotomy planes were measured. [Results] The AP of OA group was statistically larger than that of RA. The AP became larger with increasing anterior opening angle of osteotomy plane, and with decreasing thickness of osteotomy. The CT value on tibial osteotomy site of RA patients was statistically lower than that of OA. [Conclusions] In TAA, we should be aware of the increased anteroposterior length of distal tibia in OA patients, and the lower BMD in RA patients, both of which are affected by osteotomy conditions.

W17-1

Stratification of mortality based on prognostic factors in anti-melanoma-associated gene 5 antibody-associated interstitial lung disease

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Conflict of interest: Yes

[Objective] The aim of this study is to stratify mortality based on prognostic factors in patients with anti-MDA5 antibody-associated interstitial lung disease (anti-MDA5-associated ILD), using a multicenter cohort JAMI. [Methods] We selected 212 patients with anti-MDA5 from the JAMI database. We then conducted a multivariate logistic regression analysis to identify independent risk factors for mortality. We generated a stratification tree model for mortality based on the independent risk factors. [Results] Seventy-three (34%) patients died, 68 patients due to respiratory insufficiency. Independent risk factors for mortality were older age (OR 1.07, 95% CI 1.04-1.12, P < 0.0001, cut-off value 58 years), and lower SpO_2/FiO_2 ratio (OR 0.98, 95%CI 0.96-0.99, P < 0.0001, cut-off value 450). Patients older than 57 years with SpO_2/FiO_2 ratio < 450 at diagnosis had the worst outcome with mortality rate of 76%. On the other hand, Patients younger than 58 years with SpO_2/FiO_2 ratio ≧450 at diagnosis had the best outcome with mortality rate of 9%. [Conclusions] Age and SpO_2/FiO_2 ratio at diagnosis are independent predictors for mortality in patients with anti-MDA5-associated ILD.

W17-2

Risk factors for relapse of anti-synthetase syndrome

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Conflict of interest: None

[Objective] To describe the clinical features of patients of anti-synthetase syndrome (ASS) with/ without the relapse and to identify risk factors for the relapse. [Methods] Subjects were consecutive ASS patients who received first induction therapy. Relapse was judged when physicians intensified therapy for ASS. [Results] Subjects were 44 patients (DM/PM; 27/17, ILD: 44, myositis: 32). Anti-Jo1, EJ, PL-12, and PL-7 Abs were detected in 22,11,6 and 5 patients, respectively. Relapse occurred in 21cases. At the 1st relapse, 38% of cases received immunosuppressants (IS) and the mean PSL dose was 12mg/day. Moreover, 14 cases showed recurrent relapses, at which most patients received IS and the PSL dose was 12mg/day. No differences were found between patients with and without relapse in gender, age of the onset, organ involvement, levels of CK, LDH, and KL-6, and usage of IS. However, relapse occurred frequently in patients with anti-EJ Ab (72%), but rarely in patients with anti-PL12 and PL-7 Abs. Patients with recurrent relapse showed exacerbation of myositis at 1st relapse. [Conclusions] Approximately half of ARS patients showed relapse at PSL dose of 10mg dose. The specificity of AS Ab was related to the frequency of relapse. Myositis at 1st relapse was a risk factor of recurrent relapse.

W17-3

Clinical features of digital ulcers and gangrene in anti-aminoacyl tRNA synthetase (ARS) antibody-positive patients

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Conflict of interest: None

[Objective] The aim of this study is to clarify the incidence and clinical features of digital ulcers (DU) or gangrene in anti-ARS antibody-positive patients. [Methods] We retrospectively assessed 96 patients who had visited our hospital since August 2014 to September 2019, and were positive for anti-ARS antibody by RNA immunoprecipitation assay. Student's t-test and Fisher's exact test were employed to compare the patients who developed DU or gangrene (DU group) with the patients who did not (non-DU group). [Results] 7 patients (7%) developed DU or gangrene. The mean age at diagnosis was 59 years old, and 4 were female. Clinical diagnosis was dermatomyositis in 1, systemic sclerosis (SSc) in 1, myositis-SSc overlap in 4, unclassified in 1. ARS specificity recognized by autoantibodies was PL-7 in 2, PL-12 in 2, EJ in 2, KS in 1. Fever ($P = 0.0024$), puffy fingers ($P = 0.002$), and digital pitting scar ($P = 0.0027$) were more common in DU group, while the prevalence of atherosclerosis risk factors was comparable between the two groups. [Conclusions] DU and gangrene were seen in a small proportion of anti-ARS-positive patients. Vascular remodeling due to SSc might be involved in the pathophysiology of digital ischemia.

W17-4

Long-term survival and lung volume in patients with interstitial lung disease having anti-ARS and anti-MAD5 antibodies

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Conflict of interest: None

[Objective] To compare characteristics in patients with anti-ARS-positive interstitial lung disease (ILD) (Anti-ARS-ILD) and anti-MDA-5-positive ILD (Anti-MDA-5-ILD). [Methods] Fifty-one patients diagnosed with anti-ARS-ILD (n = 13) and anti-MDA-5-ILD (n = 38) were retrospectively analyzed. Chest CT was used to evaluate remained normal lung volume. [Results] The mean observation period (SD) was 44 (33) months. Serum CK (SD) were high [mean 1122 (1159) U / L vs. 56 (102) U / L, P = 0.03]. The normal lung volume (SD) at the onset of disease was 3100 (720) cm^3 in anti-ARS-ILD patients and 2796 (887) cm^3 in anti-MDA-5-ILD (NS). The survival was high in anti-ARS-ILD patients compared with

anti-MDA-5-ILD patients (P = 0.02). Thirty patients with anti-ARS-ILD (94%) and 10 patients with anti-MDA-5-ILD (77%) achieved remission, of which 11 (37%) and 2 (20%) patients relapsed, respectively. Remarkable decrease in normal lung volume was found in patients with anti-ARS-ILD having relapse [Relapsed; 2315 cm^3 (660) vs. non relapsed; 2785 (788) cm^3 P <0.01). [Conclusions] Decrease in normal lung volume was observed especially in patients with anti-ARS-ILD experienced relapse. Therapeutic strategies to preserve lung function is needed.

W17-5

The clinical features of reccurence of acute progressive interstitial lung disesase with anti-melanoma differentiation-associated gene 5 antibody

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Conflict of interest: None

[Objective] Anti-MDA5 antibody (Ab) positive dermatomyositis (DM) often develop rapidly progressive interstitial lung disease (RP-ILD), and many cases die in a short duration after the onset. After the acute phase, the disease activity is usually stable. But the long-term prognosis is still unclear. Our objective is to explore the clinical features of recurrence of anti-MDA5 Ab-positive DM. [Methods] We retrospectively collected the clinical data of anti-MDA5 Ab-positive DM patients who were treated in our hospital from April 2011 to October 2019. [Results] 3 (21%) of 14 cases showed the recurrence of RP-ILD. Interestingly, serum ferritin levels were within normal levels when the relapse symptoms were confirmed. On the other hand, anti-MDA5 Ab titers markedly increased at the time of relapse. Anti-MDA5 Ab titers were significantly elevated at the time of relapse, even once it was under the cut-off level before the recurrence. There was a discrepancy between anti-MDA5 Ab titers and ferritin levels regarding the elevation time. Men (P = 0.01) and smoking (P = 0.003) were extracted as risk factors for relapse. [Conclusions] At the time of recurrence, anti-MDA5 Ab titers markedly elevated though ferritin levels were normal. These suggesting the usefulness of measuring Ab titer over time.

W17-6

Prognostic factors of anti-MDA5 antibody positive dermatomyositis associated with interstitial pneumonia

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Conflict of interest: None

[Objective] To identify the predictors of prognosis in patients with anti-MDA5 antibody-positive dermatomyositis associated with interstitial pneumonia (DM-IP), whose prognosis is assumed to be quite poor. [Methods] Anti-MDA5 antibody-positive DM-IP patients admitted to our hospital between January 2010 and October 2019 were consecutively included and stratified into 2 groups, the survived and the deceased groups. Clinical features and prognosis of the patients were collected retrospectively and compared between groups. [Results] Twenty-one patients were involved. Eight were deceased and 13 were survived. The deceased group had a higher ratio of male (p= 0.0176). All deceased cases were with RPIP and 67% in the survived cases. Serum ferritin, CRP, CK, AST and LDH levels were higher in the deceased group (p= 0.0026, p= 0.0490, p= 0.0169, p= 0.0248, p= 0.0112, respectively). Interestingly, skin ulcers were tend to be more frequent (p= 0.0587), and anti-SS-A antibody was also more frequently detected (p= 0.0072) in the survived group. [Conclusions] Not only factors already reported, but serum CK, AST, and LDH levels were newly extracted as candidates. Also, anti-SS-A antibody was extracted as a protective factor and might associate with a good therapeutic outcome.

W18-1

Successful treatment of anti-MDA5 antibody-positive refractory interstitial lung disease with plasma exchange therapy

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Conflict of interest: None

Objectives We examined the effectiveness of plasma exchange (PE) therapy to reduce the mortality of rapidly progressive interstitial lung disease (RP-ILD) in patients positive for anti-melanoma differentiation-associated gene 5 (MDA5) antibodies. Methods Among patients newly diagnosed with PM/DM or clinically amyopathic DM from 2008 to 2019 at our hospital, 11 were diagnosed with refractory RP-ILD and were positive for anti-MDA5 antibodies. Results Anti-MDA5 antibodies were detected in 30 patients, of whom 23 were diagnosed with RP-ILD and 11 were refractory to intensive immunosuppressive therapy. Seven patients received PE (PE group) and four did not (non-PE group). The 1-year survival rate of the PE group was higher than that of the non-PE group (100% and 25%, respectively, P = 0.033). Regarding adverse events associated with PE, two patients had anaphylactic shock, one had high fever due to fresh frozen plasma allergy and one had a catheter infection. All adverse events resolved with appropriate treatment. Conclusion We evaluated the association between 1-year survival rate and PE for refractory RP-ILD in patients positive for anti-MDA5 antibodies. PE may be considered in refractory RP-ILD patients positive for anti-MDA5 antibodies.

W18-2

A case of treatment-resistant interstitial pneumonia with anti-EJ antibody positive dermatomyositis receiving brain-dead double lung transplant

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Conflict of interest: None

We report the case of a 49-year-old woman diagnosed as dermatomyositis with positive anti-EJ antibody and underwent lung transplant. She developed dyspnea on exertion and admitted to our hospital in July X-2. Gottron's sign was appeared of her fingers and elbow. Her laboratory data showed CK2377U/L, CRP3.87mg/dl and anti-ARS antibody (anti-EJ antibody)-positive. Chest CT revealed ground glass shadow and invasive shadow in lower lung field. We diagnosed dermatomyositis related interstitial pneumonia. She was treated with mPSL 500 mg pulse therapy, PSL (50mg/day), tacrolimus (5mg/day) and IVCY therapy. Her cutis and muscle symptom were improved but her respiratory symptoms were not improved. We continued treatments with PSL (15mg/day) and tacrolimus (5mg/day). IVCY therapy of 500mg/4week was administered 8 times. Her respiratory function worsened and she was introduced domiciliary oxygen therapy in June X-1. We referred her to other hospital for lung transplant. She was registered as recipient in June X and she underwent lung transplant in September X. Transplantation is an effective therapy for patients in the terminal phase of the lung disease. We discuss about lung transplant in autoimmune disease with literature review.

W18-3

Three cases of rapidly progressive interstitial lung disease and anti-MDA5 antibody-positive dermatomyositis successfully treated with additional plasma exchange therapy

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Conflict of interest: None

Case 1: A 70-year-old female had dry cough and dyspnea on exertion since March 2019. Although she was treated with antibiotics, the symptom was not improved. On clinical examination, heliotrope rash, Gottron's signs and progressive interstitial lung disease were identified. She was diagnosed as rapidly progressive ILD and dermatomyositis. Case 2: A 64-year-old female noticed skin erythema since April 2019. Subsequently, she had persistent dry cough and the symptom did not improved with antibiotics. She was diagnosed with RP-ILD and DM. Case 3: A 50-year-old male experienced skin eruption since February 2019 and exertional dyspnea was additionally noted. Further examination revealed that he had DM with RP-ILD. All three patients revealed that they had PaO2 <95%, extensive ILD on chest CT, serum ferritin >500 ng/mL and high titer of anti-MDA5 antibody at the time of admission. High dose prednisolone including methyl-prednisolone pulse therapy with calcineurin inhibitor and cyclophosphamide pulse therapy was initiated. As RP-ILD could not be fully controlled in spite of this intensive therapy, plasma exchange (3 days a month) therapy was added. After additional PE therapy, respiratory symptoms as well as skin erythema improved in all three patients.

W18-5

The efficacy of etoposide in anti-Melanoma Differentiation Associated gene-5 antibody-positive dermatomyositis

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Conflict of interest: None

The first case, a 15-year-old woman presented an erythema on her hands, polyarthralgia and difficulty in going up stairs. Serum creatine kinase (CK) elevated and anti-melanoma differentiation associated gene-5 (MDA-5) antibody was positive, so she was diagnosed as dermatomyositis (DM). She did not have interstitial lung disease (ILD). Treatment with prednisolone (PSL) and tacrolimus (Tac) was started, but serum ferritin increased. Although Intravenous cyclophosphamide (IVCY) was initiated, she developed hemophagocytic lymphohistiocytosis. Plasma exchange and intravenous immunoglobulin was not effective. Etoposide was added and serum ferritin improved. The second case, a 64-year-old woman was presented an erythema on her hands and difficulty in walking. Serum CK elevated and anti-MDA-5 antibody was positive. Computed tomography (CT) scans showed ILD, so she was diagnosed as DM. Treatment with PSL, Tac and IVCY was initiated and the erythema disappeared. 1 month after, an erythema on her face and dyspnea appeared, also CT findings showed an exacerbation of ILD. Ulinastatin and azathioprine was not effective. Etoposide was added, then the erythema and ILD was improved. These two cases suggested that etoposide could be an alternative treatment for anti-MDA-5 antibody-positive DM.

W18-6

Rituximab for inflammatory myopathy at Tokyo Metropolitan Tama Medical Center

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Conflict of interest: None

[Objective] To investigate the effects and adverse events of rituximab for patients with inflammatory myopathy. [Methods] We conducted a retrospective search of medical records for patients who were administered rituximab in our department by October 2019 and reviewed the details of patients with inflammatory myopathy. [Results] Seventy-seven patients were administered rituximab in our department within the period above, including 8 patients with inflammatory myopathy. Of these, there were 3 patients with anti-ARS antibody, 2 with anti-HMGCR, 1 with anti-TIF$_1$-γ, 1 with anti-MDA-5, and 1 with anti-SSA. Two patients continued to receive rituximab: one with anti-EJ and one with anti-SSA. Six patients discontinued rituximab. The reasons for discontinuation were infection (2 cases, one with anti-EJ and one with anti-MDA-5), insufficient effect (2 cases, both with anti-HMGCR), secondary failure (1 case with anti-Jo-1). One case with anti-TIF$_1$-γ had not been re-administered after 4 doses of induction due to favorable clinical course without rituximab thereafter. [Conclusions] Within this study, non-complicated antisynthetase syndrome responded well to rituximab, and 2 cases with anti-HMGCR were refractory to rituximab. The number of subjects is small and further study is needed.

W19-1

Estimation of the number of rheumatoid arthritis and their treatment: an analysis of the National Database of Japan

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Conflict of interest: None

[Objective] To estimate the number of rheumatoid arthritis (RA) patients in Japan by their treatment [Methods] Using the National Data Base provided by Ministry of Health, Labour and Welfare in Japan of fiscal year 2017, we estimated the number of RA patients who were ≧16 years old with combination of ICD-10 codes and the pattern of medication. [Results] The number of patients who were given the ICD codes above at least once was 1,116,122. Among them, patients who were prescribed any DMARDs for more than one month or corticosteroids for more than two months, any DMARDs for more than two months, any DMARDs for more than six months were 1,026,634, 825,772, and 583,137, respectively. In patients who were prescribed any DMARDs for more than two months, conventional DMARDs were prescribed in 95.0%, methotrexate in 63.4%, biological DMARDs in 22.9%, oral corticosteroids in 42.1%, and NSAIDs in 62.4%. When we set the RA patients as patients who were prescribed DMARDs for more than two months, the estimated the number of RA patients was 825,772 (female 76.3%), 0.65% among the nationwide residence of Japan. [Conclusions] By using the NDB, the total number of patients with RA in Japan was estimated for the first time.

W19-3

Have 5-year survival rate and mortality improved in patients with early rheumatoid arthritis? -results from the IORRA cohort-

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Conflict of interest: None

[Objective] To investigate whether the prognosis of early rheumatoid arthritis (eRA) patients has improved. [Methods] From the IORRA cohort, patients with eRA (disease duration <2 years) who participated in the survey for the first time from 2001 to 2012 were included. We observed them for 5 years from the initial survey. We classified patients into A (enrolled in 2001-2006) and B (enrolled in 2007-2012) groups. Five-year survival rate and standardized mortality ratio (SMR) were calculated and compared. The effects of untraceable cases were evaluated by multiple complementation as a sensitivity analysis of SMR. [Results] The number of patients was 1609 (79.4% female) in A and 1608 (81.8% female) in B. Deaths was confirmed in 47 cases (2.9%) in A and 45 (2.8%) in B. The 5-year survival rate was 88.8% for A and 87.8% for B, and the SMRs were 0.81 (95%CI 0.59-1.08) for A and 0.78 (0.57-1.04) for B when estimating all the lost to follow-up patients were alive. In the sensitivity analysis assuming that the mortality rate of patients who were lost to follow-up was

twice as that of general population, the SMRs were 0.90 (0.68-1.19) and 0.92 (0.68-1.23), respectively. [Conclusions] The 5-year prognosis for eRA patients was comparable to that of general population, but there was no improvement over time.

W19-4

Disease activity and treatment in RA patients on maintenance dialysis: NinJa2017 Cross-sectional cohort study

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Conflict of interest: None

[Objective] To clarify the clinical characteristics, disease activity and treatment of RA patients on maintenance dialysis (MD) in NinJa2017. [Methods] Cross-sectional study. It was researched if the patients with 1.5 mg/dL and higher serum creatinine levels are on MD. Dialysis mode, diseases leading to end-stage renal disease (ESRD) and RA treatment were described. DAS28 was compared between RA patients under MD (D), and those not under MD (nD). Median and IQR were presented. Mann-Whitney U test and Fisher's exact test were done. P value less than 0.05 was regarded as significant. Prism 8 was used for statistical analysis. [Results] We found 31 RA patients under MD. Median of Age was 70.0 years old. Twenty-seven patients were treated with hemodialysis, and 4 patients were treated with peritoneal dialys. Diseases leading to ESRD included chronic glomerulonephritis in 7 (IgA nephropathy in 4), diabetic nephropathy in 3, nephrosclerosis in 3, and renal amyloidosis in 3 patients. DAS28 in D was significantly higher than that in nD (D: 3.88, 3.25-4.39, nD: 2.85, 2.15-3.67, P=0.0008). bDMARD was used in 13 patients (TCZ 7, ABA 4, GOL 1 and IFX 1). csDMARD and ts DMARD were prescribed in 18 and 2 patients respectively. [Conclusions] Characteristics of D in NinJa2017 were clarified.

W19-5

Relationship between JADAS -27 and disease activity index of rheumatoid arthritis in non-systemic juvenile idiopathic arthritis - analysis using CoNinJa

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Conflict of interest: None

[Objective] We studied the relationship between JADAS -27 and disease activity index of RA using large-scale JIA database CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan). [Methods] The correlation between JADAS -27 of JIA and DAS 28/SDAI/CDAI/Boolean criteria was investigated using non-systemic JIA case data from 2000 to 2016 registered with CoNinJa, [Results] We evaluated 345 data from 283 patients. There was a correlation between JADAS -27 and DAS28/SDAI/CDAI (Spearman coefficients = 0.92 -0.98), with SDAI showing the strongest correlation. There was a discrepancy between patients who satisfied the remission criteria of JADAS -27 and DAS28/SDAI/CDAI (kappa coefficient = 0.54 -0.78). In oligoarticular JIA, the coincidence lowered in comparison with other disease types. Similar results were obtained in the adolescent and adult phase of patients over 16 years old. [Conclusions] It may be necessary that further validation of the use of the disease activity index of RA in adolescent and adult JIA.

W19-6

Relationship between lupus low disease activity state and quality of life in patients with systemic lupus erythematosus; From Juntendo SLE prospective registry study (JUMP study)

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) patients who achieve lupus low disease activity state (LLDAS) is known to low incidence of organ complications and disease recurrence. In this study, we examined the relationship between LLDAS and quality of life (QOL) in patients with SLE. [Methods] Seventy-four SLE patients who wewe registered in Juntendo prospective registry (JUMP study) were selected. To evaluate the QOL of the patients, SF36v2 was used. Subjects were classified into LLDAS achieved and failure to achieve groups, and the characteristics of each group were discussed. [Results] Among all patients, 32 patients fulfilled the definition of LLDAS, and 42 were never achieved. The standard scoring of SF36v2 which recognized significant difference in each group was as follows, physical functioning (RF) was 83.8 ± 15.0 and 75.2 ± 20.3 ($P < 0.05$), bodily pain (BP) was 69.8 ± 26.2 and 57.2 ± 24.3 ($P < 0.05$), role emotional (RE) was 86.2 ± 17.8 and 75.2 ± 26.3 ($P < 0.05$), and mental health (MH) was 74.7 ± 15.3 and 63.8 ± 19.9 ($P < 0.05$) respectively. Moreover, in the former group the norm-based scoring of SF36v2 was over 50 for RE and MH, but all items were less than 50 in the latter group. [Conclusions] From these results, fullfilling the LLDAS is also improve the QOL of the SLE patients.

W20-1

Optimal age cut-off of elderly-onset rheumatoid arthritis (EORA) in Japanese patients

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Conflict of interest: None

[Objective] The onset of RA has been becoming older in Japan. EORA is empirically defined as RA initiating after 60 years old. This study aimed

to determine an appropriate cut-off age of EORA in Japanese patients. [Methods] We retrospectively studied 192 RA patients meeting the 2010 ACR/EULAR criteria from 2014 to 2019 in our hospitals. Multiple regression analysis identified associated factors with elderly onset. ROC analysis determined the cut-off age of a patient group characterized by these factors. [Results] Mean onset was 64±16 years old. Multiple regression analysis revealed acute onset, large joint involvement and negative anti-CCP antibody were independently associated with elderly onset. Based on these factors, ROC analysis determined the cut-off age as 74 years old. Patients with the onset over 74 years old (n=64) were characterized by increased ratio of male, an abrupt onset and higher disease activity compared with the younger onset of patients (n=128) ($p<0.05$). Comorbidities such as hypertension, cardiovascular disease, malignancy were more in the old-age group. The significant findings were confirmed in comparison with patients between 60 and 73 years old (n=64). [Conclusions] Our study shows that the cut-off age of EORA is 74 years old in Japan.

W20-2

The change of the characteristics of EORA in the decade from 2009 to 2018 of NinJa database

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Conflict of interest: None

[Objective] To evaluate the change of the characteristics of elderly onset rheumatoid arthritis (EORA) in the decade from 2009 to 2018 of *NinJa* database. [Methods] The patients of disease duration form 5 to 6 years were divided into 3 groups according to the onset age of disease, Group Y (<65 years), Group E-1 (≧65, and <75), and Group E-2 (≧75), in the databases from *NinJa* 2009 to *NinJa* 2018. [Results] In the classification of Steinbrocker's stage, the percentages of stage III+IV were not decreased in Group E-2, whereas those were decreased gradually in Groups Y and E-1. The ratio of the medication of MTX was lower in Group E-2 than those in Groups Y and E-1. In Group E-2, the ratio of treatment with biologics or JAK inhibitors was increased markedly from 4.8% in *NinJa* 2009 to 24.7% in *NinJa* 2018. SDAI was improved from 11.24 in *NinJa* 2009 to 6.05 in *NinJa* 2018. Modified Health assessment questionnaire (mHAQ) was showed improvement tendency in Groups Y and E-1, whereas was not improved in Group E-2. [Conclusions] In Group E-2, the ratio of stage III+IV and mHAQ did not showed the improvement in the patients of disease duration from 5 to 6 years. However, these parameters were expected to improve, because the ratio of medication of biologics or JAK inhibitors was increased rapidly.

W20-3

Study of prescription pattern in elderly patients with rheumatoid arthritis using National Data Base

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Conflict of interest: Yes

[Objective] To investigate prescription patterns of medications for rheumatoid arthritis (RA) in elderly patients. [Methods] Using National Data Base provided by Ministry of Health, Labour and Welfare in Japan, we defined individuals as RA cases if they had at least one disease name code of RA and prescription of disease modifying antirheumatic drugs (DMARDs) for at least 2 months in fiscal year 2017, and were ≥16 years old. We compared the prevalence of DMARDs and oral corticosteroids (CS) among patients <65 years old (group I), ≥65 and <70 (group II), ≥70 and <75 (group III), and ≥75 (group IV). [Results] In RA cases (n=825,772), the prevalence of csDMARDs was 94.7% in group I (n=323,975), 95.8% in group II (n=127,272), 95.4% in group III (n=123,116), 94.9% in group IV (n=251,409). The prevalence of methotrexate decreased with increasing age (70.6% in group I, 68.1% in group II, 64.3% in group III, 51.2% in group IV), whereas, that of biological DMARDs was similar in patients ≥65 years old (26.3%, 22.0%, 21.9%, 19.3%). The prevalence of oral CS was 38.6% in group I, 39.5% in group II, 41.8% in group III, and 48.0% in group IV, respectively. [Conclusions] This study revealed nationwide prescription patterns of medications in elderly RA patients for the first time in Japan.

W20-4

Analysis of treatment response in elderly onset rheumatoid arthritis patients 3 years after the onset using the IORRA cohort

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Conflict of interest: None

[Objective] We evaluated the factors associated with treatment response in elderly onset rheumatoid arthritis (EORA). [Methods] We analyzed RA patients who first enrolled in the IORRA from 2010 to 2014 and who were over 60 years old within 1 year disease duration and had a DAS28-ESR over 3.2 at entry. The primary endpoint was whether DAS28-ESR after 3 years had achieved remission or low disease activity. A logistic regression analysis was conducted to examine whether patient background factors and the drug use (PSL, MTX, biologics) at baseline were related to the primary endpoint. [Results] 152 patients (age 69.9 ± 6.5, female 77%, DAS28-ESR 4.3 ± 0.8, J-HAQ 0.9 ± 0.7) achieved remission or low disease activity after 3 years (RL group), and 98 patients (age 69.4 ± 6.7, female 80.6%, DAS28-ESR 4.4 ± 0.8, J-HAQ 1.0 ± 0.7) did not (MH group). DAS28-ESR after 3 years in the RL and MH group were 2.3±0.5 and 3.4±0.9. EORA patients without steroid use (odds ratio 1.82, $p = 0.056$) and without complication of malignancy (odds ratio 10.27, $p <0.01$) were related factors for achieving DAS28 remission and low disease activity after 3 years. [Conclusion] the achievement of DAS28 remission and low disease activity after 3 years was associated with non-steroid use and absence of malignancy at baseline.

W20-5

The causes of death in deceased patients with RA by NinJa 2018 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 NinJa2018. [Methods] 146 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 77.1years old. The major cause of death in deceased patients was infection in 39patients involving in pneumonia in 32patients. Next was malignancy in 33 patients, respiratory dysfunction involving intestinal pneumonia in 20 patients, cardiovascular disease in 10 patients, unknown sudden death in 7 patients. [Conclusion] The life expectancy of Japanese patients with RA was getting better. The major causes of death were infection, especially bacterial pneumonia and/or aspiration pneumonia. It is important for us to risk management for elderly RA patients.

W20-6

Relationship between number of remaining teeth, periodontal disease prevalence and activity, and physical function in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We examined whether: (1) RA patients with long morbidity, high disease activity, and poor physical function have fewer remaining teeth; (2) periodontal disease prevalence is higher in patients with high disease activity and reduced physical function; and (3) patients with progressive bone destruction have fewer remaining teeth and higher prevalence of periodontal disease. [Methods] Number of remaining teeth, periodontal disease (periodontal pockets ≧4 mm), RA disease activity, and physical function evaluation (HAQ-DI) were compared. [Results] The average number of remaining teeth was 26.4 in patients in their 50s or younger, 19.8 in their 60s, 17.6 in their 70s, and 17.5 in their 80s. The numbers for those in their 60s and 70s were below the Japanese average. There were no clear associations between number of remaining teeth and disease duration, RA disease activity, or HAQ-DI. Periodontal pockets ≧4 mm were seen in 46 cases (78.0%), and showed no associations with disease activity or physical function. Although joint destruction patients had fewer remaining teeth, there was no association with periodontal disease. [Conclusions] The number of remaining teeth in RA patients decreased over time, and patients with advanced joint destruction had fewer remaining teeth.

W21-2

Evaluation of predictive factors for clinical remission by treatment with tofacitinib (tofa) vs. adalimumab (ADA) in patients with rheumatoid arthritis (RA) -From FIRST registry-

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Conflict of interest: None

[Objective] The aim of study was to clarify the therapeutic strategy for clinical remission by treatment with tofa in clinical practice in RA. [Methods] We analyzed retention rate and adverse events of 143 patients who received tofa from August 2013 to November 2018 at our institute. After adjusting selection bias by inverse probability of treatment weighting (IPTW) method, we compared the rate of CDAI remission at 52w with ADA and examined the factors of remission. [Results] The retention rate of tofa was 78% (Adverse event 8%), and ADA was 79% (Adverse event 20%). Compared the remission rate at 52w with ADA by IPTW method, there was no difference between treatment with tofa (35.8%) and ADA (38.3%) (LOCF) (p=0.2). Factors for CDAI remission by treatment with tofa were examined by logistic regression analysis. Low HAQ value at 0w and history of biologics treatment (less than second drug) contributed to remission. [Conclusions] Less progression in functional disturbance and treatment with less than 2 prior b/ts DMARDs could be predictive factors for clinical remission by the treatment with tofa in patients with RA.

W21-3

Infection Events in Japanese Patients with Rheumatoid Arthritis Treated with Tofacitinib: Interim All-Case Post-Marketing Surveillance

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Conflict of interest: Yes

[Objective] Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). We report serious infection (SIE) and herpes zoster (HZ) incidence with tofacitinib in a Japanese post-marketing surveillance (PMS) study. [Methods] An interim analysis of Japanese pts with RA receiving tofacitinib in an ongoing 3-year PMS study (Dec 5, 2018 data-cut). Interim data are from the safety analysis set at 6 months; frequency and types of all-causality SIEs and HZ are reported. Cumulative incidence rates (IRs; pts with events/100 pt-years) are for the 3-year treatment period +28 days. [Results] In all, 6,866 pts received tofacitinib with 7623.6 pt-years. Over 6 months, 215 pts (3.1%) had SIEs; most common were pneumonia (n=64; 0.9%), HZ (n=41; 0.6%), and *Pneumocystis jiroveci* pneumonia (n=19; 0.3%). In total, there were 249 (3.6%) pts with HZ (0.6% serious; 3.0% non-serious), including 3 cases of HZ disseminated, 2 cases of HZ oticus and 1 case of HZ meningoencephalitis. The cumulative IR (95% CI) was 5.23 (4.72 - 5.77) for SIE and 6.81 (6.23 - 7.44) for HZ. [Conclusions] HZ IR was similar to IRs previously reported for Japanese pts in tofacitinib studies. SIE IR was within the range of IRs in prior Japanese PMS studies (2.4 - 9.0) and RA registries (3.0 - 10.7) of bDMARDs.

W21-4

Safety and Malignancy in Japanese Patients with Rheumatoid Arthritis Treated with Tofacitinib: Interim Analysis of All-Case Post-Marketing Surveillance

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Conflict of interest: Yes

[Objective] Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). We report the safety of tofacitinib in a Japanese post-marketing surveillance (PMS) study. [Methods] Japanese patients (pts) with RA receiving tofacitinib were prospectively registered in an ongoing 3-year PMS study, and an interim analysis of overall safety data was conducted at 6 months (Dec 5, 2018 data-cut). All-period (36-month) data

were used to calculate cumulative incidence rates (IRs; pts with events/100 pt-years) over time for malignancies. [Results] Of 6,866 pts starting tofacitinib (safety analysis set), 22.5% discontinued by Month 6. All causality AEs and serious AEs (SAEs) were observed in 32.7% and 7.4% of pts, respectively. The most frequent AEs and SAEs by system organ class were infections and infestations (11.9% and 3.1% of pts, respectively). Cumulative IR (95% CI) of malignancy, including lymphoma, over 36 months was 1.31 (1.09-1.57). Malignancy IRs did not increase with prolonged tofacitinib exposure. [Conclusions] CumulativeIRs of malignancies were comparable with those in the tofacitinib RA clinical program. No new or unexpected safety risks were identified in this interim analysis vs the tofacitinib RA clinical program and previous data cuts from this PMS study.

W21-5

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

Kosuke Ebina[1], Toru Hirano[2], Yuichi Maeda[2], Wataru Yamamoto[3,4], Motomu Hashimoto[3], Koichi Murata[3], Tohru Takeuchi[5], Hideyuki Shiba[5], Yonsu Son[6], Hideki Amuro[6], Akira Onishi[7], Kengo Akashi[7], Ryota Hara[8], Masaki Katayama[9], Atsushi Kumanogoh[2], Makoto Hirao[10]

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Conflict of interest: Yes

[Objective] To compare the drug tolerability and discontinuation reasons of JAK inhibitors in RA patients. [Methods] 194 treatment courses (61 case of baricitinib (BAR) and 133 cases of tofacitinib (TOF), Bio/JAK naïve 22.2%, 2nd Bio/JAK 23.2%, 3rd or more Bio/JAK 54.6%; age 60.4y, female 78.4%, disease duration 10.6y, DAS28-CRP 3.7, CDAI 18.6, HAQ-DI 1.0, combined MTX dose 8.8mg/week, rate 58.8%, and combined PSL dose 4.0mg/day, rate 53.1%, were included in this multi-center, retrospective study. Data was adjusted by potent confounders (age, sex, disease duration, combined MTX and PSL, and Bio/JAK switched number) with a Cox proportional hazards model and evaluated at 12 months. [Results] There was no significant difference in baseline backgrounds except for female rate (BAR 90.2% vs. TOF 72.9%; P=0.012) between two groups. Discontinuation rate due to ineffectiveness was BAR 12.0% vs. TOF 15.2% (Cox P=0.76), due to toxic event was BAR 6.4% vs. TOF 7.7% (Cox P=0.97). Overall retention rates (%) excluding non-toxic events and remission were BAR 80.7% vs. TOF 76.7% (Cox P=0.84). [Conclusions] In spite of relatively high rate of Bio/JAK switched patients, both BAR and TOF showed low ineffectiveness and toxic discontinuation rate, as well as high overall retention in short-term follow-up.

W21-6

Herpes zoster in baricitinib-treated patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We evaluated characteristics of patients who developed HZ during baricitinib treatment. [Methods] One hundred five patients with RA (82 females) were enrolled. Patients were scheduled to receive bari 4 or 2 mg once daily dose. We evaluated characteristics and clinical course of patients who developed HZ. [Results] At baseline, mean age and disease duration of all patietns were 67.0 ± 12.0 years and 7.4 ± 9.0 years, respectively. We studied 8 patients with HZ (including 7 females). The incidence ratio (IR) was 8.9 per human-year. Mean age and disease duration of patients with HZ were 66.2 ± 10.1 years and 11.6 ± 12.5 years, respectively. Six patients were treated with baticitinib by a dose of 4mg/day. HZ incidence period after baricitinib administration were 2 - 16 months. Predonosolone (mean 1.0 ± 1.9 mg/day) and MTX (mean 6.5 ± 3.8 mg/week) were combined in 2 cases and 7 cases, respectively. Four patients had a history of HZ and their severity were all mild. All of the patients were cured with antiviral therapy. Six patients restart baricitinib therapy after the withdrawal period between 1 week and 6 weeks. [Conclusions] The IR of HZ was high as reported by clinical trials. However, HZ events were nonserious and many patients could restart baricitinib.

W22-1

Pain Improvement in Japanese Rheumatoid Arthritis Patients Treated with Baricitinib Compared to Adalimumab or Placebo

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Conflict of interest: Yes

[Objectives] Time and % of pain control with Baricitinib (BARI) vs. Adalimumab (ADA) and placebo (PBO) was evaluated in Japanese RA patients (pt). [Methods] In a phase 3 study (RA-BEAM), MTX-IR RA pt were randomized 3:3:2 to PBO, BARI 4 mg, or ADA 40 mg. Pain was assessed with VAS. The % achieving 30/50/70% VAS improvement through Week 24 and the median time when 50% of pt achieved these pain improvement were assessed in Japanese subpopulation (249 pt). Pain improvement was also analyzed by baseline pain VAS subgroup (≦med vs. >med). [Results] Pt treated with BARI were more likely to achieve 30/50/70% pain improvement than ADA and PBO with HR of 1.1/1.4/1.8 vs. ADA and 1.6/1.9/2.8 vs. PBO. The median time for 50% pt to achieve 30/50/70% pain improvement was 1/4/12 weeks for BARI, 1/8/>24 weeks for ADA, and 4/14/>24 weeks for PBO. The median time for 50% pt to achieve 30/50/70% pain improvement varied by baseline pain severity in pt treated with ADA or PBO; while did not vary in pt treated with BARI. [Conclusion] BARI demonstrated greater and faster pain improvement than ADA or PBO through Week 24 in Japanese RA pt. In addition, unlike ADA and PBO, BARI showed consistent improvement regardless of baseline pain severity. These results were consistent with those in whole population.

W22-2

Dose Reduction of Baricitinib (Bari) in Patients with RA Achieving Sustained Disease Control

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Conflict of interest: Yes

[Objectives] In 2018, we reported efficacy and safety of Bari in DMARD-IR patients who achieved sustained low disease activity (CDAI≦10; LDA) for ≧3 months with Bari 4mg, then stepped-down to 2mg. We report effects of Bari step-down in subpopulation who maintained LDA longer (≧6 months). [Methods] In the long-term extension study of Bari, DMARD-IR patients from RA-BUILD/BEAM/BEACON who maintained LDA ≧6 months were re-randomized in a blinded manner to continue 4mg or step down to 2mg to assess disease activity through 48 weeks. Patients could rescue (4mg) if CDAI >10. [Results] Most patients maintained LDA with patients who maintained 4mg (85%) having higher rate than those reduced to 2mg (71%); which is consistent with the previous results in patients who maintained LDA ≧3 months (4mg: 80% and 2mg: 68%). Mean CDAI change from baseline to Week 48 were smaller in patients who maintained 4mg (+0.84) than those who reduced to 2mg (+2.49). Similar trends were obtained for other activity parameters. AEs were lower in 2mg than 4mg. [Conclusion] Dose reduction may be

reasonable to attempt in patients achieving sustained disease control with Bari 4mg.

W22-3

Short-term clinical effectiveness and safety of baricitinib in rheumatoid arthritis patients in routine clinical practice: Results from data of a Japanese multicenter registry system

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Conflict of interest: Yes

[Objective] To evaluate the short-term clinical effectiveness and safety profile of baricitinib (BAR) in patients with rheumatoid arthritis (RA) treated in routine clinical practice. [Methods] There were 121 participants with RA treated with BAR in a Japanese multicenter registry (TBCR). They were followed up for at least 24 weeks. [Results] Mean age was 66.1 years and RA disease duration was 14.0 years. 82.1% of patients were ACPA positive, 71.1% experienced previous biologics, 48.3% used concomitant methotrexate, and 40.0% used oral prednisone. Mean DAS28-CRP was significantly decreased from 3.55 at baseline to 2.32 at week 24. Multivariate logistic regression showed that no previous biologics history and lower DAS28-CRP score at baseline were independently associated with achievement of LDA at week 24. Overall retention rate of BAR treatment was 86.5% at week 24, estimated by Kaplan-Meier analysis. Discontinuation rate due to adverse events was 6.5% at week 24. Seven patients developed herpes zoster and all of which re-started BAR after treatment with antiviral agents. There was no significant decreasing in mean hemoglobin level and lymphocyte count. [Conclusions] BAR demonstrated reasonable effectiveness and acceptable safety profile in RA patients in the routine clinical practice.

W22-4

Long-term Safety (up to 7 years [yrs]) of Baricitinib (Bari) in Patients (pts) including Japanese (JP) with Moderate to Severe Active Rheumatoid Arthritis (RA): an Integrated Analysis

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Conflict of interest: None

[Objective] To evaluate long-term safety of Bari in pts with moderate to severe active RA including JP. [Methods] Incidence rates (IR per 100 patient-year [PY]) of adverse events (AEs) were calculated using data in the All Bari RA analysis set which included pts exposed to any Bari dose, and from completed phase 1-3 studies and an ongoing long-term extension study. [Results] 3770 pts (514 JP pts) were exposed to Bari for 10127 (JP: 1240) total PY (maximum exposure: 7 yrs) as of Feb 2018. Compared with previously reported (cut off Apr 2017), similar trend was observed in IRs of deaths (0.4), malignancies excluding non-melanoma skin cancer (0.8), major adverse cardiovascular events (0.5), serious infections (2.8), Herpes zoster (HZ) (3.3), lymphoma (0.1), GI perforation (0.04), tuberculosis (0.2), and pulmonary embolism (0.2) and deep vein thrombosis (0.3). In JP, IRs of AEs except for HZ were not notably different from those of overall. HZ (6.8) were more frequent than overall, but the HZ IR was similar to previously reported and stable with longer exposure. [Conclusions] With longer exposure (maximum exposure: 7 yrs), Bari had an acceptable safety profile in pts with active RA as described in the previous report. Conclusions in JP are same as overall.

W22-5

Safety of Baricitinib (Bari) in Patients with Rheumatoid Arthritis (RA): Interim Report from All-case Post Marketing Study in Clinical Use

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Conflict of interest: Yes

[Objectives] Evaluate Bari safety in RA patients (pt) in clinical use. [Methods] An all-case PMS of Bari, started in Sep 2017, collects safety and effectiveness for the first 24wk of treatment and continues to collect SAEs for 3yrs. We report pt baseline demographics and AEs for pt completing 24wk case report or discontinued before 24wk as of Jul 2019. [Results] Data from 1262pt were collected (females 82%). At dosing, mean age 64yr (median 66yr), ≥65yr 55%; mean RA duration 12yr (median 9yr), Bari dose regimen 4mg 62%, 2mg 25%, 4mg→2mg 5%, 2mg→4mg 4%, others 3%. Pre-use of bDMARDs 75%, tsDMARDs 23%; concomitant use of MTX 62%, corticosteroid 49%. 71% continued treatment for 24wk. AE 350pt (28%). 5pt died of adenocarcinoma, liver failure, aspiration pneumonia, bacterial pneumonia, pulmonary hypertension. SAE 63pt (5%): pneumonia (8), bacterial pneumonia (5), herpes zoster (3), interstitial lung disease (3), osteonecrosis (3). Major AESIs: herpes zoster (56), serious infections (21), low hemoglobin/anemia (15), liver dysfunction (39), high lipid/hyperlipidemia (10), MACE (15), interstitial pneumonia (6), malignancy (6), VTE (1). [Conclusion] No new safety concern has been indicated. Encourage guideline-compliant use of Bari, as SAEs including infections have been reported.

W22-6

Cardiovascular Safety in treatment with Baricitinib (Bari) for patients (pts) with Rheumatoid Arthritis (RA) (up to 7 Years)

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Conflict of interest: Yes

[Objective] This analysis provides CV safety in RA pts treated with Bari for up to 7 years. [Methods] Incidence rates (IR) per 100 patient-year (PY) of MACE, arterial thrombotic events (ATE), and deep vein thrombosis and/or pulmonary embolism (DVT/PE) were calculated using data which were pooled from 9 Phase 1-3 studies, including a long-term extension study (LTE), and analyzed in 3 sets: 1) Placebo (PBO)-controlled; 2) Bari 2- vs 4-mg, including LTE data (Extended 2 vs 4 mg); 3) All pts exposed to any Bari dose (All Bari RA). [Results] 3770 pts (514 Japanese [JP] pts) were exposed to Bari (10127 PY [JP: 1240 PY], maximum exposure: 7 yrs) as of Feb 2018. For IRs of MACE and ATE were low, both were comparable across treatments and analysis sets, and did not increase with prolonged exposure (MACE: 0.3 - 0.7, ATE: 0.4 - 0.6). For DVT/PE, 6 events were reported for BARI 4-mg but not PBO during the 24-week PBO-controlled period. IR of DVT/PE were comparable between Bari 2 and 4 mg within the Extended 2 vs 4 mg (2mg 0.6; 4mg 0.6). Results from All Bari RA, IRs didn't increase over time (IR 0.5). [Conclusions] MACE and ATE IRs were low and did not increase with prolonged exposure. For DVT/PE, IR were similar between Bari doses and in line with published rates (0.33 - 0.79) in RA in general.

W23-1

Subcutaneous Tocilizumab for Patients with Juvenile Idiopathic Arthritis: Single Center, Retrospective Survey

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Conflict of interest: None

[Objective] To investigate the efficacy and safety of subcutaneous TCZ (TCZsc) in juvenile idiopathic arthritis (JIA). [Methods] The subjects were 18 patients with JIA treated with TCZsc in a single center. Patient characteristics, clinical and laboratory findings, duration of using TCZsc and adverse events were retrospectively investigated. [Results] JIA classification was as follows: systemic type (sJIA) 6, polyarthritis (pJIA) 10 and oligoarthritis (oJIA) 2. The median age at initiation of TCZsc were 23.6, 19.8 and 28.3 years in sJIA, pJIA and oJIA, respectively. For 17 patients, TCZsc is the second biologics. The median duration of TCZsc were 10, 13 and 3.5 months in sJIA, pJIA and oJIA, respectively. In sJIA, all patients had continued TCZsc at the last visit. Two pJIA and 2 oJIA patients discontinued TCZsc due to arthritis flare 2, uveitis flare 1 and chronic urticaria 1. There were no significant differences regarding active joint counts, WBC, CRP and MMP-3 between at the initiation of TCZsc and the last visit. [Conclusions] Continuation rate of TCZsc was favorable, especially in sJIA. However, care should be taken for allergic reaction and flare of uveitis.

W23-2

Prevalence of Joint Disorders in Juvenile Idiopathic Arthritis Adult Transition cases

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Conflict of interest: None

[Objective] The purpose of this study is to investigate the disease type and joint disorders in JIA adult transition cases in our hospital. [Methods] Fifty JIA adult transition cases who have visited orthopedics department since 2008 were enrolled in this study. The average age was 29.6 years, and the average disease duration was 22.9 years. Survey items included JIA disease type classification, therapeutic drugs, remission achievement rate, Steinbrocker classification, and history of orthopedic surgery. [Results] As the disease type classification, the most common type was polyarthritis type (52%) followed by systemic (28%) and monoarthritis (16%). As therapeutic agents, the usage rate of biological therapy was 60% and the usage rate of MTX was 44%. Only 4 patients were able to achieve remission during the course, and the overall remission rate was 8%. The proportion of patients classified as stage III or IV as Steinbrocker classification was 43%, 40%, and 50% for systemic type, polyarthritic type, and small arthritic type, respectively. Six cases (12%) underwent orthopedic surgery in their early age. [Conclusions] Since most of our JIA cases have joint disorders after transition to adult, certain JIA cases may require earlier orthopedic intervention and continueous orthopaedic follow-up.

W23-3

Tacrolimus as an alternative treatment of methotrexate for oligoarticular and polyarticular juvenile idiopathic arthritis

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Conflict of interest: None

[Objective] Methotrexate (MTX) is the first-line disease modifying anti-rheumatic drug for oligoarticular and polyarticular juvenile idiopathic arthritis (JIA). However, some patients show the resistance to MTX. Furthermore, some patients show intolerance to MTX due to gastrointestinal symptoms. In this study, we investigated the effect of tacrolimus (Tac) as an alternative treatment of MTX for JIA. [Methods] Eight patients with JIA including 6 patients with the resistance to MTX and 2 patients with MTX intolerance due to nausea were included. We retrospectively examined clinical manifestations of these patients and evaluated the efficacy and adverse events of Tac. [Results] In 6 patients with the resistance to MTX, 3 achieved remission, and the other 3 patients showed low disease activity after adding Tac or switching MTX to Tac. In 2 patients with MTX intolerance, one achieved remission after switching MTX to Tac. Furthermore, this patient achieved medication off remission 2 years later. There were no significant adverse events in these patients. [Conclusions] Tac might be an effective alternative treatment of MTX for JIA in cases with resistance and intolerance to MTX. Further larger studies are necessary to define the true value of Tac as an alternative of MTX for JIA.

W23-4

Evaluation of efficacy of canakinumab against refractory systemic juvenile idiopathic arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy of canakinumab (CAN) against refractory systemic juvenile idiopathic arthritis (sJIA). [Methods] This is a retrospective cohort study of 20 patients with refractory sJIA. Patients were divided into systemic inflammation group (n=4) and systemic-onset arthritis group (n=16). Furthermore, systemic-onset arthritis type were categorized into active arthritis group (n=3) and inactive arthritis group (n=13) according to the clinical findings 12 months (mo) after CAN therapy. [Results] All patients successfully continued CAN at 12mo and their dose of prednisolone (PSL) was decreased. In comparison between active and inactive arthritis group, there was no difference regarding age of initiation of CAN, sex, disease duration, but the PSL dose at CAN initiation was more in inactive arthritis group (0.13 vs 0.34 mg/kg/d, p=0.022). At 12mo, Pt-VAS and PSL dose was significantly higher in active arthritis group, but there was no difference in CRP, ESR, IL-6 and IL-18 at 6 and 12mo. In inactive arthritis group, median PSL dose before and at 12mo was 0.13 vs 0.06 mg/kg/d (p=0.027), MMP-3 before and at 12mo was 194.2 vs 45.2 ng/dl (p=0.002). [Conclusions] CAN was effective against refractory sJIA. CAN allows the reduction of reduce PSL and controls disease activity.

W23-5

Clinical characteristics of chronic recurrent multifocal osteomyelitis in children

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Conflict of interest: None

[Objective] CRMO has chronic bone pain as the chief complain, and has difficulty in making a definitive diagnosis. We summarized the clinical course and characteristics of pediatric CRMO diagnosed at our hospital. [Methods] From 2008 to 2019, we extracted children under the age of 16 who were diagnosed with CRMO at our hospital. [Results] We diagnosed five cases (male: female = 2: 3) with CRMO. The median age of onset is 8 years, the median duration of disease umtil diagnosis was 1.5 years. All case have bone pain, 2 cases with palmoplantar pustulosis (SAPHO syndrome) and 1 case with Crohn's disease. Initial treatment used pamidronate in 4 cases and NSAIDs in 1 case. In the pamidronate group, pain disappeared within 3 days, but 3 patients relapsed. All patients used TNF inhibitors (Etanercept 3 patients and infliximab 1 patient). One patient in the NSAIDs group also used adalimumab without symptom improvement. [Conclusions] CRMO has a low degree of disease recognition and does not have a specific test, so it takes a long time to be diagnosed. Pamidronate and TNF inhibitors are effective for treatment, but the effects of pamidronate are temporary, and TNF inhibitors are considered useful for maintaining remission therapy.

W23-6

A Prospective cohort study on the short and long-term prognosis, including pregnancy outcomes, of patients with systemic lupus erythematosus in Japan (PLEASURE-J study): Interim report of childhood-onset patients

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Conflict of interest: None

[Objective & Methods] The Pleasure-J prospective cohort study was launched in Nov. 2017. The interim report of childhood-onset patients has been evaluated. [Results] Of a total of the 88 enrolled individuals in the two years, 15 are childhood-onset before the 18th birthday. Their median age at diagnosis and SLEDAI-2K were 15 and 5, respectively. Of the 12 diagnostic criteria for pediatric SLE established by Japan Ministry of Health, Labor and Welfare in 1986, hematologic disorder immunological disorder, positive anti-nuclear antibody, and hypocomplementemia were most frequently met (9 cases). Renal disorder defined by proteinuria and cellular urinary casts were positive in only 4 patients, however renal biopsy, applied to 8, revealed findings consistent with lupus nephritis in all the 8 patients. Methylprednisolone pulse therapy was used for 9 cases and the mean maintenance dose of prednisolone was 40 mg/day. Regarding immunosuppressants, hydroxychloroquine, mycophenolate mofetil, cyclophosphamide was applied to 11, 8, and 3 children, respectively. [Conclusions] The unprecedented long term prospective cohort study for childhood-onset lupus beyond transition has just started but is expected to contribute to pediatric and transitional care and research in rheumatology.

W24-1

Clinical features of patients with Behcet's disease complicated with arthritis

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Conflict of interest: None

[Objective & Methods] We compared the clinical features in patients with Behcet's disease (BD), diagnosed according to the revised diagnostic criteria proposed by the BD Research Committee of Japan of the MHLW, complicated with arthritis (n=91) or without arthritis (n=119). [Results] 83.5% were incomplete type. Uveitis and recurrent aphthae were significantly less and nodular erythema was frequent in patients with arthritis (HLA-B51: 41.7, A26: 9.6, RF: 15.9 and ACPA: 1.8%). 4.4% were diagnosed complicated with RA. Mean TJC was 4.4 and SJC was 1.9 (knee 44, ankle 30.6, wrist 28, elbow 24, shoulder 22.4, MPJ 16, PIPJ 14, DIPJ 2%). Bone erosions in X-ray were observed in 3 of 4 patients diagnosed RA. Colchicine (82.4%), NSAIDs (39.6%), MTX (53.8%), PSL (25.3%; mean dose 10mg/day), IFX (25.3%) and ADA (11%) were administrated. In 31 patients followed over a year, TJC (3.7→1.1) and SJC (2.2→0.2) were notably decreased. Moreover, SJC was tend to be more decreased in patients treated with biologics compared to those treated with others. [Conclusions] Frequency of mucocutaneous lesions in patients with arthritis differ from those of without arthritis. Not only large-joint but small-joint arthritis was relatively frequent, and they were treated with Colchicine, MTX and anti-TNF Ab rather than PSL.

W24-2

Sustained disease activity and underestimation by clinicians in patients with Behçet's disease

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Conflict of interest: None

[Objective] The Behçet's Disease Current Activity Form (BDCAF) is one of the disease activity measures of Behçet's disease (BD) frequently in clinical trials, but its use in Japanese patients has not been established. This study aimed to survey the disease activity by BDCAF in Japan. [Methods] A cross-sectional study of BD patients was conducted from February to September 2019 at Yokohama City University Hospital. BDCAF and patients' and clinicians' overall disease perceptions by face scale (FS) were assessed. BDCAF was scored out of 12 based on symptoms present the previous 28 days. Clinical data were compared between groups with and without BD symptoms along with BDCAF and FS. [Results] A total of 137 patients were evaluated. The median of BDCAF was 2 (interquartile range 1-4). Active oral ulcers and arthralgia were found in 56.9% and 49.6% of the patients, respectively. Patients' FS was significantly higher (indicating worse global assessment) than those evaluated by clinicians ($p<0.05$). The rates of patients having mucocutaneous and joint symptoms were significantly higher in patients with active oral ulcers ($p<0.05$). [Conclusions] Our data suggest that active BD symptoms are remaining in large proportions of the patients, but clinicians are underestimating their disease activity.

W24-3

Identification of physical and psychosocial problems in patients with Behçet's disease and fatigue

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Conflict of interest: None

[Objective] This study aimed to identify physical and psychosocial problems in patients with Behçet's disease (BD) and fatigue by developing a checklist base on the International Classification of Functioning, Disability and Health (ICF). [Methods] Thirty patients with BD were interviewed using the original ICF Checklist (128 categories), from which they selected 79 categories related to physical and psychosocial aspects of BD. Moreover, 13 categories were added based on experts' discussions. Another 100 patients were interviewed using these 92 categories. Odds ratios (OR) for the presence of problems were compared between patients with BD, with and without fatigue. [Results] Multivariate logistic regression models revealed that patients with BD and fatigue had more difficulties with instrumental activities of daily living (IADL), namely, needlework (OR, 2.4), eating (2.4), domestic duties (2.7), and neighborhood relationships (2.9), compared to those without fatigue. [Conclusions] This study demonstrated

that patients with BD who experience fatigue face not only physical symptoms caused by BD, but also difficulties with IADL. These results suggest that providing support for IADL as well as physical aspects of the disease is important for patients with BD who experience fatigue.

W24-4

Identification of a Distinct Intestinal Behçet's Disease Cluster in Japan: A Nationwide Retrospective Observational Study

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Conflict of interest: None

[Objective] Behçet's disease (BD) patients with poor prognoses must be identified to receive individualized care. This study aimed to identify a subgroup of BD patients with distinct clinical manifestations. [Methods] A total of 707 patients registered to the Yokohama City University (YCU) regional BD registry, and 7,399 BD patients to the Japanese MHLW database were included. Hierarchical cluster analysis of clinical phenotype was independently performed on both populations. [Results] YCU registry identified four clusters including a unique GI variant, which has been recently increasing and required potent immunosuppressive therapy and frequent hospitalization despite of a low ISG criteria fulfillment. The likelihood of developing GI involvement during the follow-up was clearly stratified by numbers of the following 3 factors at the entry; arthritis, absence of ocular disease, and negative HLA-B51. Similar findings were reproduced in the MHLW registry. [Conclusions] Clustering analysis shows that a serious form of GI cluster, which requires intensive care in absence of ocular lesions and HLA-B51, is increasing in Japanese BD patients. We propose a simple instrument to predict the GI cluster based on extra intestinal findings.

W24-5

Three Cases of Intestinal Behçet's Disease like Symptoms Associated with Trisomy 8-Positive Myelodysplastic Syndrome (MDS)

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Conflict of interest: None

[Introduction] Recently, cases of trisomy 8-positive MDS associated with Behçet's disease have been reported, especially from Japan. [Case 1] A 72-year-old male was hospitalized due to arthralgia and fever. CT and colonoscopy showed ileocecal ulcer similar to intestinal Behçet's disease. Since thrombocytopenia persisted, bone marrow aspiration (BMA) was performed. He was diagnosed as trisomy 8-positive MDS. Treatment with steroids and adalimumab was insufficient, and he improved after switching to infliximab. [Case 2] A 75-year-old male was hospitalized due to fever. BMA was performed due to thrombocytopenia and she was diagnosed as was trisomy 8-positive MDS. CT and colonoscopy showed ileocecal ulcer. Mesalazine, azathioprine and adalimumab were effective. [Case 3] A 76-year-old woman was hospitalized due to stomatitis, weight loss and shortness of breath. BMA was performed due to anemia and she was diagnosed as trisomy 8-positive MDS. Although azacitidine was started, esophageal ulcer and ileocecal ulcer developed. Steroid and adalimumab were administered, and the symptoms improved. [Conclusion] All 3 patients responded well to biologics or immunosuppressants. In elderly patients with intestinal Behçet's disease-like ulcer, complication of MDS should be taken into account.

W25-1

How best to perform musculoskeletal ultrasonography by a sonographer in clinical practice

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Conflict of interest: None

[Objective] We examined whether US examination for RA by our sonographers could meet the physicians' needs. [Methods] A sonographer is in charge of 30 minutes of an inspection, examining hand and forefoot routine, and additional requested sites if necessary. The lesions with GS≧2 and/or PD≧1 were considered active findings. [Results] Among 158 cases who received US examination, 83 were established RA and 68 were early RA suspects. Forty-six (55%) of established RA had active wrist lesions, whereas 12 had active lesions in only the non-wrist routine joints. Additional tests were performed in 64 cases with 148 joints, and steroid was injected locally in 3 of 6 cases where the active lesion was a sole additional site. US helped determine the management of 76 RA cases. Among 32 newly diagnosed RA cases, 28 were diagnosed with reference to US findings. Routine active findings were detected in 24 cases at the wrist, and 2 cases at only the joints except for wrists. Three had active lesions in only additional joints, and other 3 were confirmed as having polyarthritis by additional tests. [Conclusions] US for RA detects active lesions of the wrist with the highest rate. By adding other routines and regions of interest to the test, comprehensive examination that meets physician's needs is possible.

W25-2

Ultrasound assessment and findings of knee in polymyalgia rheumatica

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Conflict of interest: None

[Objective] This study aimed to assess the musculoskeletal ultrasound (MSUS) findings of knee in PMR patient. [Methods] We recruited 47 patients who were diagnosed PMR in our hospital from June 2016 to September 2019. We investigated longitudinally their clinical, laboratory and MSUS data including shoulder and knee before and after treatment. Presence or absence of articular synovitis, tenosynovitis and bursitis were evaluated by GS and PD. Tendonitis were evaluated by presence or absence of PD alone. [Results] Mean age at onset was 72 years. Female was 60%. Median of CRP and MMP-3 was 5.5 mg / dL and 152.5 ng / mL. Median of patient VAS and mHAQ was 70 and 1.5. The MSUS findings were identified GS 88%/PD 64% in long head of biceps tendon sheath, GS 21%/PD 13% in subdeltoid bursa, GS 26%/PD 17% in subacromial bursa, GS 0%/PD 0% in scapulohumeral joint, PD 52% in supraspinatus tendon, PD 51% in subscapular tendon, GS 27%/PD 25% in suprapatellar bursa, PD 35% in medial collateral ligament, PD 20% in lateral collateral ligament and GS 88%/PD 77% in popliteal tendon. After treatment, these MSUS findings improved. [Conclusions] We identified MSUS findings of knee in PMR patient. Especially, US findings of popliteus tendon may be useful to diagnose and evaluate activity in PMR.

W25-3

Power Doppler Ultrasonography findings in Systemic Lupus Erythematosus

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Conflict of interest: None

[Objective] Musculoskeletal symptoms are common in SLE. However, there are less evidence of Power Doppler ultrasonography (PDUS) findings in SLE. We investigated the PDUS findings in SLE with musculoskeletal symptoms. [Methods] A total 21 patients with SLE who were assessed by PDUS between January 2014 and September 2019 in our hospital were recruited. We evaluated the articular synovia, tendons and tendon sheaths, and entheses in finger and wrist joint, and the other symptomatic joint by PDUS as well as clinical findings. [Results] In SLE with musculoskeletal symptoms, the prevalence of articular synovitis, tenosynovitis and enthesitis in PDUS were 48% (n=10), 38% (n=8) and 43% (n=9), respectively. PDUS synovitis was mainly found at PIP, MCP and Wrist joints. PDUS tenosynovitis was mainly found at finger flexor tendons and wrist extensor tendons. PDUS enthesitis was mainly found at entheses of finger collateral ligament, quadriceps tendon and distal patellar ligament. There were 6 cases (29%) who had musculoskeletal symptoms without any PDUS findings. [Conclusions] This study indicated that various PDUS findings such as synovitis, tenosynovitis and enthesitis were found in SLE patients with musculoskeletal symptoms.

W25-4

Clinical significance of finger extensor paratenonitis detected by musculoskeletal ultrasound

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Conflict of interest: None

[Objective] To determine the clinical significance of finger extensor paratenonitis (PTN) detected by ultrasound (US). [Methods] We reviewed the reports of the US examination underwent in our division since April 2015. Cases with finger extensor PTN at the level of the dorsal the MCPJ were determined. The severity of articular synovitis in the perilesional MCPJ were subjectively scored for grey-scale and power Doppler on a four-step scale (0-3). In RA patients, US5 scores (the 'hand-limited version' of the German US7) were determined for the involved hands. [Results] 32 cases were analyzed. Diseases/disorders were RA in 22 cases and non-RA in 10 cases. PTN were distributed to right (R-) MCP2 in 10, R-MCP3 in 10, L-MCP2 in 4, L-MCP3 in 4, L-MCP4 in 4, R-MCP1 in 3, R-MCP4 in 3, and L-MCP1 in 2. Articular synovitis in the perilesional MCPJ were found more frequent in the cases of MCP2 (71%) than in the cases of MCP3 (21%). Among 22 RA patients, US5 scores were significantly higher in those with moderate to severe perilesional MCP synovitis than in those without it. [Conclusions] US can be useful in determining the presence or absence of perilesional active articular synovitis in the cases of finger extensor PTN.

W25-5

Characteristics of the patients with peritenon extensor tendon inflammation of MCP joint detected by ultrasonography

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Conflict of interest: None

[Objective] Peritenon extensor tendon inflammation (PTI) of MCP Joint (MCPJ) are demonstrating to be a specific feature of Psoriatic arthritis (PsA). However, it can be seen other rheumatic patients. The aim of this study is to clarify the characteristics of newly diagnosed PTI positive arthritis patients. [Methods] We enrolled the newly diagnosed patients of our university in October 2018 who had MCPJ swelling and all patients were examined joint ultrasound (US). We divided the patients into two groups by positivity of PTI detected by US. Clinical diagnosis characteristics and laboratory data were compared. [Results] A total of 345 patients, 268 RA, 50 connective tissue disease (CTD) including SLE, Sjogren syndrome and 27 spondyloarthritis (SpA) were recruited. PTI of MCPJ were observed 86 patients and the mean age was 53.8 years old and 70% were female. The presence of PTI were significantly seen in SpA patients (81.5%) and CTD patients (82.0%) than that in RA (8.6%). Over 70% of PTI positive patients had other enthesitis. The positivity of anti SS-A antibody was significantly high, although that of anti-CCP antibody less than PTI negative patients. [Conclusions] We found that PTI on MCPJ is associated not only SpA but also other CTD arthropathy including SLE and Sjogren syndrome.

W25-6

Early improvement of the power Doppler signal can predict to continue the biological DMARDs after 1 year

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA), biologics treatment is one of the effective treatment options. On the other hand, the effects of biologics cannot be obtained satisfactorily in all patients, and there are some cases in which treatment is interrupted due to ineffective or adverse events. In this study, we investigated whether continuation of biologics treatment can be predicted by ultrasonographic findings in the early phase. [Methods] Fifty-four RA patients who started the first biologics from September 2016 to December 2018 were included. 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, 42 cases were able to continue treatment until one year later, and the continuation rate was 80.8%. Multiple regression analysis was performed with treatment continuation as the dependent variable and improvement of CRP, MMP-3, DAS28-CRP, grayscale score and power Doppler score in 4 weeks as explanatory variables. Only improvement of power Doppler score was extracted as a significant predictor ($p = 0.045$). [Conclusions] The early improvement of power Doppler signal in 4 weeks could be a predictive factor for the continuation of 1 year biological treatment.

W26-1

The relationship between thickness of cortex in 3rd carpal bone at proximal one-third and bone mineral density of patient with rheumatoid arthritis

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Conflict of interest: None

[Objective] The relationship between thickness of cortex in 3rd carpal bone at proximal one-third (C3) and bone mineral density of patient with rheumatoid arthritis (RA) was investigated. [Methods] As a fundamental rule, right hand was measured. Roentgenogram of hands taken for measurement of Sharp/van der Heijde Score (SHS) was used to measure. Width of carpal bone (W) and thickness of cortex (TC) at C3 were measured, and TC per W (TC/W) was calculated. Correlation between TC/W and patient's clinical parameters including bone mineral density in lumbar spine (BMD_LS) and in femoral neck (BMD_FN) was evaluated statistically with multivariate linear regression analysis, and the relationship between TC/W and T-score less than -2.5 (OP_C) at each bone was evaluated with Receiver Operation Characteristics Method (ROC), [Results] TC/W calculated from 300 RA patients demonstrated significant correlated with age, SHS, and BMD in both bones. With ROC, cut-off index was 0.2 for

OP_C, of which sensitivity was 67.9% and 76.1%, and specificity was 83.0% and 81.6% for LS and FN, and odds ratio was 4.19 and 4.90, respectively. [Conclusions] TC/W correlates with BMD, with that suggested to work as a screening tool for judgment of osteoporosis.

W26-2

Development of detecting bone erosion using AI

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Conflict of interest: Yes

[Objective] We intended to establish a technology for detecting temporal changes in bone erosion in patients with rheumatoid arthritis (RA) using artificial intelligence (AI). [Methods] X-ray images of RA patients registered in KURAMA Cohort were used. We used Deep Learning to identify bone erosion. Two hand images of the same patient with one year or more X-ray interval are aligned using contour lines and image features. The contours of both finger joints were compared, and bone erosions were identified as differential. The consistency with the existing evaluation method mTSS (modified Total Sharp Score) was examined. [Results] Images of 13 RA patients were analyzed. As the result comparison between scoring by a rheumatologist and erosion progression detected by our AI, AI judged two out of four that the rheumatologist scored. Also, AI detected the progression of erosion that is not enough to score by mTSS. This is exciting for future study. However, there are some awaiting solutions such as misjudgment caused by rotation of X-ray images. [Conclusions] Differences in detection of bone erosion progression with AI from existing evaluation methods were proved. We will continue to develop methods for detecting bone erosion of wrist joints and feet, and detecting Joint Space Narrowing.

W26-3

AI-based automated same cross section detection system for ultrasound imaging in rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the accuracy of AI based automated same cross section detection system for ultrasound imaging in rheumatoid arthritis. [Methods] Ultrasound images were acquired from the wrist of healthy persons. These images were classified into three types of radial, medial and ulnar images. To obtain a large amount of teacher images from few cases, teacher images were separated to single images from moving images. AlexNet and VGG-based transfer learning scheme was performed to train the network. Using the vector output from the convolutional layer of the network, the closest distance between the images were calculated. Using this system, we calculated the closest image, and evaluated visually. The software was written in Matlab (MathWorks, MA, USA) language. [Results] The correct answer rate of AlexNet and VGG were 79±12%, 85±11%. [Conclusions] Using AI, we can detect the same cross-section of ultrasound images. Although accuracy is a problem, there is a possibility that accuracy can be increased by increasing the amount of data.

W26-4

Evaluation of anti-CCP antibody and carpal bone erosion confirmed by 2D and 3D images of HR-pQCT

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Conflict of interest: None

[Objective] In this study, we investigated the relationship between bone erosion and ACPA using HR-pQCT. [Methods] Subjects were 129 DMARD naïve arthralgia cases without bone erosion on plane X-ray, 82 caes were ACPA negative group (NG), 47 cases were ACPA positive group (PG). Wrist joints were imaged with HR-pQCT. Rupture of the cortical bone in contact with the trabecular bone where the trabecular bone disappeared was confirmed by coronal and axial sections and defined as bone erosion. [Results] The percentage of cases with bone erosion was significantly higher in PG (30 cases, 64%) than in NG (33 cases, 40%) ($p = 0.011$). In PG, 28 cases were diagnosed with RA, and 10 out of 18 cases diagnosed with RA at the first visit had bone erosion, of which 6 cases had synovitis in US. In NG, the number of bone erosions showed a positive correlation ($r = 0.325$) with age, and was especially observed at 50 years and older. Under the age of 50 years, bone erosion was observed in 21 of 30 cases in PG, and the rate was significantly higher than in 4 of 22 cases in NG ($p = 0.0003$). In 13 of19 cases who did not diagnose RA at the first visit, bone erosion was observed. [Conclusions] In ACPA positive cases, it was suggested that bone erosion observed by HR-pQCT already existed before the onset of RA.

W26-5

The longitudinal analysis of joint structure of rheumatoid arthritis by HR-pQCT

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Conflict of interest: None

[Objective] To investigate bone erosion, joint space and bone micro-architecture detected by HR-pQCT in rheumatoid arthritis (RA) during 12 months after initiation of new treatment. [Methods] This study included 10 RA patient. HR-pQCT imaging analyses quantified bone erosion and joint space in 2,3 metacarpophalangeal joints, bone micro-architecture in 2,3 Metacarpal Head. Synovitis were assessed by ultrasonography (US). [Results] 8 patients were treated with biologics and 2 patients were treated with MTX. The mean DAS28-ESR decreased from 4.36 to 2.48 at 24 weeks. 11 erosions in 8 joints were detected by HR-pQCT. Erosion volume of 9 erosions were decreased during 12 months (mean Δerosion volume was -1.31 mm^3). Whereas, new erosion was appeared in 3 patients. DAS-ESR was improved in 2 patients and cumulative US-PD score (0,6,12 months) were 0,0,1, respectively. Joint space narrowing did not progress (Δjoint space volume was 0.119 mm^3). Regarding microarchitectures, the trabecular volumetric densities and trabecular number were increased. [Conclusions] The repair of bone erosion during treatment were detected by HR-pQCT. There were progression of bone erosion even in the patients whose disease activity was improved or without US-proven active synovitis.

W26-6

Usefulness of alignment evaluation using ultrasound for forefoot deformity in patients with rheumatoid arthritis: including comparison with hallux valgus deformity patients

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patients have a high incidence of forfoot deformities. However, it is difficult to evaluate the alignment change of the metatarsal head that affects the formation of the callosities that causes pain in the forefoot. In this study, we examined whether metatarsal head alignment can be evaluated by ultrasound assessment. [Methods] Twenty-one patients with RA who underwent forefoot surgery from January 2017 to September 2019 and 33 patients with hallux valgus (HV) were performed ultrasound examination on the plantar side with or without manual max pressure. [Results] In patients with RA, the third metatarsal head was closer to the skin than the fourth due to compression. This abnormality was not observed in patients with HV patients. The patients in which the distance between the skin and metatarsal heads of the second and third metatarsal heads less than 5 mm were not observed in patients with HV alone, but were high in patients with RA. [Conclusions] There is a possibility that the forefoot alignment change can be evaluated by ultrasound from the plantar side with manual max pressure. This methods may be useful to identify forefoot deformity and early therapeutic intervention such as insole can be performed for prevention the surgery.

W27-1

Serum semaphorin3A elevated in patients with rheumatoid arthritis who complained of continuous joints pain despite low inflammation

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Conflict of interest: Yes

[Objective] To detect which humoral factors were associated with sustained joint pain under low inflammatory condition in patients with rheumatoid arthritis (RA). [Methods] Patients with RA that had never been treated with biologics were selected. Patients were divided into three groups; remission group (Pr) [PtVAS<20mm, CRP<1.0mg/dL], inflammatory group (Pi) [PtVAS≧20, CRP≧1.0mg/dl], and low-inflammatory pain group (Pp) [PtVAS≧20, CRP<1.0mg/dL]. Serum IL-1b, 2, 4, 6, 8, 17A, IFN-g, TNF-a, GM-CSF, NGF, CXCL13, serotonin, semaphorin (Sema) 3A, and Sema4C were measured. [Results] Total of 39 patients were enrolled in this study (group Pr, Pi, and Pp contained 7, 16, 16, respectively). GM-CSF increased in group Pi and Pp and Sema3A increased in group Pp compared with Pr (Pr 9.05, Pi 9.93, Pp 12.03pg/mL, Pr vs Pi p=0.268, Pr vs Pp p=0.039). Sema3A was moderately positively correlated with PtVAS in non-inflammatory patients (Pr+Pp) (r=0.439, p=0.036), but not CRP. The proportion of patients whose Sema3A level was higher than maximum level in group Pr was higher in Pp (56.25%) than Pi (18.75%) (p=0.028). Interestingly, Sema3A was also correlated with serotonin (r=0.444, p=0.035). [Conclusions] Our results indicates that Sema3A may be associated with the low-inflammatory sustaining joint pain.

W27-2

The relationship between adipocytokine and inflammatory markers/disease activity in the patients with rheumatoid arthritis form five-year data of TOMORROW study

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Conflict of interest: None

[Objective] The aim of this study was to investigate the relationship between adipocytokine and inflammatory markers/disease activity in RA patients by using 5-year data of TOMORROW study. [Methods] We compared leptin (Lep)/adiponectin (Adipo) concentrations in 183 RA patients and190 controlsfrom 2010 (BL) to 2015 (5Y) and investigate the relationship between Lep/Adipo and CRP/DAS in patients. [Results] Lep/Adipo of patients were significantly higher than them of controls at BL/5Y, and significantly increased from BL to 5Y. In patients, Adipo was significantly negatively related with CRP at BL/5Y (BL: R=-0.174, 5Y: R=-0.240; p<0.05), however, not with DAS. Lep was significantly positively related with CRP at 5Y (R=0.207; p<0.05), however, not with CRP at BL and DAS at BL/5Y. Adipo at BL/5Y were significantly higher in patients with biologics (Bio) at BL compared to patients without Bio, but there were no significant relationships between Lep of both groups. [Conclusions] Adipo of RA patients with continuous treatments for 5 years was increased, and moreover in patients with Bio, which should be stronger agents than csDMARDs, Adipo was higher at BL/5Y. Adipo was significantly negatively related with CRP at BL/5Y, thus it can be considered that Adipo may have anti-inflammatory effects.

W27-3

Bone density and body composition in patients with rheumatoid arthritis, and its involvement of serum myokines

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Conflict of interest: None

[Objective] To investigate the bone density and body composition of rheumatoid arthritis (RA) patients, and its involvement of myokines. [Methods] Eighty-three RA patients who visited Niigata University Hospital from April to June 2017, were participated in this study. We measured the right femoral neck bone density using the dual energy X-ray absorption method (DEXA) and the body composition using the bioimpedance (BIA) method. Serum myostatin, IL-6, and FGF-2 levels were measured using ELISA. Patients' laboratory findings and disease activities were also measured, and the correlations between bone mineral density and these factors were analyzed. [Results] In Spearman rank correlation analysis, the right femoral neck bone density had a negative correlation with age, body fat percentage, fat mass index, and number of swollen joints, and a positive correlation with skeletal muscle mass, fat-free mass, and serum myostatin level. In stepwise multiple regression analysis, fat-free mass was selected as a significant positive independent factor for bone density in the right femoral neck, and age and number of swollen joints were selected as negative independent factors. [Conclusions] Our results indicated the usefulness of serum myostatin level as a predictor of sarcopenia and flail in RA.

W27-4

Analysis of lipid metabolome in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Although many proteins associated with inflammation have been elucidated in rheumatoid arthritis (RA), few studies have reported endogenous metabolites associated with RA. Recently, several lipid metabolites have been reported to have inflammatory/anti-inflammatory function. To explore lipid metabolites associated with RA, we characterized plasma lipid profiles using lipidomics approach. [Methods] Blood samples from 21 healthy controls and 373 RA patients were collected and untargeted metabolomics for 336 lipid molecules was conducted by liquid chromatography-mass spectrometry. Patients were classified into low disease activity (LDA) group (DAS28-ESR of less than 2.6) and high disease activity (HDA) group (DAS28-ESR of more than 2.6). [Results] Metabolites of belong to groups of acylcarnitine (Car), free fatty acid (FFA) or lysophosphatidylcholine (LPC) significantly increased in RA patients compared with controls. Some molecules exhibited significant difference between the LDA group and HDA group. [Conclusions] We found increases in lipid molecules of Car, FA as well as LPC in RA patients. We are planning to examine further correlational analyses between each fatty acid and clinical informations to explore their involvement in the pathology of RA.

W27-5

Peptidyl-arginine deiminases in peripheral blood and peripheral blood neutrophils and their associations with single nucleotide variants in patients with rheumatoid arthritis

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Conflict of interest: Yes

Objective: Single nucleotide variants (SNVs) of peptidyl-arginine deiminase 2 (PADI2) and PADI4 genes are associated with RA susceptibility. We aimed to elucidate expressions of PADIs in patients with RA and their associations with SNV. **Method:** We enrolled 23 patients with RA and 20 healthy controls (HC). PADI2 and PADI4 were measured by using ELISA. SNVs were determined by using TaqMan SNP Genotyping Assays. Quantitative real-time RT-PCR was used to measure mRNA levels. **Results:** Serum concentration of PADI2 in patients with RA were significantly higher (p=0.028) than HC while that of PADI 4 were not different. Fresh neutrophils from patients with RA expressed significantly larger amounts of PADI2 (p = 0.001) and PADI4 (P = 0.003) mRNA than those of HC. Neutrophils from RA and HC spontaneously released PADI2 and PADI4. Linear regression analyses revealed that RA (versus healthy controls) (p = 0.001) and numbers of the risk allele of PADI2 rs761426 (p = 0.04) were significantly associated with the levels of PADI2 mRNA in neutrophils. RA (versus healthy controls) was also associated with the levels of PADI4 mRNA in neutrophils (p = 0.002), but not numbers of the risk allele of PADI4 rs11203367. **Conclusions:** Different roles of PADIs in patients with RA were suggested.

W27-6

Mass cytometry identifies enhanced Histone H3 citrullination and TNFa production by CD14 monocytes in subjects At-Risk for future development of rheumatoid arthritis

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Conflict of interest: None

[Objective] We explored Histone H3 (H3) citrullination and cytokine/chemokine signatures in peripheral blood immune cells following *ex vivo* Toll-Like receptor stimulation. [Methods] 13 ACPA (+) subjects At-Risk of future development of rheumatoid arthritis (RA), 14 early RA patients, and 13 controls were studied. Freshly drawn whole blood was incubated with or without LPS and R848 (TLR7/8 agonist) in the presence of Golgi stop for 6 hours and then fixed. Cells were stained with 39 metal conjugated antibodies, and mass cytometry analysis was performed. Separately, $CD14^{high}$ monocytes were stimulated with R848 after pretreatment with GSK484 (PAD4 inhibitor), and $CD14^{high}$ monocytes were cultured on coverslips with R848 to performe immunofluorescence (IF) staining. [Results] CITRUS analysis identified significant expansion of $CD14^{high}$ monocyte cluster with H3 citrullination and TNFα, IL-12, and MIP1β production following LPS and R848 stimulation in At-Risk subjects ($p<0.01$). GSK484 significantly suppressed H3 citrullination. IF revealed monocyte extracellular trap (MET) formation. [Conclusions] $CD14^{high}$ monocytes in At-Risk subjects demonstrate increased cit-H3 expressing MET formation with aberrant cytokine production, a process which may play a role in the development of RA.

W28-1

Potent induction of CXCL10 by citrullinated fibrinogen (cFb) in rheumatoid synovial cells (RSC)

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Conflict of interest: None

[Purpose] Citrullinated fibrinogen (cFb) is well known as a corresponding antigen of ACPA, which is an autoantibody of rheumatoid arthritis (RA). Therefore, the effect of cFb on inflammatory cytokines and chemokines in RA synovial cells was investigated. [Method] The synovium obtained at the surgery for RA patients was treated with collagenase, and the dish-adherent cells were used as rheumatoid synovial cells (RSC). RSCs were cultured with cFb, and the gene expressions of various cytokines was examined by qPCR. In addition, cytokine levels in the culture supernatant were measured by ELISA. [Results] First, among 15 cytokines/chemokines, CXCL10 expression was remarkably enhanced at mRNA levels. This effect was also observed in a concentration-dependent manner at the protein level. Among IFN, IFN-β was significantly induced by cFb. In addition, a JAK-inhibitor, which suppresses the downstream signal of IFN, strongly suppressed the induction of CXCL10 by cFb. [Conclusion] cFb strongly induced CXCL10 in RSC possibly via IFN-β. CXCL10 is capable of migrating T cells and monocytes to inflammatory sites, and involved in osteoclastogenesis. Therefore, cFb and CXCL10 may be deeply associated with rheumatoid inflammatory process.

W28-2

Cooperative regulation in cell cycle gene expression by SPACIA1 and TNF-alpha in rheumatoid arthritis-synovial fibroblasts

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Conflict of interest: None

[Objective] In previous study, we identified SPACIA1 as a factor related to proliferation in rheumatoid arthritis (RA) synovial fibroblasts (RASFs), and reported that SPACIA1 associated with CDK6 mRNA stability. It is known that CDK4 and CDK6 generally compensates their functions each other. TNFα upregulates both CDK4 and CDK6 gene expression in a certain cancer cell line. On the other, SPACIA1 associated with CDK6 expression, but not CDK4, therefore we confirmed the G1 phase cell cycle regulation by TNFα in RASFs. [Methods] Gene expression analysis on the G1 phase factors was performed using RASFs stimulated with TNFα, IL-1β or IL-6. TNFα signaling pathways on CDK6 gene expression were observed using their inhibitors. [Results] CDK6, but not CDK4, mRNA level was significantly increased by TNFα or IL-1β stimulation in RASFs. TNFα signaling upregulated CDK6 gene expression through NF-κB and AP-1 via MEK pathway in RASFs. [Conclusions] From the results so far, we concluded that TNFα activates CDK6 transcription and SPACIA1 could stabilized CDK6 mRNA in RASFs. Unlike in a cancer cell line above, the both of SPACIA1 and TNFα didn't affect CDK4 expression. The CDK4/6 compensation maybe not function in RASFs.

W28-3

Death receptor 3 regulates the gene expression of various key molecules in rheumatoid synovial fibroblasts

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Conflict of interest: None

[Objective] Death receptor 3 (DR3) is involved in the mechanism of cell proliferation and apoptosis through NF-kB signaling. Suppression of DR3 in rheumatoid synovial fibroblasts (RA-FLS) is associated with hyperplasia of rheumatoid synovial tissue. In this study, we investigated the gene expression profiles regulated by DR3 in RA-FLS to reveal how DR3 is involved in the pathogenesis of RA. [Methods] RA-FLS were incubated with DR3-Fc for 12h. Gene expressions were detected by microarray assay. [Results] The most up-regulated 2 genes by DR3 were KIAA1109, and adhesion G protein-coupled receptor A3 (ADGRA3). KIAA1109 gene is strongly associated with RA in European descent populations. ADGRA3 is a member of G protein-coupled receptors which associate with the regulation of the cell adhesion and migration, and cell proliferation and apoptosis. The most down-regulated 2 genes by DR3 were RNA exonuclease 2 (REXO2), and family with sequence similarity 120A (FAM120A). REXO2 was identified as a target gene for inflammatory bowel disease-associated variants. FAM120A regulates activity of Src kinase to protect cells from oxidative stress-induced apoptosis. [Conclusions] DR3 regulates the expression of various genes in RA-FLS and may affect the pathogenesis of RA.

W28-4

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] We previously showed ADAM-15 was expressed in RA serum and synovial tissues (STs). VE-cadherin concern with cell adhesion and is shedded by ADAM-15. In this study, we investigate the relation between ADAM-15 and VE-cadherin. [Methods] To examine whether ADAM-15 and VE-cadherin was expressed by RA serum, enzyme linked immune sorbent assay (ELISA) were performed. To determine VE-cadherin expression on RA synovial tissues, immunohistochemistry was performed. To investigate correlation between ADAM-15 and VE-cadherin, Spearman's rank correlation coefficient test was performed. [Results] VE-cadherin in RA (n=23) was significantly elevated compared with NL (n=13) (RA 1301 ± 242 pg/ml, NL 274 ± 141 pg/ml, respectively, $p<0.05$). We found that VE-cadherin was expressed on RA synovial tissue. ADAM-15 and VE-cadherin was correlated ($rs=0.549$, $p<0.05$). [Conclusions] VE-cadherin is expressed on RA serum and STs. These data show ADAM-15 and VE-cadherin is correlated in RA.

W28-5

GRK5 (G protein-coupled receptor kinase 5) deletion suppresses the progression of inflammatory arthritis

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Conflict of interest: None

[Objective] The present study aimed to investigate the role of GRK5 in progression of arthritis. [Methods] Human OA, RA, and normal synovium were used for analysis of GRK5 expression in immunohistology. Collagen antibody-induced arthritis (CAIA) was induced in wild type (WT) and GRK5 knock out (KO) mice. We isolated fibroblast-like synoviocytes (FLS) from synovium of WT mice and GRK5 KO mice, cultured, and analysed the gene expression of various cytokines and chemokines after incubating with LPS. Human FLS were transfected with siGRK5, and then transfected with pNL3.2 (NlucP/NF-κB-RE/Hygro), and pGL-CMV (luc2/CMV/Neo) vectors. NF-κB luciferase assay was performed. [Results] In human synovium, GRK5 expressed in synovium despite of normal, OA, or RA. Especially at synovial lining layer, GRK5 expressed significantly stronger in RA than in normal. Following the induction of CAIA, the progression of arthritis was significantly suppressed in GRK5 KO mice both in terms of clinical score and histological analysis. After incubating FLS with LPS, gene expressions of various cytokines and chemokines were significantly suppressed in GRK5 KO mice. Transcription activity of NFκB were suppressed by GRK5 knockdown in human FLS. [Conclusions] GRK5 is deeply involved in pathogenesis of synovitis.

W28-6

Pathological significance of cell type-specific RANKL in the autoimmune arthritis

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA), RANKL expression is upregulated accompanied with inflammation, resulting in joint destruction. Although synovial fibroblasts rather than T cells relatively contribute to the joint destruction, but the precise evaluation using collagen-induced arthritis (CIA) sensitive DBA1/J background has not been done. In addition, the contribution of B cell-RANKL to the joint damage has been unclear. [Methods] Synovial fibroblast (Col6a1-Cre), B cell (Mb1-Cre), and T cell (Lck-Cre) RANKL cKO C57BL6 mice were generated and back crossed to collagen-induced arthritis (CIA) sensitive DBA1/J background. CIA of these mice was evaluated. [Results] All the Cre lines exhibited comparable arthritic score to the control mice. Joint destruction was inhibited in Col6a1-Cre cKO mice, whereas joint destruction in CIA Mb1-Cre or Lck-Cre cKO mice was comparable to the control mice. [Conclusions] RANKL derived from T cells, B cells or synovial fibroblasts was dispensable for the inflammation of autoimmune arthritis. B cell or T cell-RANKL was found to be dispensable, whereas synovial fibroblast-RANKL was indispensable for joint destruction. This study suggests importance of therapies targeting joint damage-oriented synovial fibroblasts in RA.

W29-1

Newly Diagnosed Lupus Nephritis in Elderly Predicts Good Renal Outcome: a Distinct Disease Subset from Young-onset Lupus Nephritis

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Conflict of interest: Yes

[Objective] The purpose of this study is to compare renal prognosis and clinical characteristics between elderly and young-onset LN. [Methods] We reviewed SLE patients with LN from 2000 to 2018 in our hospital. LN was defined as biopsy-proven LN or persistent proteinuria (more than 0.5 g/gCr or ≧3+ for more than 3 months). Patients were classified into two groups based on disease onset: young-onset LN (<50 years old) and elderly-onset LN (≧50 years old). Deterioration of renal function (more than 30% eGFR decline from baseline) and circulating regulatory T (Treg) cell counts were compared by fluorescence-activated cell sorting (FACS) analysis using anti-CD3, 4, 25, 127 antibodies. [Results] Forty-four patients with young-onset LN and 12 with elderly-onset LN were evaluated. Baseline eGFR was significantly lower in patients with elderly than young-onset LN. There was no significant difference in baseline SLEDAI, observational periods, treatment between them. Cumulative deterioration rate of renal function was significantly lower in the elderly than young-onset LN (p=0.026). A higher tendency of peripheral Treg counts by FACS analysis was observed in the elderly than young-onset LN. [Conclusions] This study suggests that elderly-onset LN may have better renal prognosis than young-onset LN.

W29-2

Impact of salt intake restriction, blood pressure control, and weight management on clinical outcomes for patients with lupus nephritis

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Conflict of interest: None

[Objective] To evaluated the impact of adjunctive care on clinical outcomes for patients with lupus nephritis (LN) who receive the identical immunosuppressive treatment. [Methods] We retrospectively examined 36 LN patients who received induction therapy with glucocorticoids, mizoribine, and tacrolimus according to our protocol. All patients received education including dietary guidance while staying hospital. [Results] (1) Achieving management goals for adjunct therapy in 12 and 24 months were as follows: BMI (<25) 94%, 85%, systolic blood pressure (<130 mmHg) 81%, 81%, HbA1c (<6.0%) 69%, 72%, LDL-C (<120 mg/dl) 83%, 81%, salt intake (<6 g/day) 63%, 48%. (2) Salt intake restriction at 6 months improved proteinuria. Blood pressure management at 12 months correlated with achieving complete remission (CR). Successful blood pressure control group both at 6 and 12 months showed a significantly higher CR rate at 24 months. (3) Strict body weight management (BMI<21) at 12 months represented successful management of blood pressure, HbA1c, and salt intake restriction. [Conclusions] Salt intake restriction and blood pressure management may enhance the improvement of induction phase LN. Monitoring body weight is useful as a daily evaluation index for visualizing adjunctive care.

W29-4

Evaluation of the correlation between renal pathology and clinical course of lupus nephritis

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Conflict of interest: None

[Objective] Lupus nephritis (LN) is one of important prognostic factors in systemic lupus erythematosus (SLE). Our goal is to assess the correlation between renal pathology and clinical course of LN. [Methods] 68 patients with LN proven by renal biopsy from 2001 to 2018 were enrolled. We assess the correlation among clinical characteristics, laboratory data, and pathohistological findings. [Results] Female were 56. Mean age was 46±2.2 years old. According to ISN/RPS classification, I, II, III, IV, III/IV+V, and V were 3, 5, 14, 13, 29 and 4 cases, respectively. Intensive therapies included mPSL pulse therapy (51.4%), IVCY (23.5%) and oral immunosuppressants (76.4%). In all cases, oral PSL was administrated and the average of initial PSL dosage was 30.5±2.0 mg daily. Urinary protein excretion levels in LN I/II, LN III/IV, or LN III/IV+V and LN V, were 0.5±0.2, 1.8±0.4, or 4.3±0.9g/gCr (p<0.05). Ds DNA antibodies levels in above three groups were 70.3±36.1, 128.4±32.1, or 104.9±23.8 IU/mL. [Conclusions] In LN exhibiting LN V, severe proteinuria was observed. In LN III/IV+V, renal function and prognosis tended to be poor.

W29-6

The utility of mycophenolate mofetil in patients with systemic lupus erythematosus during maintenance phase

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Conflict of interest: None

[Objective] To investigate the efficacy of combination therapy with mycophenolate mofetil (MMF) in patients with systemic lupus erythematosus (SLE). [Methods] Thirty-one SLE patients who had been referred to Niigata University Hospital between 2017 and 2018 were participated in this study. We investigated patients' prednisolone dosage (PSL), concomitant medications, laboratory findings, and SLE disease activity index (SLEDAI) at the start of MMF. Next, the changes and adverse events at 12, 24, 36, and 52 weeks after the MMF administration were investigated. [Results] 2 males and 29 females were included in the analysis. The age was 42.0 (37.5-56.5) years old, The PSL was 10.0 (9.50-12.8) mg/day, SLEDAI was 2.00 (0.00-2.00) at the start of MMF. The PSL was reduced to 9.0 (8.0-10.0) mg/day at 52 weeks (p <0.01). SLEDAI remained low to 2 (0-2) at 12 weeks, 0 (0-2) at 24 weeks, 0 (0-2) at 36 weeks, and 0 (0-2) at 52 weeks. CH50 was increased from 33 (30-43.5) U/mL to 36 (31-46) at 52 weeks (p = 0.033). Adverse events were observed in 3 patients of nausea, 1 of anorexia, and 2 of infection, but no patients were discontinued. [Conclusions] Combination therapy with MMF in patients with SLE may be safe in the short term, and effective in reducing PSL dosage and improving disease activity.

W30-1

Changes in treament for stable SLE cases of our institute over past 5 years - focusing on new drugs and steroid sparing effect -

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Conflict of interest: None

[Objective] Recently new drugs such as Mycofenolate mofetil (MMF), Hydroxychloroquine (HCQ), and Belimumab (BER) were introduced to SLE treatment. We aim to know actual usage of such new drugs and corticosteroid (CS) aparing effect for past 5 years. [Methods] Among our cases at the end of September 2019, we choose cases who have been stable for the past 5 years (stable cases). We reviewed prescriptions of these cases. [Results] Among our 381 cases with 39 males, there are 204 stable cases with 20 males. Treatment for these cases at early October 2014 consists of 92% CS (average prednisolone (PSL) 7.0 mg, 21% CS only cases), 43% tacrolimus (Tac), 28% azathioprine (AZP), 18% mizoribin (Miz). Treatment for these cases at the end of September 2019 consists of 92% CS (average PSL 6.0 mg, 15% CS only cases), 53% Tac, 27% AZP, 14% Miz, 15% MMF, 9% HCQ, 5% BER. 49 cases were treated with new drugs. In new drug using cases PSL could be reduced from 9.8mg to 7.5mg, but in cases not using new drugs PSL could be reduced from 6.1mg to 4.9mg. The PSL sparing effect of former cases almost double that of latter cases. [Conclusions] For stable SLE patients, the addition of immunosuppressants have CS sparing effect. Especially newly introduced drugs for SLE

were further useful for CS sparing.

W30-2

Transition of systemic lupus erythematosus treatment in our hospital

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Conflict of interest: None

[Objective] To compare the time course changes of SLE treatment and outcome in our hospital [Methods] We analyzed 36 patients with SLE receiving first remission induction therapy between 2008 and 2012 (group1) and 52 patients receiving first remission induction therapy between 2013 and 2018 (group2). We compared clinical characteristics and treatment between group1 and group2 at the time of remission induction therapy and maintenance therapy. Maintenance therapy was analyzed at 2014 for group1 and at 2019 for group2. [Results] Disease activity measured by SLEDAI was significantly higher in group2 at the time of diagnosis. The initial dose of PSL comparable between the groups, but the concomitant use of immunosuppressive agents was more frequently observed in group2. In maintenance therapy, the dose of PSL was significantly lower in group2 (11.7±3.4 vs. 9.2±2.8, $p<0.001$). Concomitantly used immunosuppressive agents were TAC for 33% in group1 and MMF for 35.4%, TAC for 35.4% in group2. SLICC/ACR damage index and rate of disease flare were comparable between the groups. [Conclusions] Lately, there was tendency to use immunosuppressive more frequently and reduce the dose of PSL. Further research is needed for long-term maintenance of disease activity and accumulated complication.

W30-3

Safety of mycophenolate mofetil for the patients with systemic lupus erythematosus; single-center, retrospective cohort

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Conflict of interest: None

[Objective] We analyzed the continuous rate, adverse events, and reason for withdrawal of mycophenolate mofetil (MMF) in patients with systemic lupus erythematosus (SLE). [Methods] We enrolled 142 patients who received with MMF from 31 July 2015 to 31 May 2019. [Results] Patients consisted of 21 males and 121 females. Median age was 38 years old (interquartile, 29-46). Forty patients were withdrawal of MMF, and accumulative withdrawal rate was 44%. The reasons for withdrawal were followed; 11 of infection, 9 of diarrhea, 6 of exacerbate of SLE, 4 of remission of SLE, 4 of wish for pregnancy, 2 of cytopenia, 1 of rash, 1 of renal dysfunction, and 1 of liver dysfunction. We examined the concentration of MMF (trough level) in only 8 patients. Two patients complicated with irreversible disorder due to viral meningitis, and their concentration of MMF were 8.3 and 6.3 ug/ml, respectively. The median dose at the last observation was 1000 mg (1000-1500 mg) overall. [Conclusions] We analyzed the continuous rate, adverse events, and reason for withdrawal of MMF in retrospective single center study. The Japanese transplantation guideline recommend that the concentration of MMF was controlled below 4.5 ug/ml. We want to discuss the necessity of concentration measurement of MMF.

W30-4

Evaluation of the EULAR/ACR-2019 classification criteria in cases of juvenile systemic lupus erythematosus

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Conflict of interest: None

[Objective] To compare the sensitivity and specificity of the EULAR/ACR-2019 new classification criteria with those of the ACR-1997 criteria, the diagnostic criteria developed in 1985 by the Pediatric Study Group of the Japanese Ministry of Health and Welfare (JMHW), and the SLICC-2012 criteria for patients with childhood-onset systemic lupus erythematosus (SLE). [Methods] This single-center retrospective study examined 53 cases of childhood-onset SLE and 46 cases of non-SLE with positive antinuclear antibodies (ANAs) as controls. [Results] All SLE cases had positive ANAs. The sensitivities of the new EULAR/ACR, ACR-1997, JMHW, and SLICC-2012 criteria were 100%, 86.8%, 98.1%, and 100%, respectively, and their specificities were 87.0%, 95.7%, 93.5%, and 84.8%, respectively. Among controls, three patients with mixed connective tissue diseases and two patients with Sjögren's syndrome met the new EULAR/ACR criteria. [Conclusions] The sensitivities of the EULAR/ACR-2019 and SLICC-2012 criteria were higher than the sensitivities of the ACR-1997 and JMHW criteria. The specificity of the EULAR/ACR-2019 criteria was lower than the specificities of the ACR-1997 and JMHW criteria; however, the specificity of the EULAR/ACR-2019 criteria was higher than the specificity of the SLICC-2012 criteria.

W30-5

Clinical features, disease activity and prognosis of elderly-onset systemic lupus erythematosus: a single-center study

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Conflict of interest: None

[Objective] To characterize the clinical and serological features, disease activity, damage accrual and comorbidities in elderly-onset systemic lupus erythematosus (SLE), especially diagnosed at the age ≧75 years. [Methods] Twenty-three patients diagnosed with SLE were divided into three groups based on the age of onset: <50, 51-74, ≧75 years of age. We retrospectively compared clinical data among three groups. [Results] Compared to 8 patients of the <50 years-onset group, 8 patients of the 51-74years-onset group and 7 patients of the ≧75 years-onset group more often had arthritis and less rash, alopecia and nephritis with lower SLE-disease activity score (DAS) at diagnosis. Anti-Sm antibodies were negative in all cases of two older groups. Despite the comparable doses of initial glucocorticoid therapy and less frequent use of hydroxychloroquine, disease flares were less frequent while organ damages accrued in older groups. Patients of ≧75 years-onset group had lower SLE-DAS at the last visit and more cardiac complications. [Conclusions] Elderly-onset SLE have different clinical and serological features, in whom disease activity and flare rate were lower while damages accrued. Patients diagnosed at ≧75 years of age may have different treatment outcome and prognosis.

W30-6

The relationship between components of SLICC/ACR Damage Index (SDI) and prescription on SLE patients other than immunosuppressants

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Conflict of interest: None

[Objective] This study is aimed to investigate the relationship between SLICC/ACR Damage Index (SDI) and prescription in SLE patients other than immunosuppressants. [Methods] This retrospective study consisted of 21 male and 203 female patients who were registered with SLE database in our hospital between March 19th and September 30th 2019. Prescription drugs were classified into some categories: calcium antagonist, angiotensin converting-enzyme inhibitor (ACEi) / angiotensin receptor blocker (ARB), diuretic, H2 receptor antagonist, proton pump inhibitor (PPI), warfarin, direct oral anticoagulant (DOAC), statin, and bisphosphonate. [Results] 103 patients recorded one or more SDI scores, with the most frequent component was avascular necrosis, followed by eGFR<50, diabetes. The multivariate logistic regression analysis showed that the

odds of avascular necrosis were 5.43 (95% CI, 1.44 to 20.5, p=0.0126) times higher in patients with H2 receptor antagonist than in patients without H2 receptor antagonist. Pearson's chi-square test showed that the significant difference was observed in the incidence of the avascular necrosis between patients with H2 blocker, PPI, and no prophylaxis against gastric ulcer (26.1% vs 8.5% vs 6.1%, P=0.0134). [Conclusions] SDI might be affected by prescriptions.

W31-1

Examination of CYP3A5 genotype is useful for introduction of tacrolimus treatment in outpatients with rheumatic diseases

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Conflict of interest: None

[Objective] CYP3A5 genotype was reported to play an important role in clinical outcomes in rheumatic diseases. Several reports showed that TAC concentration with a CYP3A5 *1 allele (EX) was lower than with a CYP3A5 *3/*3 (NEX). In this study we examined the possibility for screening patients suitable for TAC treatment by CYP3A5 genotype. [Methods] We investigated CYP3A5 genotype and TAC concentration in outpatients with rheumatic disease without renal dysfunction. Tac was taken after the evening meal and we measured trough level of TAC. TAC concentration normalized to the corresponding dose per body weight (C/D) was analyzed according to CYP3A5 genotype. [Results] The C/D value in the NEX group (n=16) was 124.8±59.2, which was significantly higher than that in the EX group (n=23; 67.7±29.8; P<0.001). When comparing patients using concomitant drugs which are strong inhibitors of or metabolized by CYP3A4/5 with patients not using those drugs, the each C/D value of NEX group was 122.9±52.3 (n=9) and 127.1±71.6 (n=7), and that of EX group was 71.3±32.2 (n=12) and 63.8±28.0 (n=11), with no significant differences. [Conclusions] EX patient may be impossible to gain sufficient TAC concentration even though using 3mg/day, suggesting that we should consider induction of TAC in NEX patients.

W31-2

Efficacy of Plasma Platelet-Derived Microparticles in the Diagnosis of Rheumatoid Arthritis-Associated Interstitial Lung Disease

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Conflict of interest: None

[Objective] Platelet-derived microparticles (PDMP) are membrane vesicles released from the activated platelets and have been reported to be elevated in rheumatoid arthritis (RA), but the relationship between plasma PDMP levels and the clinical characteristics of RA is unclear. PDMP level is elevated in respiratory diseases, and We analyzed the plasma PDMP levels obtained from 65 patients including rheumatic diseases with interstitial lung disease (ILD). [Methods] In total, plasma PDMP levels of 65 patients (including 8 RA with ILD, 11 non-RA with ILD and 46 patients without ILD) were analyzed using enzyme-linked immunosorbent assay. Moreover, the PDMP levels were compared with KL-6 levels in patients with ILD. [Results] The PDMP levels of RA patients with and without ILD were 81.17 ± 29.63 U/ml and 48.07 ± 42.42 U/ml, respectively. RA patients with ILD showed significantly higher PDMP levels than those without ILD. Furthermore, the PDMP levels were significantly higher in RA with ILD compared with those in non-RA with ILD; however, KL-6 levels between the two groups were not significantly different. Thus, plasma PDMP level can be a potential independent biomarker for the diagnosis of RA with ILD. [Conclusions] Plasma PDMP level is useful for RA with ILD diagnosis.

W31-3

Glycosylation abnormalities in the serum IgG of RA patients

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Conflict of interest: Yes

[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.

W31-5

Impact of anti-mutated citrullinated vimentin and anti-cyclic citrullinated peptide antibodies on rheumatoid arthritis disease activity

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Conflict of interest: None

[Objective] We investigated the associations of anti-mutated citrullinated vimentin (MCV) and anti-cyclic citrullinated peptide (CCP) antibodies (Abs) with disease activity in patients with rheumatoid arthritis (RA). [Methods] Two hundred and fifty patients with RA (female 79%, mean age 62.5 years, duration 10.4 year, and DAS28-ESR 3.09) in our hospital were enrolled. Anti-MCV and anti-CCP Ab titers in their sera are measured in the same sera and then divided into negative (Q0), low-positive (Q1), and high-positive (Q2) groups. High-positive was defined as titer higher than 3 times of the normal upper limit. Anti-MCV Ab was measured using ELISA kit (Anti-MCV®, ORIGENTEC Diagnostika GmbH). [Results] Q0, Q1 and Q2 groups in anti-MCV titer were 22%, 15% and 63%. Also, Q0, Q1 and Q2 groups in anti-CCP titer were 19%, 8% and 73%. Mean age of anti-MCV-Q0 patients tended to be higher than anti CCP-Q0 (67.3 vs. 62.7 years, P=0.054). DAS28 of Q0, Q1, and Q2 in anti-MCV Ab were 2.66, 2.93, and 3.28, respectively and the values of Q2 were higher than Q0 (P=0.0018). In anti-CCP Ab, however, the values of Q0 (2.97), Q1 (2.93), and Q2 (3.13) were not statistically different. [Conclusions] High-positive of anti-MCV Ab, but not anti-CCP Ab, is associated with an increased disease activity.

W31-6

The serum N-acetylglucosamine concentration in patients with rheumatoid arthritis

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Conflict of interest: None

In RA, synovitis results in articular cartilage disorders. The condition evaluation of cartilage is often mainly by image testing, serum marker use is not common. The serum concentration of N-acetylglucosamine, a polysaccharide of cartilage substrates, was measured and its significance was examined by examining its relationship to clinical effects. [Objective] 60 RA cases were enrolled [Methods] The internal standard, using N-acetylglucosamine-d3, after the serum was deproteinized using acetonitrile, injected into a high-speed liquid chromatography mass spectrometer (LC-MS / MS) fitted with an amino-based column. [Results] The correlation

between positive was age 0.644, knee joint disease 0.425, HAQ0.340, BUN 0.412, RF0.287, negative correlation, MTX-0.389, basal metabolism -0.313, sex difference -0.272eGFR-0.59 There were positive correlations between The serum N-acetylglucosamine and age and HAQ, and negative correlation between and BUN, MTX [Conclusions] We conducted serious measurements of The serum N-acetylglucosamine concentration under these hypothesis using more RA patients. By measuring the serum N-acetylglucosamine, cartilage state (image findings, various glycosaminoglycan), inflammation, amount of exercise, it was considered necessary to examine the nutritional changes.

W32-1

Multi-center study of clinical features and HLA typing in Japanese patients with ankylosing spondylitis

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Conflict of interest: Yes

[Objective] To analyze the clinical characteristics and HLA typing in Japanese patients with ankylosing spondylitis (AS). [Methods] We collected the clinical characteristics of the patients who fulfilling the modified New York criteria for AS. The clinical characteristic included the demographic data, histories, disease activity and HLA-B allele. [Results] A total of 84 patients of Japanese AS were enrolled from August 2018 to October 2019. The age at the survey was 42.1, the age at onset was 22.4, the disease duration was 19.7, and the diagnostic delay from the onset was 11.3years. Inflammatory back pain, enthesitis, dactylitis, uveitis, psoriasis, IBD were seen in 60, 30, 4, 30, 1 and 3, respectively. In treatment, 30 patients were treated any disease modifying anti rheumatic drugs salazosulfapyridine 24cases, methotrexate 16cases, biologics 35cases (Infliximab 15cases, adalimumab 18 cases and secukinumab 1 case). BASDAI was 3.1±2.2, ASDAS was 2.3±2.3. Sixty six patients were HLA-B27 positive (78.6%), in HLA-B27 negative patients, B7, B35, B37, B46, B48, B51, B54, B55, B60, B61, B62, B75 were seen. [Conclusions] The clinical characteristics of Japanese AS patients were not similar to those in other countries, and the HLA-B27 prevalence was 78.6%.

W32-2

Efficacy and Safety of Ixekizumab (IXE) in Patients with Active Non-Radiographic Axial Spondyloarthritis (nr-axSpA): COAST-X, a Phase-3 Randomized, Placebo-Controlled Study

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Conflict of interest: Yes

[Objective] Assess efficacy and safety of IXE in patients (pts) with active nr-axSpA. [Methods] Enrolled pts with an established diagnosis of axSpA [met ASAS classification (but not mNY) criteria], BASDAI≧4, back pain≧4, inflammation (sacroiliitis on MRI or CRP>5 mg/L), and inadequate response or intolerance to NSAIDs. Pts were randomized 1:1:1 to placebo (PBO), or 80mg IXE every 4 wks (Q4W) or 2 wks (Q2W). Primary endpoint was ASAS40 at Wk16. [Results] 303 pts (16 Japanese pts) were randomized: PBO, IXE Q4W, IXE Q2W (N=105, 96, 102). Significantly more pts achieved ASAS40 at Wk16: IXE Q2W (40%, p=0.002), IXE Q4W (35%, p=0.009) vs PBO (19%), and the efficacy was maintained until Wk52. Pts on either IXE regimen had significantly greater changes from baseline at Wks 16 and 52 for disease activity, functional status, and sacroiliac joint SPARCC scores vs PBO. The frequency of serious adverse events (AEs) and AEs that led to treatment discontinuation was low and similar across all arms. No new safety signal was identified. [Conclusions] The primary endpoint of ASAS40 and all major secondary endpoints for IXE Q4W and Q2W were met at Wk16 and maintained through Wk52 with no unexpected safety findings. IXE treatment improved signs, symptoms, and inflammation on MRI in pts with nr-axSpA.

W32-3

Efficacy and safety of 52-week ixekizumab (IXE) treatment in patients (pts) with active ankylosing spondylitis (AS)/radiographic axial spondyloarthritis naive to biologic DMARD (bDMARD-naive) or those with prior inadequate response/intolerance to tumor necrosis factor inhibitors (TNFi-IR): COAST-V and COAST-W

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Conflict of interest: Yes

[Objectives] To report efficacy and safety in 2 phase-3 studies in active AS pts receiving IXE for Wk52. [Methods] bDMARD-naive (COAST-V)/TNFi-IR (COAST-W) pts with established diagnosis of AS with radiographic sacroiliitis defined by mNY criteria were included. Pts were randomized equally to PBO, 80mg IXEQ2W or Q4W, or 40mg Q2W adalimumab (ADA, COAST-V only). At Wk16, pts in PBO or ADA arm were re-randomized equally to IXEQ2W or Q4W. Primary endpoint (EP) was ASAS40 response at Wk16 and other EPs included ASDAS, BASDAI and MRI. [Results] ASAS40 response at Wk16 was significantly higher for IXEQ2W or Q4W than PBO, and sustained up to Wk52 (COAST-V Wk16 PBO 18%, IXEQ2W 52%, Q4W 48%, p<.001; Wk52 IXEQ2W 51%, Q4W 53%: COAST-W Wk16 PBO 13%, IXEQ2W 31%, Q4W 25%, p<.05; Wk52 IXEQ2W 31%, Q4W 34%). The sustained improvement was found in other EPs. Of 7 pts in Japan in COAST-V, the 1 pt in IXEQ4W arm achieved EPs including ASAS40, and sustained to Wk52, whereas all 3 pts in PBO arm did not respond. TEAE/SAE frequency was comparable among all arms. Majority of TEAE were mild or moderate. [Conclusion] In bDMARD-naive/TNFi-IR AS pts, IXE significantly improved the signs and symptoms of AS at Wk16, and the efficacies were sustained up to Wk52. No unexpected safety signals were noted.

W32-4

The clinical features, cytokine levels and HLA phenotype of SAPHO syndrome/ palmoplantar pustulotic arthro-osteitis (PAO), PsA

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Conflict of interest: None

[Objective] To investigate the clinical features, clinical background, HLA phenotype trends, Cytokines levels of SAPHO syndrome / PAO and PsApatients in our hospital. [Methods] We examined the clinical features, clinical background, HLA phenotype, and serum TNFαR, IL-6, IL-17and IL-23 levels of SAPHO syndrome / PAO and PsApatients in our hospital. [Results] HLA-B27 was only 1/30 cases. Three phenotypes of HLA-B51, B61 and B62 were mainly detected in this study. There was no significant association between clinical symptoms and HLA phenotype. The age of onset in patients with HLA-A26 was significantly higher, and in patients with HLA-B52 lower than those who had the other HLA phenotype. The levels of serum IL-23 were significantly higher in patients with stoclavicular hyper ostosis (SCCH) and smoking history. Serum IL-17 titers were elevated in all available cases, but which of serum TNFαR1,2, and IL-6 was increased only in a few cases. [Conclusions] These results suggested that SAPHO syndrome is associated with at least two phenotypes; for example, one type involves the TNFα/IL-6 axis, while the other involves the IL-17 axis.

W32-5

Clinical features of 19 patients with SAPHO syndrome

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Conflict of interest: None

[Objective] SAPHO syndrome presents a wide variety of clinical features. There is no single, optimal approach to the treatment. The aims of this study were to facilitate the understanding of SAPHO syndrome. [Methods] Patients diagnosed having SAPHO syndrome in our department from December 2010 to September 2019 were analyzed retrospectively. [Results] 4 male and 15 female patients were diagnosed. Their mean age at diagnosis was 57.9±7.3 year old. Among 19 patients, 17 had cutaneous involvement, all of them had palmoplantar pustulosis. Osteoarthritis symptoms involved chest rib chain hyperplasia symptom in 13, sacroiliitis in 6, spondyloarthritis in 8, osteomyelitis in 4, peripheral arthritis in 14. Cutaneous involvement occurred before, after, and concurrently with osteoarthritis symptoms in 10, 5, and 1, respectively. We treated 3 patients with only NSAIDs, 6 with methotrexate, 3 with salazosulfapyridine, 10 with bisphosphonate, 1 with no drug. In the refractory cases, 4 patients were treated with biologics against to TNFα (all with infliximab), and 1 with IL-23p19, without using corticosteroids. [Conclusions] There was various approach to the treatment of SAPHO syndrome in our hospital.

W32-6

The study of incidence and HLA phenotype of reactive arthritis in Japanese patients with bladder cancer following intravesical BCG therapy: a single center prospective study

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Conflict of interest: None

[Backgroud] Intravesical instillation of Bacillus Calmette-Guerin (iBCG) is used as an effective immunotherapy of bladder cancer. However it may have, as adverse event, a reactive arthritis (ReA) and the frequencies are known as about 0.5 to 1 % in Western countries. We previously reported that the frequency of iBCG-induced ReA was 2.0% in Japan as a result of retrospective study for 20 years. [Objective] To prospectively evaluate the incidence and HLA phenotype of ReA in Japanese patients with bladder cancer following iBCG therapy. [Methods] The clinical findings of Japanese patients who received iBCG (n = 26) for bladder cancer from January 2018 to April 2019 were prospectively assessed, with specific attention to patients with ReA. We also looked at HLA phenotypes of patients with ReA. [Results] Patient age was 73 ± 9 and male/female ratio was 19/7. Of the 26 cases, ReA, uveitis and conjunctivitis were revealed in 1 (3.8%), 0 (0%) and 1 (3.8%), respectively. Notably, HLA-B27 was not detected in ReA patient. [Conclusions] Although this study was short-term prospective, the 3.8% ReA incidence in iBCG-treated Japanese patients exceeds that in previous study from Western countries and Japan. We will continue as large-scale and long-term prospective study.

W33-1

Immunogenicity of sarilumab, a fully human IgG1 monoclonal antibody against the IL-6 receptor, in two phase 3 trials in patients (pts) with active rheumatoid arthritis (RA) (KAKEHASI and HARUKA)

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Conflict of interest: Yes

[Objective] To report immunogenicity and relationship with safety and efficacy in pts with active RA treated with sarilumab. [Methods] Pts received subcutaneous sarilumab 150 mg q2w (S150) or 200 mg q2w (S200)+MTX for 52 or 28 weeks (wks) (after 24 wks placebo) (KAKEHASI; NCT02293902) or, S150 or S200 with/without non-MTX conventional synthetic (cs) DMARDs (HARUKA; NCT02373202) for 52 wks. Antidrug antibodies (ADAs) and neutralizing antibodies (NAbs) were assessed. [Results] In KAKEHASI, 5/81 (6.2%) (S150+MTX) and 6/80 (7.5%; 1/80 [1.3%] NAbs) (S200+MTX) pts were ADA positive (+ve). Lack of efficacy occurred in 18/150 (12.0%) ADA negative (-ve) pts and 1/11 (9.1%) ADA +ve pts, and loss of efficacy in 4/150 (2.7%) ADA -ve pts. In HARUKA, 5/30 (16.7%) (S150), 2/31 (6.5%) (S200), and 0/30 (S150/S200+csDMARDs) pts were ADA +ve. One ADA -ve pt receiving monotherapy reported lack of efficacy (no other reports of lack or loss of efficacy). There were no cases of anaphylaxis. No relationships between ADA formation and hypersensitivity reactions or between ADA status and sarilumab pharmacokinetics were evident in either trial. [Conclusions] ADAs to sarilumab when administered in combination or as monotherapy in pts with RA did not alter the safety or efficacy of sarilumab 150 or 200 mg q2w.

W33-2

Efficacy of sarilumab plus methotrexate (MTX) in patients (pts) with active rheumatoid arthritis (RA): subgroup analysis by baseline characteristics in a phase 3 trial (KAKEHASI)

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Conflict of interest: Yes

[Objective] To report the results of a subgroup analysis by baseline characteristics on efficacy outcomes in the placebo (P)-controlled period of the phase 3 KAKEHASI trial (NCT02293902). [Methods] Pts with a prior inadequate response to MTX, received subcutaneous sarilumab 150 mg q2w (S150), 200 mg q2w (S200), or P switching at week (wk) 24 to S150 or S200, all plus MTX, for 52 wks. ACR20 response at wk 24 was the primary endpoint. Subgroup analyses (by age, gender, weight, BMI, prior biologic DMARD use, rheumatoid factor, anti-CCP, baseline CRP, RA duration, and smoking history) were conducted. [Results] At wk 24, ACR20 response for S150+MTX was 67.9% (55/81) and for S200+MTX was 57.5% (46/80) vs 14.8% (12/81) for P+MTX ($p<0.0001$) (Tanaka 2019. *Arthritis Res Ther* 21:79). In the current analysis, there were no significant treatment-by-subgroup interactions based on the prespecified subgroups for ACR20 response (all $p>0.05$). Similarly, in post-hoc analyses, there were no significant treatment-by-subgroup interactions for HAQ-DI improvements at wk 16 or for CDAI improvements at wk 24 (all $p>0.05$). [Conclusions] Improvements in ACR20 at 24 wks, HAQ-DI at 16 wks, and CDAI at 24 wks observed in the overall population were consistent across all subgroups.

W33-4

Sarcopenia can be prevented by withdrawing glucocorticoids in patients with rheumatoid arthritis - from the CHIKARA study -

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Conflict of interest: None

[Introduction] We previously reported that glucocorticoid (GC) use is an independent predictive factor for developing sarcopenia in patients with rheumatoid arthritis (RA) using the prospective observational CHIKARA study. Based on this fact, we have tried to withdraw GCs. We investigated if withdrawing GCs can lead to preventing sarcopenia. [Methods] We investigated the body compositions, laboratory data, disease activity, physical function, and treatment of 100 patients with RA participated in the CHIKARA study at baseline, 1, 2, and 3 years. Among 20 patients using GCs at baseline, factors associated with changes of appendicular skeletal muscle mass index (ASMI) and sarcopenia development during 3 years were analyzed. [Results] Of 14 patients withdrawing GCs, there was no sarcopenia development and ASMI increased by 0.22 kg/m^2 during 3 years. On the contrary, of 6 patients continuing GCs, 2 developed sarcopenia (p=0.02) and ASMI decreased by 0.22 kg/m^2 (p=0.04). GC withdrawal (dummy variable) was a significantly associated factor for ΔASMI (β=0.39, p=0.02) when GC and age were used as explanatory variables by multiple regression analysis. [Conclusion] Patients withdrawing GCs showed increased ASMI and no sarcopenia development. Sarcopenia might be prevented by withdrawing GCs.

W33-5

Satisfaction with treatment in the patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Recently, patient-reported outcome measure has recognized as one of the standard evaluation methods for treatment and surgical procedures. In rheumatoid arthritis (RA), disease activity score include global assessment of patient, but there are few reports examined the relationship with patients' satisfaction. In this study, we investigated the satisfaction rate and examined the factors affected satisfaction. [Methods] We analyzed 264 RA patients (mean age 64.8 years; mean disease duration 12 years). We evaluated disease activity by simplified disease activity index (SDAI). [Results] The drugs used are: MTX usage rate 60.6%, mean amount 6.0mg, PSL usage rate 27.3%, mean amount 3.46mg, biological drugs usage rate 54.5%. SDAI was remission 34%, low 46%, medium 7%, and high 3%. Satisfaction with treatment was very satisfied 19%, satisfied 46%, normal 33%, dissatisfied 2%, and very dissatisfied 0%, and there was a significant correlation between satisfaction and SDAI, pain, and global assessment of patient. On the other hand, there were 22% cases who answered normal or unsatisfied even whom disease activity was remission. [Conclusions] Although disease activity is most impact on patient satisfaction, further investigation was needed for other factors affected satisfaction.

W33-6

Study of patients with rheumatoid factor-negative rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify the features of Japanese patients with seronegative rheumatoid arthritis (RA). [Methods] 112 RA patients were subjected for the study. 19 patients were seronegative (SNRA: 59±16 year-old, male: female=5:14, disease duration 12±8.5 years). 93 patients were seropositive (SPRA: 62±14 year-old, 19:74, 14±11 years). Disease activity, treatment and comorbidities were compared between SNRA and SPRA. [Results] DAS28-CRP was significantly better in SNRA (2.02±1.08) compared to SPRA (2.45±1.00, p<0.05). HAQ-DI was also significantly better in SNRA (0.18±0.28) compared to SPRA (0.47±0.59, p<0.05). There was no significant difference in bDMARDs or csDMARDs between SNRA and SPRA. bDMARDs were used in 8/19 (42%) of SNRA, and in 50/93 (54%) of SPRA. In csDMARDs, tacrolimus and iguratimod were frequently used in SNRA (TAC21%, IGU26%) and SPRA (TAC28%, IGU16%). The most common comorbidities were respiratory disorders (SNRA26%, SPRA 43%), followed by hypertention (SNRA32%, SPRA25%). However, there was no significant difference in comorbidities between the two groups. [Conclusions] Seronegative RA patients had better clinical outcome compared to seropositive RA patients although the treatment and comorbidities were not significantly different between the two groups.

W34-1

Pathogenic roles of Toll-like receptor 7 in systemic lupus erythematosus (SLE)

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Conflict of interest: Yes

[Objective] SLE is an autoimmune disease characterized by autoantibody production and multiple organ damages. TLR7 is suggested to play pathogenic roles in SLE, but molecular and cellular mechanisms behind TLR7-dependent pathology are largely unknown. By using anti-mouse TLR7 monoclonal antibody (mAb), we here studied pathogenic roles of TLR7 in lupus-prone mice, NZBWF1. We also established anti-human TLR7 mAb and studied TLR7 expression in peripheral blood leukocytes (PBLs) from SLE patients. [Methods] NZBWF1 were administered with anti-mouse TLR7 mAb to study pathogenic roles of TLR7. Furthermore, we established anti-human TLR7 mAb and examined TLR7 expression in PBLs from SLE patients. We also studied antagonistic effect of the anti-human TLR7 mAb. [Results] Administration of anti-mouse TLR7 mAb increased mouse survival. Anti-mouse TLR7 mAb decreased levels of kidney damage. Glomerulonephritis was ameliorated. Serum autoAbs and deposition of IgG were decreased. In parallel, TLR7 expression was not altered in PBLs from SLE patients. The anti-human TLR7 mAb inhibited cytokine production by PBLs. [Conclusions] Anti-mouse TLR7 mAb showed protective effect in NZBWF1. We also found TLR7 expression in PBLs from SLE patients. These results suggest that TLR7 might play pathogenic roles in SLE.

W34-2

Role of SOCS1 (suppressor of cytokine signaling 1) in SLE

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Conflict of interest: None

[Objective] T cell-specific SOCS1-deficient mice exhibited the pathology of SLE. The immunological mechanism of them was elucidated to be an increase in plasticity of regulatory T cells (Treg). It was considered that the expression of SOCS1 in Treg plays an important role in stabilizing the suppressive function of Treg and suppressing SLE pathology. In this study, we investigate whether the pathology of SLE is suppressed in SOCS1 transgenic mice (SOCS1 Tg). [Methods] In SOCS1 Tg and wild-type mice (control), imiquimoid cream was applied to induce SLE. The presence and mechanism of SLE were analyzed. [Results] 1) The pathology of SLE was not suppressed in SOCS1 Tg, but rather worse than that in which SLE was induced in wild-type mice. 2) In flow cytometry analysis, SLE-induced SOCS1 Tg showed a decrease in IL-2 producing cells and an increase in IFNγ producing cells from CD4 positive T cells in spleen and lymph nodes compared to control. On the other hand, the number of Foxp3-positive cells increased. [Conclusions] SOCS1 exacerbates SLE regardless of whether it is constantly expressed at high or low levels, and there is a possibility that a decrease in inhibitory function including Treg plasticity is involved in both mechanisms.

W34-5

Elucidating the role of Juxtaposed with another zinc finger gene 1 (JAZF1) gene in lupus

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Conflict of interest: None

[Objective] The immunological function of the JAZF1 gene, one of the susceptibility genes for Systemic Lupus Erythematosus (SLE), remains unclear. In this study, we aimed at clarifying the Jazf1 function in lupus. [Methods] Jazf1-GFP reporter mice and Jazf1 KO mice were generated. Quantitative RT-PCR was performed on FACS-sorted various types of immune cells. $CD4^+$ T cells from Jazf1 KO or WT mice were cultured under Tr1 condition, and IL-10 in the culture supernatant was quantified by ELISA. The skin of Jazf1 KO or WT mice was treated topically with imiquimod cream to generate lupus model mice. [Results] Jazf1 was preferentially expressed in IL-10-producing $CD4^+CD25^-LAG3^+$ regulatory T cells ($LAG3^+$ Tregs) among various immune cells. Interestingly, Jazf1 expression was inversely correlated with IL-10 expression in $LAG3^+$ Tregs. The deficiency of Jazf1 was associated with the enhanced production of IL-10 in Tr1 cells. Jazf1 KO lupus model mice demonstrated significantly elevated serum IL-10 level and proteinuria compared to WT mice. [Conclusions] Jazf1 plays an essential role in IL-10 production from $LAG3^+$ Tregs. Furthermore, Jazf1 deficiency caused exacerbation of lupus-like disease activity. These findings suggest that JAZF1 can be a therapeutic target for SLE.

W35-2

Clinical study on the development of interstitial pneumonitis in patients with rheumatoid arthritis

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Conflict of interest: None

Purpose: To clarify features of rheumatoid arthritis (RA) patients who developed interstitial pneumonitis (IP) and who had not had IP before. Method: We performed chest high-resolution computed tomography (HRCT) in patients at their first visit to our clinic from 2009 to 2014 and annually thereafter. Information on patients' background and serological data were obtained from their charts. Results: 280 RA patients (onset age, 59.1±14.4yo; duration of RA, 6.1±9.6 years) underwent chest HRCT at the first visit, and 91 (32.5%) had an IP shadow. The presence of IP at the first visit was significantly associated with male gender (52.7% vs. 31.2%), higher onset age of RA (62.1yo vs. 57.7yo), positivity for rheumatoid factor (82.4% vs. 62.4%), and positivity for anti-CCP antibody (68.9% vs. 51.9%). 3 patients (1.6%,3/189) without IP at the first visit had new interstitial abnormality on HRCT 5 years later. Positivity for IP shadows 5 years later was not associated with gender, age at onset, positivity for RF, and positivity for anti-CCP antibody. Of the 3 patients, one was treated with prednisolone (PSL) and two with methotrexate (MTX). PSL tended to reduce the onset of IP (p=0.27). Conclusion: IP exists before the onset of RA in some patients. IP rarely occurs after the onset of RA.

W35-3

Sustained disease activity is a risk factor for worsening of interstitial pneumonitis in rheumatoid arthritis

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Conflict of interest: None

[Objective] To identify the risk factors for worsening of interstitial pneumonitis (IP) in RA patients under bDMARD therapy. [Method] Subjects were consecutive 116 RA patients with IP detected by HRCT at starting bDMARD therapy. Among them, 91 patients who received sequential HRCT scans were analyzed. The presence of and change in ILD were judged by HRCT findings. Data on demographics, clinical features including disease activity and treatment were collected. [Results] In 91 patients with IP, 37 (41%) showed worsening of IP and 54 (59%) (3 with improvement) did not. Between worsening and no worsening groups, no differences were found in sex, age, disease duration, the positivity for anti-CCP antibody and RF, levels of KL-6 and Sp-D and disease activity at the entry. Therapy for RA was similar in both groups; two-thirds of patients of both groups were treated with TNF inhibitors as the first bDMARDs. Change in CDAI during the observation periods (mean: 2.7 years) of non-worsening groups was greater than that of the worsening group (non-worsening vs. worsening; -11.7 vs. -6.1). [Conclusion] Sustained disease activity was a risk factor for worsening of IP in RA.

W35-4

Prognostic factors of pulmonary injury in RA

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Conflict of interest: None

[Objective] To identify the prognostic factors of pulmonary injury in RA. [Methods] Subjects were consecutive RA patients who admitted our hospital to treat pulmonary injury. Patients with bacterial pneumonia were excluded. Medical records were reviewed. [Results] Subjects were 48 patients (male/female: 13/35, age: 64.9 years). Causes of pulmonary injury were 34 IP, 9 drug-induced lung injury, 3 PJP, and 2 others. Survivors were 38 and non-survivors were10. No differences were found in demographics and medication for RA between 2 groups. Non-survivors had more extended fibrosing lung disease and airway diseases as pre-existing lesions than survivors. No differences were found in symptoms on admission, time from onset of respiratory symptoms to admission, WBC counts, and CRP levels between 2 groups. Non-survivors had extended GGO, poor respiratory condition, and elevated levels of LDH, KL-6, and ferritin compared to survivors. Moreover, exacerbation of IP caused high mortality compared to other causes of lung injury. [Conclusions] Pre-existing extended fibrosing lung disease and airway disease, poor respiratory condition on admission, and exacerbation of IP as a cause of lung injury were poor prognostic factors of pulmonary injury in RA.

W36-1

Prognostic significance of pulmonary involvement in rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the characteristics and prognostic significance of lung involvement in rheumatoid arthritis (RA). [Methods] RA patients with regular follow-up in December 2012 were included. They were divided into 8 groups; without CT/normal CT, UIP pattern, NSIP pattern, OP pattern, unclassified interstitial change, bronchiolitis, nontuberculous mycobacterium (NTM), and others. Five-year survival rate was compared to without CT/normal CT group by proportional hazard model. Adjusted variables were selected using all possible models. [Results] Among 1639 RA patients, 57 patients died; 3 from interstitial lung disease, 23 from malignancy, 4 from infectious disease, 1 from myocardial infarction, 4 from other reasons, 23 from unknown causes. Hazard ratios [95% confidence interval] adjusted by age, CRP, and glucocorticoid use were 9.5 [3.6-25.6] for UIP pattern (n=37), 7.7 [0.9-61.5] for NSIP pattern (n=8),

4.5 [1.7-12.0] for unclassified interstitial change, 1.9 [0.6-5.9] for bronchiolitis (n=104), 4.0 [1.2-13.3] for NTM (n=40), and 2.7 [1.2-5.9] for others (n=452). [Conclusions] Mortality risk was different among groups divided by lung involvement in RA. UIP pattern, unclassified interstitial change, and NTM showed significantly higher mortality risk.

W36-2

Relationship between rheumatoid arthritis lung lesions, autoantibodies (anti-CCP antibodies and RF) and joint echo findings

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Conflict of interest: None

[Objective] Pulmonary lesions in RA patients, particularly interstitial lung disease (ILD) and airway lesions (bronchiectasis / bronchiolitis (AL)), is associated with the prognosis of RA patients. We investigated the relationship between ILD / AL, ACPA, RF and joint findings in RA patients. [Methods] 101 RA patients (30 males, 71 females, average age 62.2 years old) who underwent chest CT, 22 hand joint echocardiography, smoking history and ACPA/RF test were analyzed in this study. [Results] Of 101 cases, ILD / AL was observed in 47 cases (47%), ILD was 30 cases (30%), AL was 26 cases (26%), and ILD / AL combined was 9 cases (9%). The prevalence of AL was higher in the ACPA high-titer group, and the ILD was higher in the RF high-titer group. Hand joint echo showed high blood flow in the group with both high RF and ACPA high-titer groups. [Conclusions] The prevalence of AL is higher in RA patients with high titer of ACPA. The prevalence of ILD is higher with high titer of RF and abnormal joint blood flow.

W36-3

Risk Factors for Developing and Mortality for Acute Exacerbation of Rheumatoid Arthritis associated Interstitial Lung Disease

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Conflict of interest: None

[Objective] To investigate the risk factors associated with acute exacerbation (AE) and its survival in patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD). [Methods] We examined the clinical features of 165 RA-ILD patients admitted to our hospital between July 2010 and October 2019 to identify variables significantly associated with AE occurrence. [Results] The mean patient age was 73.6±9.7 and 97 (71.9%) were female. 30 (22.2%) developed AE and 13 of them (43.3%) died (with the mean follow-up period of 64.9 months). Univariate analyses revealed that UIP pattern was associated to the AE (OR 2.68, 95% confidence interval 1.10-6.52, p=0.03). Age (median 70 vs. 80 years, p=0.003), without MTX use (70.6% vs. 23.1%, p=0.025) and high level of C reactive protein (median 9.38 vs. 18.12 mg/dL, p=0.02) on admission were significantly higher in patients who died of AE. Cox proportional hazard model revealed that age over 65 years (HR 1.79, 95% confidence interval 0.38-8.30), UIP pattern (HR 4.67, 95% confidence interval 1.02-21.5) and MTX use (HR 0.16, 95% confidence interval 0.04-0.72) were associated with death. [Conclusions] Our data may suggest that UIP pattern relates to the AE, and MTX use, UIP pattern and age relate to AE survival in patients with RA-ILD.

W36-4

Correlation between osteoporosis treatment and fractures in patients with rheumatoid arthritis: from the CHIKARA study

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Conflict of interest: None

[Objective] Osteoporosis is a common feature in patients with rheumatoid arthritis (RA). Osteoporosis treatment is important to prevent physical dysfunction due to fractures. We investigated osteoporosis treatment and changes in bone mineral density (BMD) in RA patients. [Methods] The data from a prospective observational study (CHIKARA study) were used. We measured BMD by Dual Energy X-ray Absorptiometry (DEXA). [Results] 83 RA patients were included. Mean age was 66.7 years old, median disease duration was 8.6 years. Mean DAS28-ESR was 2.9. The baseline BMD was 1.08 ± 0.2g/cm^2 at lumbar spine and 0.74 ± 0.15g/cm^2 at femoral neck. 32 patients had Osteoporosis treatment at baseline. There was no significant change in BMD at whole body and lumbar spine, regardless received osteoporosis treatment at baseline (p=0.251, p=0.089, Mann-Whitney u-test). BMD at femoral neck increased significantly in osteoporosis treatment group (p=0.011, Mann-Whitney u-test). Four new fractures occurred. 2 patients received osteoporosis treatment at baseline, but other 2 patients did not receive. [Conclusions] We investigated osteoporosis treatment and changes in BMD in RA patients. RA patients should be careful about fractures even if they do not fulfill osteoporosis criteria.

W36-5

Skeltal muscules atrophy is related to RA disease activity, joint destruction, athrosclerotis change and osteopenia among the patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify whether skeletal muscle atrophy in RA patients is related to disease activity and joint destruction of RA, and whether skeletal muscle atrophy is related to arteriosclerosis and bone mineral loss. [Method] A cross-sectional study was conducted on 168 patients with RA. We examined the relationship between the skeletal muscle mass index (SMI) measured by the direct bioelectrical impedance measurement method (DSM-BIA) for each site and the index of RA disease activity, and the Carpal height ratio (CHR) of both wrist joints. We also measured bone mass density (BMD) of the lumbar spine and femoral neck, and in some cases, various arteriosclerosis indices, and investigated the relationship with SMI. [Results] SMI significantly correlated with CDAI, SDAI, and erythrocyte sedimentation rate. There was a positive correlation between SMI and CHR. Furthermore, SMI has a positive correlation between BMD and ankle brachial blood pressure ratio, and a negative correlation with brachial ankle pulse wave velocity and Intima media thickness. [Conclusion] In patients with active RA, skeletal muscle atrophy are advanced. Moreover, in the case with skeletal muscle atrophy, bone mineral and arteriosclerosis has progressed.

W36-6

The screening using FibroScan Ultrasonography for Non Alcoholic Fatty Liver Disease in Rheumatoid Arthritis

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Conflict of interest: None

(Objective) The prevalence of fatty liver disease in patients with rheumatoid arthritis is currently unknown. If indeed a high prevalence of NAFLD will be found in the RA patients, further support will be landed for the link between inflammation and fatty liver disease. These findings may also have implications regarding the management and follow up of RA patients. The validity of sonographic imaging for detection of fatty liver diseases is currently accepted. (Methods) Ultrasonography, Fibroscan has a sensitivity of 89% and a specificity of 93% in detecting steatosis and sensitivity and specificity of 77% and 89% respectively in detecting increase fibrosis. We researched the fatty liver and liver fibrosis in patients with RA

and suspectable NAFLD/NASH. (Results) 21 patients was diagnosed the fatty liver by the rate of Controlled Atenuation Parameter (CAP). 5 patients of 21patients was diagnosed the progressive liver fibrosis by Liver stiffness measurement (LSM) by transient elastography and discontinued MTX. (Conclusion) Ultrasonography, Fibroscan is usefulness for patients with RA complicated NAFLD/NASH. Especially, it is important to diagnose the progressive liver fibrosis by Liver stiffness measurement (LSM) by transient elastography

W37-1

Consideration of development risk of lymphoma in rheumatoid arthritis treated with methotrexate

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Conflict of interest: Yes

[Objective] Recently, although development of MTX-LPD in RA patients are attention, its correct frequency is unknown. In this study, we show the frequency of the lymphoma in RA patients, the frequency of lymphoma in RA patients treated with MTX or non-MTX using “Nihon University Clinical Database System”, we consider MTX-LPD development in RA. [Methods] We pick up 21,228 RA patients in “Nihon University Clinical Database System” from 1993 to 2011, and checked number of lymphoma, compared treated with MTX to non-MTX in these patients. [Results] Number of lymphoma diagnose RA (3.5%) were significantly higher to diagnosed OA (0.8%). Number of lymphoma treated with MTX in RA patients was significantly higher to treated with non-MTX. Although there were no significant with after treated MTX and non-MTX in RA patients before 2010, number of lymphoma after treated with MTX (7.5%) were significantly higher to after treated with non-MTX after 2011. [Conclusions] There was no reports to development risk of lymphoma treated with MTX compared to treated with non-MTX. Use of high dose of MTX was permitted in Japan after 2011, it was suggested that the development of lymphoma was associated with dose of MTX.

W37-2

Clinical characteristics of lymphoproliferative disease spontaneous regression factor and RA treatment in patients with rheumatoid arthritis treated with methotrexate

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Conflict of interest: None

[Objective] The purpose of this study is to demonstrate the characteristics of LPD spontaneous regression factor and RA treatment after LPD among RA patients concurrently treated with MTX. [Methods] We retrospectively evaluated 51 RA patients with LPD (Average age 66.3 years) from 2007 to 2019 regarding their clinical features. [Results] After cessation of MTX, LPD spontaneously regressed in 31 patients (Regressive group), but 20 patients required chemotherapy (Persistent group). In the Regressive group, significantly low level of serum sIL-2R, EBV positive and high count of lymphocyte after 2 weeks cessation of MTX were observed. With an average observation period of 48 months, 6 patients died and 3 were caused by LPD. After cessation of MTX, 24 patients relapsed with RA. In the RA relapse group, significantly high titer of RF, LPD spontaneous regression, and high SDAI at the onset of LPD were observed. In RA relapse group, 7 patients were treated with TAC, 12 patients were treated with biologics (TCZ: 9, ABT: 3, CZP: 1, RTX: 1), but no LPD relapse was recognized. [Conclusions] Our data indicated that the titer of sIL-2R was an important marker of spontaneous regression of LPD and high titer of RF and high disease activity at the onset of LPD were important risk factors for RA relapse.

W37-3

Predictive factor of spontaneous regression in MTX related lymphoprolipherative disorder and Rheumatoid arthritis treatment after LPD onset

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Conflict of interest: None

[Objective] Recently, there are many reports from Japan about methotrexate related lymphoproliferative disorder (MTX-LPD). We investigate the characteristics of infiltrating cells at the biopsy lesion as predictors of spontaneously regression (SR). In addition, it has not been established for RA treatment after the onset of MTX-LPD. We clarify the histopathlogical features of LPD with SR and current status of RA treatment after onset of LPD. [Methods] Of the 83 MTX-LPD cases diagnosed from 2005 to 2019, 16LPD specimens were steined using immunohistochemistry (IHC). In addition, we enrolled 76 cases that could be followed up after the onset of LPD. RA treatment after MTX-LPD was extracted from medical records. [Results] In LPD with SR, the CD8 positive T cell rate at the biopsy lesion was low. As regards 76 MTX-LPD cases, the mean age of MTX-LPD onset was 66.6 ± 10.8 years. Fifty-three cases were SR, and 23 cases were treated with chemotherapy. As regards RA treatment after MTX-LPD onset, csDMARDs alone, biologics or JAK inhibitors and NSAIDs or PSL alone treatment were 36, 20 and 20 cases respectively. [Conclusions] Treatment with csDMARDs and/or biologics was performed for RA patients after onset of MTX-LPD. In addition, we suggested that IHC is useful for predicting of SR.

W37-4

Pathological analysis of lymphoproliferative disorders in patients with rheumatoid arthritis: Results of multicenter collaborative research

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Conflict of interest: None

[Objective] Nowadays, Rheumatoid arthritis (RA) associated lymphoproliferative disorders (LPD) and methothrexate (MTX) induced LPD are major problems among the patients with RA that remain to be resolved. The present study analyzed a large number of patients with RA-LPD and MTX-LPD in a multicenter collaborative study, focusing on histologic findings. [Methods] A total of 518 patients with RA who developed LPDs between 1999 and 2018 were enrolled into a multicenter collaborative study across 33 member hospitals of the National Hospital Organization (NHO) and 18 representative specialized rheumatology hospitals in Japan.

[Results] Of the RA-LPD cases, 390 (75.3%) RA-LPD cases were B-cell type; 30 (5.8%), T-cell type; and 7 (1.4%), NK/T cell type according to the WHO classification. The most frequent types of RA-LPD were diffuse large B cell lymphoma (265, 51.2%), followed by Hodgkin lymphoma ([HL]; 63, 12.2%), mucosa-associated lymphoid tissue lymphoma (36, 7.0%), polymorphic LPD (32, 6.2%), follicular lymphoma (22, 4.2%), angioimmunoblastic T-cell lymphoma (12, 2.3%), and HL-like lesion (10, 1.9%). Of the RA-LPD patients, 51.9% were positive for EBER-1. [Conclusions] A multicenter collaborative study could showed the detailed characteristics of RA-LPD according to histological subtype.

W37-5

Lymphoproliferative Disorders in Patients with Rheumatoid Arthritis: Results from Japanese Nationwide, Multi-institutional Study

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Conflict of interest: None

Objective: To reveal clinical features and risk factors of lymphoproliferative disorders (LPD) in Japanese patients with rheumatoid arthritis (RA). Methods: We enrolled patients with RA aged ≧ 20 who visited hospitals between 1st April 2011 and 31st July 2011 using REDCap and observed retrospectively for 3 years. The first visit of each patient during the 4 months was defined as the start of the observation. Patients were registered at each site by the order of their first visit. A patient who developed LPD were followed for up to 5 years from the onset of LPD. LPD included lymphoma with pathological diagnosis (PD), LPD other than lymphoma with PD, and clinical LPD without PD. We calculated odds ratios (OR) of risk factors for LPD using a logistic regression model. Results: 10,807 patients from 59 sites were analyzed. The mean age was 63 years old and 79.3% were female. LPD were reported from 91 patients, and diffuse large B cell lymphoma was the most frequent pathological subtypes (54%), followed by Hodgkin lymphoma (16%). Mortality was 20%. The major COD was lymphoma (78%). Age by decade (OR 1.55) and MTX use (OR 3.40) were independent risk factors of developing LPD. Conclusion: This study revealed pathological subtypes, prognosis, and risk factors of LPD in patients with RA.

W37-6

The difference in pathogenetic mechanism of rheumatoid arthritis-complicated lymphoproliferative disorders in follow-up of 35 cases

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Conflict of interest: None

[Objectives] Lymphoproliferative disorders (LPD) develop in some patients (pts) with rheumatoid arthritis (RA). It is hypothesized that pathogenesis of LPD are immunosuppression and reactivation of EB virus (EBV) caused by immunosuppressant (IS) including methotrexate (MTX), chronic inflammation of RA and Sjogren's syndrome (SS), and so on. [Methods] We followed up 35 RA pts (12 males and 23 females) with LPD from January 2010 to October 2019. [Results] MTX was administered to 32 pts, and biological DMARDs or JAK inhibitors were 10 pts. 16 pts were diagnosed to have DLBCL, 6 pts were B cell lymphoma, 3 MALT, 2 Hodgkin lymphoma, and 2 follicular lymphoma (FL). EBV was detected in tumor tissues from 11 of 26 analyzed-pts. 19 pts were in remission by withdrawal MTX. After treatment of LPD, 18 pts experienced relapse of RA at mean 14±11 months. In 132 person-years, LPD relapsed in 4 pts, in which EBV was not detected. 2 pts were FL, which relapsed frequently. A patient was treated by withdrawal MTX for primary LPD. 2 pts had been treated by tacrolimus, iguratimod and biological DMARDs for relapsed RA, and 2 pts had IS-free. A patient was complicated by SS. [Conclusion] We followed up RA pts with LPD. The clinical histories suggested the difference in pathogenetic mechanisms of RA-LPD.

W38-1

Pregnancy triggers the onset of anti-transcriptional intermediary factor 1 antibody-positive dermatomyositis

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Conflict of interest: None

[Objective] Risk factors for dermatomyositis (DM) have not been well-known. Some patients develop DM in pregnant periods, and the association was still obscure. We aimed to observe cases of pregnancy-associated DM. [Methods] We performed a retrospective, single center study on 62 DM cases who visited our department from 2010 to 2018. The profiles of myositis-specific autoantibodies (MSAs) were distinguished to anti-ARS, TIF1γ, Mi2b, MDA5, NXP2 and SAE antibodies. [Results] Thirteen female patients out of 62 all DM patients in our series developed DM within their reproductive ages. The 13 female cases included 7, 4 and 2 cases of anti-TIF1γ, ARS and MDA5 antibody-positive DM, respectively. In this series, 3 cases of developed anti-TIF1γ antibody-positive clinically amyopathic DM in their pregnancy/postpartum periods. [Conclusions] Our observation study suggested that anti-TIF1γ antibody-positive DM, never any other MSAs-positive DM, might be triggered by pregnancy. TIF1γ autoantigens are also ubiquitously expressed in mammalian embryo and mammary epithelial cells during pregnancy and lactation period. Overexposure to foetal/maternal TIF1γ autoantigens, like as a high expression of TIF1γ in malignant tumours, may have contributed to the development of autoimmunity to TIF1γ.

W38-2

Semi-open muscle biopsy is safe and useful for the diagnostic of idiopathic inflammatory myopathies

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Conflict of interest: None

[Objective] TMuscle biopsy is essential for classification of the idiopathic inflammatory myopathies (IIM) without dermatomyositis (DM)-specific skin rash. However, the muscle biopsy is not widely conducted for their diagnosis, partly because of the invasiveness of the open biopsy technique, which is the most common method in Japan. In this study, we evaluated the safety and usefulness of the semi-open muscle biopsy, which is less invasive than the open biopsy. [Methods] Patients with clinically suspected IIM without DM-specific rash were enrolled. The web calculator for the EULAR/ACR classification criteria of IIM was employed. [Results] The semi-open muscle biopsies were performed in all of the enrolled 20 cases including 6 cases, who were not eligible for the open biopsy. Although muscle biopsy is required for classification, the web calculator classified 7 and 8 patients tentatively as having IIM definitely and probably, respectively. With the biopsies, 6 out of the 8 probable cases were classified authentically in definite IIM. Two out of the 5 unclassified cases were classified authentically in probable IIM. No complications were observed except abnormal sensation on the biopsy site in one case. [Conclusions] Semi-open muscle biopsy is safe and useful for the diagnosis of IIM.

W38-3

Exosomal membrane proteins as novel biomarkers of polymyositis/dermatomyositis and clinical application

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Conflict of interest: None

[Objective] To identify novel biomarkers of polymyositis/dermatomyositis (PM/DM) using proteomic analysis of serum exosome, and to establish sandwich ELISA of exosomal membrane protein for clinical application. [Methods] We performed proteomic analysis of serum exosome from 10 healthy individuals, 10 PM/DM patients and 23 non-PM/DM patients using LC-MS/MS. The expression of target membrane proteins in serum exosome was confirmed by Western blot. We established sandwich ELISA to measure serum exosome expressing target membrane proteins. [Results] We identified several exosomal membrane proteins that were significantly increased in PM/DM, and confirmed that one of them was abundant in exosome fraction in the sera by Western blot. In addition, we established sandwich ELISA that directly detects serum exosome expressing the target membrane protein using specific antibodies against exosome marker (CD9 or CD63) and target membrane protein. In our in-house sandwich ELISA, the levels of exosome expressing target membrane protein in the sera were significantly higher in PM/DM patients (n=50) than those in healthy individuals (n=12) and non-PM/DM patients (n=63) ($p<0.01$). [Conclusions] Serum exosomal membrane protein could be a novel biomarker for PM/DM.

W38-4

Clinical features and type 1 IFN signature of anti-TIF1-gamma antibody positive dermatomyositis patients

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Conflict of interest: None

[Objective] Inflammatory myopathy (IM) includes various disease courses with different autoantibodies. Anti-TIF1-γ antibody (+) patients were compared with other IM in terms of clinical features and type I interferon-stimulated genes (ISGs) expression. [Methods] IM patients in our department were divided into 2 groups according to autoantibody positivity (TIF1-γ (+) and TIF1-γ (-); subdivided into 3 groups; MDA5 (+), ARS (+) and all (-)). Clinical features and serum ISGs expression were examined. [Results] Eleven dermatomyositis (DM) cases were in TIF1-γ (+) group and 41 IM cases were in TIF1-γ (-) (20 in MDA5 (+), 16 in ARS (+) and 5 in all (-)). Interstitial pneumonia was observed 1 case in TIF1-γ (+) and 34 cases in TIF1-γ (-). Malignancy complicated 8 cases in TIF1-γ (+), and 2 cases in TIF1-γ (-). ISGs expression of TIF1-γ (+) patients was lower than that of MDA5 (+) cases and higher than that of ARS (+) cases. In one TIF1-γ (+) patient, ISGs expression was down-regulated after IV-Ig treatment, following improvement of her DM symptoms. [Conclusions] Intermediate ISGs expression was observed in TIF1-γ (+) DM patients, suggesting relationship between type I IFN signature and clinical state of the disease.

W38-5

Examination of CYP3A5 genotype is useful for introduction of tacrolimus treatment of interstitial pneumonia in dermatomyositis

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Conflict of interest: None

[Objective] CYP3A5 genotype was reported to play an important role in TAC consentration. Several reports showed that the TAC consentration in patients with a CYP3A5 *1 allele (EX) was lower than that of patients with a CYP3A5 *3/*3 (NEX). In this study we examined the usefulness of CYP3A5 genotype in interstitial pneumonia in dermatomyositis (DM-IP) treatment which requires the enough blood level for treatment in early stage. [Methods] We investigated CYP3A5 genotype and TAC consentration in patients with rheumatic diseases without renal dysfunction. Tac was taken after both morning and evening meals and blood samples were taken 12h after TAC administration. TAC consentration normalized to the corresponding daily dose per body weight C/D was analyzed according to CYP3A5 genotype. [Results] The C/D value in the NEX group (n=6) was 154.6±25.6, which was significantly higher than that in the EX group (n=3; 79.0±2.8; P=0.028). When the target consentration was set at 5-10 ng/ml, the required dose was (0.0316 to 0.0633) mg/kg in the EX group and (0.0162 to 0.0324) mg/kg in the NEX group. [Conclusions] EX patient may be impossible to gain sufficient TAC consentration introducing 0.0375mg/kg dose, suggesting that examination of CYP3A5 genotype is useful for introduction of early treatment of DM-IP.

W38-6

The differences of muscle magnetic resonance imaging findings between anti-SRP antibody-positive myopathy and anti-ARS antibody-positive dermatomyositis

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Conflict of interest: None

[Objective] The aim of this study is to compare the findings of muscle magnetic resonance imaging (MRI) between anti-SRP antibody-positive necrotizing myopathy (anti-SRP myopathy) and anti-ARS antibody-positive dermatomyositis (ARS-DM). [Methods] This is a case-controlled observational study. Four patients with anti-SRP myopathy and 10 patients with ARS-DM were enrolled. These participants were satisfied inclusion criteria of this study as follows: the existence of muscle weakness of the lower legs according to manual muscle testing, and the high levels of serum creatinine kinase (CK) more than 2,000 U/L. The muscles of the thigh MRI findings such as edema, fascial edema, fatty replacement, and atrophy were evaluated. [Results] Inflammatory edema was high frequency findings of MRI in both groups. The findings of fascial edema were observed in only ARS-DM patients. Anti-SRP myopathy patients had more prevalent edema in the gluteus muscle than in ARS-DM patients (75% vs 30%, respectively). In contrast, ARS-DM patients had findings of inflammation in the anterior compartment of muscles compared to anti-SRP myopathy patients (90% vs 50%, respectively). [Conclusions] These differences of MRI findings in thigh muscles may be helpful to distinguish between anti-SRP myopathy and ARS-DM.

W39-1

Clinical features of pneumatosis cystoides intestinalis associated with polymyositis/dermatomyositis

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Conflict of interest: None

[Objective] Pneumatosis cystoides intestinalis (PCI) is a relatively rare disease. Polymyositis (PM) and dermatomyositis (DM) are often associated with PCI, but details are unknown. Clinical characteristics were examined. [Methods] We examined 6 PCI patients Dokkyo Medical University Hospital whose clinical history and examination results were clearly described in charts. [Results] This hospital examined 4 cases of PM with PCI, 1 DM, and 1 clinically amyopathic dermatomyositis (A-DM). The average age was 57 ± 7.1 years old, 3 men and 3 women. The period from the start of steroids to the onset of PCI was 35-2588 days (median 304 days). Three cases of PM showed Raynaud's phenomenon and false bowel obstruction and met the diagnostic criteria for systemic sclerosis. It was considered a double syndrome. Three of them developed PCI repeatedly. Autoantibodies were observed in 3 cases of ARS antibody and 1 case of MDA-5 antibody. For treatment of myositis, PSL was administered in all cases, cyclosporine was used in 5 cases, and IVCY was used as an immunosuppressant in 2 cases. Two cases of PM died of repeated PCI infections. [Conclusion] PCI combined with PM had many clinical similarities

to PCI with systemic sclerosis.

W39-2

Clinical features of polymyositis/dermatomyositis with left ventricular systolic failure

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Conflict of interest: None

[Objective] To clarify the clinical features of polymyositis/dermatomyositis (PM/DM) with left ventricular systolic dysfunction (LVSD). [Methods] PM/DM cases who visited our department from 2010 to 2019, and were performed echocardiography at the first occurrence or recurrence of PM/DM were included. LVSD was defined as ejection fraction (EF) <50%. [Results] Thirty six cases (mean age 56.3 ± 13.2 years old, female 69.4%) were included. Mean EF was 63.8±13.6%. Pericardial effusion was observed in 13.9%. Five cases (13.9%) had LVSD, and 2 of them were proved myocarditis by myocardial biopsy. EVSD group had significant lower frequency of anti-aminoacyl-tRNA-synthetase antibody positivity (0% vs 54.8%) and higher those of diabetes (40.0% vs 3.2%) and arrhythmia (60.0% vs 6.5%) than non-LVSD group. Age and frequencies of hypertension, other auto-antibodies positivity, valvular disease, pericardial effusion, and interstitial pneumonia (IP) were similar. EF improved after treatment in 80% of LVSD group. During the observation period (52.0 ± 51.0 months), one each case died in these groups due to IP. [Conclusions] The frequency of LVSD in PM/DM was low, but it may be related to specific auto-antibody and underlying diseases.

W39-3

Clinical experience of anti-MDA5 antibody positive dermatomyositis in our institution

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Conflict of interest: None

[Objective] Prognostic predictors of rapidly progressive interstitial pneumonia associated with anti-MDA5 antibody-positive dermatomyositis have been reported. Meanwhile there are few reports on the long-term prognosis of surviving cases. The purpose of this observational study is to investigate the prognostic factors and the course of surviving cases at our institution. [Methods] The clinical features of cases treated at our institution were retrospectively investigated. [Results] There were 8 subjects and 2 died. The chief complaint was joint pain and rash. The maximum serum ferritin level at diagnosis averaged 404 ng / mL in surviving patients and 1498 ng / mL in dead patients. A-aDO2 was 47.4 for survivors and 34.3 for deaths. The period from PSL pulse to IVCY was 6.5 days for survivors and 14 days for deaths. The HRCT score in middle lobe was 0 to 1 for both groups. Elevated βDG, CMV antigenemia, and oral candidiasis was occurred in 2 cases. The 2 deaths both developed sepsis and pneumomediastinum. After discharge, there were no relapse, 1 required home oxygen therapy, and 3 shingles observed. [Conclusions] Ferritin level was likely to be useful in predicting poor prognosis. Simultaneous triple therapy is important. Attention should be paid to opportunistic infections.

W39-5

Clinical and Immunological Characteristics of Patients with Anti-KS Antibody

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Conflict of interest: None

[Objective] To clarify the clinical and immunological features of patients with anti-KS antibody. [Methods] PM/DM or ILD patients who visited our Hospital between 2010 and 2019 were screened. Autoantibodies were identified by immunoprecipitation assays and the clinical and immunological features were assessed retrospectively. [Results] Fifteen anti-KS positive were identified. Ten were female and 5 were male. Final diagnoses were 6 patients with ILD alone, 4 with clinically amyopathic DM (CADM), 3 with Sjögren's Syndrome (SjS), one each with rheumatoid arthritis, or CADM/SjS overlap. Although various diagnoses were determined, all patients had ILD with a chronic course. As for skin manifestations, 9 (60%) had mechanic's hands, 4 (27%) had Gottron's sign and one (7%) each had the heliotrope rash. Interestingly, all anti-KS positive showed no clinical muscle weakness or serum creatine kinase elevation. Moreover, seven (47%) had SjS/ sicca syndrome. There was a significantly high frequency of SjS/ sicca syndrome in anti-KS positive patients compared with anti-Jo-1 positive patients (47% vs. 12%, P=0.022). [Conclusions] These results suggest anti-KS antibody positive might form a distinguishable subset that is closely associated with SjS/sicca syndrome and CADM as well as chronic type ILD.

W40-1

Clinical correlations with nailfold capillaroscopy findings associations in systemic sclerosis A ten-year follow-up study

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Conflict of interest: None

[Objective] Nailfold capillaroscopy is an important tool, and nailfold capillary abnormalities is known as an evaluation of microvascular damage in systemic sclerosis (SSc). [Methods] Of the SSc patients measured from March 2006 to July 2019, seventy-three patients who could be re-evaluated 10 years later were included. We compared capillaroscopy patterns at the first visit and 10 years later. We also investigated the relationship between nailfold capillary abnormalities and clinical findings such as skin ulcer, pitting scar, MRSS, finger contructure, ILD, PAH, renal crisis, and specific antibodies. [Results] In capillaroscopy pattern, the pattern deteriorated at 26% and improved at 22%. The risk of skin ulcer 10 years later was late pattern at the first visit, skin ulcer, and anti-Topo-I antibody positive. The risk of finger contructure 10 years later was late pattern, severe MRSS, and anti-Topo-I antibody positive. However, clinical findings related to pattern deterioration could not be shown. [Conclusions] It was shown that cases with anti-Topo-I antibody-positive microvascular damage and a late pattern that are prone to skin ulcers and finger contractures.

W40-3

Characteristics of systemic sclerosis (SSc) complicated with calcinosis

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Conflict of interest: None

[Objective] Cutaneous calcinosis is often observed in SSc patients. This study aimed to identify how calcinosis linked to other clinical manifestations. [Methods] A retrospective cohort study analyzed 416 SSc patients using our SSc database. We examined the relationship between gender, clinical symptoms, disease type, complications, and autoantibodies in SSc cases with and without calcinosis. [Results] The proportion of SSc patients with calcinosis was 24%. The positive association was observed in the group of women (P = 0.04, OR 4.2), diffuse types (P = 0.00001, OR 2.9), Raynaud (P = 0.03, OR 2.9), nail fold bleeding (NFB) (P = 0.000001, OR 7.4), peripheral bone resorption (P = 0.000001, OR 8.0), myositis (P = 0.00001, OR 3.5), pulmonary hypertension (PH) (P = 0.04, OR 2.0), and anti-Scl70 antibody positive (P = 0.02, OR 1.9). The group with calcinosis

had higher mTSS value than the group without calcinosis (P = 4.8e-32). [Conclusions] Calcinosis was associated with Raynaud, NFB, peripheral bone resorption, PH, mTSS and diffuse type. These observations suggest that a peripheral circulatory insufficiency may causes calcinosis and common skin fibrosis grade linked with development of calcinosis. Calcinosis requires further studies including molecular cell biology search.

W40-4

Clinical significance of esophageal dilation on computed tomography (CT) in systemic sclerosis (SSc)

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Conflict of interest: None

[Objective] To investigate the clinical significance of esophageal dilatation on CT in SSc. [Methods] Among 260 SSc patients in our database, we enrolled 128 patients based on disease duration <10 years and availability of CT. After measuring the largest diameter at cross section in upper, middle, and lower thoracic esophagus on CT, we conducted multivariate analysis to identify factors associated with the diameters. [Results] Ninety nine patients were women, 60 were diffuse cutaneous SSc (dcSSc). The largest diameters at upper, middle and lower parts were 11.8±5.8, 9.8±6.8, and 12.4±8.1 mm, and maximal diameter was 15.8±6.5 mm. In the multivariate analysis, maximal diameter were correlated with presence of interstitial lung disease (ILD), long disease duration (all $p<0.05$), and middle part was correlated with presence of ILD, and lower part was correlated with presence of ILD, dcSSc and long disease duration (all $p<0.05$). In 75 patients of SSc-ILD, maximal and lower part diameters were negatively correlated with %FVC and %DLCO (all $p<0.05$). [Conclusions] Lower thoracic esophagus dilatation on CT might reflect SSc features, particularly with regard to restrictive impairment and severity of ILD.

W40-5

Vonoprazan for treatment of proton pump inhibitor-resistant reflux esophagitis in patients with systemic sclerosis

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Conflict of interest: None

[Objective] To investigate the efficacy of vonoprazan for PPI-resistant reflux esophagitis in SSc patients. [Methods] Among 260 SSc patients who visited our clinic between 2014 and 2019, we enrolled 10 consecutive SSc patients who were treated with vonoprazan for PPI-resistant reflux esophagitis. Reflux esophagitis was graded using Los Angeles (LA) classification, and patient-reported outcomes were assessed using a frequency scale for the symptoms of GERD (FSSG) questionnaire. Safety was also evaluated by retrospective chart review. [Results] Nine of 10 patients were female. Mean age was 57 ± 12 years with 11 ± 8 years of disease duration. LA classification was A in 2, B in 3, C in 3, and D in 2. Follow-up endoscopy revealed LA classification was M or N, indicating complete healing of reflux esophagitis, in 6 of 10 patients after switching to vonoprazan. FSSG score was also significantly improved (P = 0.043). Lower gastrointestinal involvement was found in 3 of 4 non-responders, but none of responders. Vonoprazan has been continuously used for 18 ± 11 months without any adverse events in all patients. [Conclusions] This pilot study suggests that vonoprazan is beneficial for PPI-resistant reflux esophagitis in patients with SSc.

W41-1

A nationwide survey of Takayasu arteritis (TAK) and giant cell arteritis (GCA) in Japan

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Conflict of interest: None

[Objective] A nationwide survey was conducted to estimate the number of patients, and to assess clinical aspects and prognosis of Takayasu arteritis (TAK) and giant cell arteritis (GCA) simultaneously in Japan using same questionnaires. [Methods] A primary questionnaire was sent to randomly selected medical institutions in order to estimate the number of patients according to the following 8 categories by the hospital size and number of beds: 100% of the university hospitals, the hospitals with 500 beds or over, and the specialty institutions; 80% of the hospitals with 400-499 beds; 40% of the hospitals with 300-399 beds; 20% of the hospitals with 200-299 beds; 10% of the hospitals with 100-199 beds; and 5% of the hospitals with 99 beds or less. We next sent a secondary questionnaire to the same institutions to characterize the clinical features and treatment of TAK and GCA. [Results] Of 3515 institutions, 1951 (55.1%) replied. The number of the TAK patients was estimated at 5320 (95% CI, 4810-5620) and GCA patients was estimated at 3200 (95% IC, 3830-3570). Ratios of numbers of patients with clinical diagnosis to patients meeting the diagnostic criteria were 1.08 for TAK and 1.22 for GCA. [Conclusions] Nationwide survey of TAK and GCA provided the estimated number of the patients.

W41-2

Search for novel biomarkers of large vessel vasculitis by comprehensive gene analysis using whole blood RNA-sequencing

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Conflict of interest: Yes

[Objective] Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are defined as different types of primary large vessel vasculitis (LVV). While inflammatory markers are used as indicators of disease activity, arterial lesions progress even asymptomatically. The purpose of this study is to search for biomarkers involved in the pathology of LVV. [Methods] Consecutive patients with active LVV (n=24; GCA: n=17, TAK: n=7) and healthy controls who visited our institution between August 2013 and May 2019 were enrolled. RNA from peripheral blood samples was extracted and gene expression was assessed. Gene Set Enrichment analysis (GSEA) and GO analysis identified gene candidates characteristically expressed in LVV. Furthermore, genes characteristic of GCA and TAK were examined. [Results] GSEA revealed 468 genes ($p<0.05$, FC> 1.5) differentially expressed in LVV. Among them, 267 genes showed increased expression in LVV, and 89 terms were identified using GO analysis. Of these 267 genes, 22 genes were upregulated in GCA but not in TAK ($p<0.05$), which were independent from age. [Conclusions] We identified the specific gene sets and pathways characteristic of LVV by RNA-sequensing using peripheral blood. In addition, we found independent characteristic gene expression between GCA and TAK.

W41-3

Clues for Diagnosis and treatment of polymyalgia rheumatica with normal CRP and blood sedimentation

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Conflict of interest: None

[Objective] Using 2012 EULAR/ACR PMR classification criteria, abnormal CRP or ESR is an essential item. If CRP and ESR are negative, PMR-like symptoms are present, but PMR cannot be diagnosed. Using Bird diagnosis criteria we can diagnose PMR patients with normal CRP and ESR and prescribe steroids. [Methods] Compared with PMR cases,

blood test data and myalgia sites, joint pain sites, and joint echo findings of CRP and blood sediment negative PMR cases. [Results] Among 119 PMR cases, 4 were CRP negative and 4 were ESR normal. Two cases (1.6%) had normal CRP and ESR. Articular echo showed tendon sheath synovitis in both shoulder biceps long muscles. Both patients started taking prednisolon, respectively 12.5mg and 15mg, but the effect recurred during predonisolone tapring. Relapse of PMR investigated with echo, predonisolone was increased. Without of use of immunosuppressants, one was able to discontinue predonisolone while one was continuing small amount of predonisolone. [Conclusions] Although CRP is useful for diagnosis and treatment evaluation in general PMR, rarely CRP negative PMR exists. In patients with CRP negative, joint echo is useful for determining the therapeutic effect.

W41-4

Optimal maintenance dose of corticosteroid in large vessel vasculitis

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Conflict of interest: None

[Objective] EULAR set the optimal doses of prednisolone (PSL) as 10 mg/day or 5 mg/day for Takayasu arteritis (TAK) or giant cell arteritis (GCA), respectively. The aim of this study was to evaluate the optimal dose in large vessel vasculitis (LVV). [Methods] 153 LVV patients (GCA, 31) who visited our department during 2008 to 2019 were retrospectively evaluated. The maintenance doss of PSL, disease duration, the use of immunosuppressive drugs and biologics, clinical backgrounds were evaluated. [Results] The mean maintenance doses of PSL (mg/day) after 1, 2-3, 4-5, or 6-10 years after treatment were 11.8, 6.2, 3.8, or 6.0 for TAK and 9.0, 2.0, 4.0, or 4.3 for GCA, respectively. The frequency of maintenance doses of PSL (mg/day) at 0, 1-4, 5, 6-9, or 10 was 12. 7%, 22.8%, 31.6%, 24.0%, or 7.6% for TAK, and 20%, 20%, 50%, 0.0 %, or 10% for GCA, respectively. While it was difficult to taper PSL to 5 mg/day in 30% of TAK patients, it was able to stop PSL in more than 10% of TAK patients. Biologics were used in 30 cases of TAK patients, and PSL was stopped in 6 cases. [Conclusions] It was possible to taper PSL to 5 mg/day in approximately 70 % of TAK patients after a couple of years, suggesting that it is better to set 5 mg/day as the optimal maintenance dose in TAK as well as GCA.

W41-5

The differentiation of clinical characteristics of patients with large vessel vasculitis between ages at onset

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Conflict of interest: None

[Objective] Takayasu arteritis (TAK) and giant cell arteritis (GCA) are affecting mainly large sized arteries, and age at onset is a important factor of diagnosis. However, histopathological loci are difference between TAK and GCA. The aim of this study is to clarify the difference of clinical characteristics in patients with large vessel vasculitis (LVV) between ages at onset. [Methods] The patients with TAK and GCA who were diagnosed at our hospital between April 2004 and December 2018 were included. We defined early onset group as the age at onset under 50 years old, and late onset group as greater 50 years old. The patients who only be affected temporal arteritis were excluded. The data from patients were retrospectively analyzed. [Results] Eventually, 22 patients were included: 7 with early onset group, 15 with late onset group. Vertebral artery, iliac artery, and femoral artery were significantly more affected in late onset group than early group. The dose of corticosteroid at 12 months, and the rate of immunosuppressant use at the last observational point were significantly lower in late onset group, whereas the recurrent rate was not significantly different. [Conclusions] The response of treatment and affected vessel in patients with LVV may be difference by ages at onset.

W42-1

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 in case of accompanying early stage of onset or active findings of CTD, use of immunosuppressive therapy is recommended. However, the effectiveness at PH associated with SSc is low. The pathogenesis of PH with SSc may be different from that of other CTD. [Methods] We analyzed 21 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 (n=13), non-SSc group (n=8). 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] Diastolic pressure gradient was significantly lower in the SSc group (7.8 ± 1.5 vs 17.3 ± 3.9, $t = 0.007$). [Conclusion] 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.

W42-2

Delayed recovery of elevated pulmonary arterial pressure after exercise as an early sign of pulmonary vascular remodeling leading to pulmonary hypertension in patients with systemic sclerosis

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Conflict of interest: None

[Objective] Pulmonary arterial hypertension (PAH), a fatal complication of systemic sclerosis (SSc). It is not clear that reversible vascular damage precedes the irreversible decrease in PA vascular bed. To clarify this hypothesis, we investigated characteristics by exercise echocardiography among patients with SSc having normal PA pressure. [Methods] We retrospectively studied 36 patients with SSc who showed normal mPAP (<25mmHg) by right heart catheterization (RHC). According to the RHC data, patients were divided into 3 groups; mPAP ≦17, 18-20, and 21-24. [Results] TRPG just after the exercise were higher in patients with mPAP 18-20 and 21-24 than in those with ≦17 (P=0.006). Patients with mPAP 18-20 and 21-24 tended to have higher TRPG at 3 min after the exercise than those with mPAP ≦17. Patients having mPAP 18-20 had frequently TRPG≧50 at 3 min after the exercise while no patients with mPAP ≦17 had TRPG≧50 (P=0.01). Five patients developed PH, and 4 patients showed an elevation of TRPG at 3 or 5 min after the exercise at the onset of PH. [Conclusions] Delayed recovery of elevated PA pressure after exercise may reflect an early sign of vascular remodeling losing reversibility by repeated spasmic change of PA.

W42-3

Cytokine analysis in pulmonary capillary of pulmonary hypertension complicated with onnective tissue disease and its relation to pathogenesis

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Conflict of interest: None

Since CTD-PH has various organ involvement, the pathological factors are complicated and it is difficult to select treatment. It is known the cytokines such as IL-6, IL17, and IL-21 is associated in the pathogenesis of collagen disease and PH. [Objective] To clarify the relationship between cytokine profile and disease states in CTD-PH. [Methods] 14 cases of CTD-PH (SSc-PH: 8, MCTD-PH: 4, SLE-PH: 2), Other-PH: 6, and scleroderma controls: 2. Right heart catheterization was performed and serum IL-6, IL-17, IL-21 and MCP-1 in pre and post-capillary were measured. In addition, the relationship between cytokines and clinical information in each group was compared. [Results] Serum MCP-1, IL-6, and IL-21 were higher in the SSc-PH group than in the other disease groups. In the SSc-PH group, post-capillary serum MCP-1 decreased as compared to pre-capillary. On the other hand, serum IL-17 tended to be higher in non-SSc group compared to the SSc-PH group. In addition, patients with decreased serum IL-17 and IL-21 before and after treatment showed improved pulmonary hemodynamics. [Conclusions] SSc-PH had a different cytokine profile than non-SSc-PH. In addition, it was suggested that serum IL-17 and IL-21 may be involved in improving the pathological conditions associated with treatment.

W42-5

Associated factors with chest wall muscle atrophy in patients with systemic sclerosis associated interstitial lung disease

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Conflict of interest: None

[Objective] We previously reported reduced chest wall muscle volume is correlated with decline of forced vital capacity independently with interstitial lung disease (ILD) area on computed tomography (CT) in systemic sclerosis (SSc) patients with ILD. We investigated the factors associating with chest wall muscle atrophy in patients with SSc-ILD. [Methods] This is a retrospective study enrolling 36 patients with SSc-ILD who repeated both of respiratory function tests and chest CT with 1 to 3 years of interval. Chest wall muscle area (CWMA) was determined at the level of 9th thoracic spine on CT by independent two examiners. [Results] Twenty six were female, 19 were diffuse cutaneous SSc (dcSSc), and 20 were corticosteroid users. Mean age was 54.9±13.5 years with 2.8±3.0 years of disease duration and 22.6±2.5 on body mass index (BMI) of. Multivariate analysisshowed BMI decline and maximum dose of corticosteroid were independently associated with reduction of CWMA. Stratified analyses according to sex and disease subtype revealed the consistent results. [Conclusions] Our study suggested use of corticosteroids and decline of BMI were associated with chest wall muscle atrophy in patients with SSc-ILD.

W42-6

Angiogenic humoral factors associated with the development of systemic sclerosis

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Conflict of interest: None

[Objective] To clarify cytokines and/or chemokines associated with systemic sclerosis (SSc) development, we examined angiogenic humoral factors in sera from patients with pre-clinical stage, early, and typical SSc. [Methods] We divided 9 patients into 3 groups according to the ACR/EULAR 2013 and ACR1980 classification criterion. Serum samples were obtained from patients with anti-centromere antibody, who met neither criterion (group 1, pre-clinical stage), ACR/EULAR 2013 but not ACR1980 (group 2, early SSc) or both criterion (group 3, typical SSc). We examined the expression levels of 20 humoral factors using commercially available array kit. [Results] Average values of EGF, ENA-78, bFGF, IGF-I, IL-8, MCP-1, TGF-β1, thrombopoietin, VEGF, and VEGF-D in group2 were more than 2-fold higher in comparison with those of group1. Significant difference was found in serum expression levels of IGF-1, RANTES, and VEGF between in group1 and group2. There was significant correlation between serum IGF-1 and RANTES levels ($r=0.721$, $p=0.028$). The expression level of VEGF in group 3 was higher than that of group1. [Conclusions] Among angiogenic humoral factors, IGF-1, RANTES and VEGF may be involved in the development from pre-clinical stage of patients to SSc.

W43-2

An Analysis of Biological Markers Predicting Tofacitinib Efficacy in Japanese Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Objectives] Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). We evaluated whether laboratory data could predict tofacitinib efficacy in Japanese patients (pts) with RA. [Methods] Data were pooled from 2 Phase (P) 2 (NCT00603512, NCT00687193) and 1 P3 study (NCT00661661). Pts received tofacitinib 1, 3, 5, or 10 mg twice-daily, with/without methotrexate (MTX), and 15 mg BID without MTX. Laboratory data and efficacy measures (DAS28-4 [CRP], DAS28-4 [ESR], ACR-N response) were recorded at months (M) 1 and 3. Multivariate analyses were used to assess the predictive value of laboratory data at M1 for changes from baseline (Δ) in M3 efficacy measures. [Results] In all, 467 pts were included. Decreased platelet count at M1 was predictive of M3 ΔDAS28-4 (CRP), ΔDAS28-4 (ESR), and ΔACR-N (all $p<0.05$). Increased low density lipoprotein cholesterol (LDL-c) at M1 was predictive of M3 ΔDAS28-4 (CRP) and ΔACR-N (all $p<0.05$). Increased hemoglobin (Hb) at M1 was predictive of M3 ΔDAS28-4 (ESR; $p<0.05$). [Conclusion] Tofacitinib efficacy at M3 in Japanese pts with RA was associated with decreased platelet counts, and increased LDL-c and Hb levels at M1. However, disease- and treatment-specific changes in select laboratory data and other factors may confound interpretation.

W43-3

Do osteoporotic drugs affect daily function in patients with rheumatoid arthritis?

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Conflict of interest: None

[Objective] The function of RA is affected by multiple factors. We assumed that drugs for RA and osteoporosis would affect the RA-function. We analyzed the factors related to the RA-function with RA cohort. [Methods] We recruited 369 RA-patients treated for 2 years. Osteoporotic drugs, Steroids, MTX, Biologics (Bio), Janus Kinase Inhibitor (JAK-i), HAQ sub-items (Dressing, Arising, Eating, Walking, Hygiene, Reach, Grip, Activities) were recorded. We adopt change of HAQ sub-items as the objective variable and each parameter as the explanatory variable. Then univariate and multivariate analysis were performed. [Results] The averages of age, DAS28-ESR and MTX-dose were 63.5, 2.71 and 7.29. Factors extracted on both univariate and multivariate analysis were described below; Dressing: Sex, Arising: Sex, Eating: DAS28-ESR and osteoporotic drug count, Walking: Steroid and osteoporotic drug number, Hygiene: None,

Reach: DAS28-ESR, MTX, osteoporotic drug count, Grip: osteoporosis drug count, Activities: gender and MTX. [Conclusions] For maintenance of RA patients-function, RA-activities might have to be suppressed with MTX rather than Steroid and osteoporosis might have to be treated with the minimum number of drugs.

W43-4

Glucocorticoid use associates with deterioration of muscle quality and function - from the CHIKARA study -

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Conflict of interest: None

[Introduction] We previously reported that glucocorticoid (GC) use was risk for developing sarcopenia and that sarcopenia was not associated with muscle function in patients with rheumatoid arthritis (RA). We longitudinally investigated factors associating to deterioration of muscle quality and function. [Methods] We examined muscle quality and function (power, speed, and balance in standing-up motion) using exercise functional analysis device (BM-220, Tanita, Japan) at 1- and 3-year follow-up in the prospective observational CHIKARA study. We assessed associations between changes of these parameters and body composition, disease activity, treatment, physical function and history of falls. [Results] Eighty-one RA patients completed survey. Average GC dose during 2 years negatively correlated with changes of muscle quality, power and speed. SDAI at 1 year negatively correlated with power and speed. No factor associated with HAQ and history of falls. No factor was detected by multiple regression analysis. [Conclusion] GC use associated with deterioration in muscle quality and function, as well as sarcopenia development. GC may adversely affect muscle mass and quality. In addition, as high disease activity may lead low exercise function, its control is important.

W43-5

Cross-sectional study to explore characteristics of rheumatoid arthritis patients who do not achieve treatment goal yet

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Conflict of interest: Yes

[Objective] Although treatment goal of RA is REM or LDA, there are not a few patients who don't achieve goal. The aim of this study is to identify characteristics of those patients. [Methods] Toyohashi RA database in 2018 was used. All patients were seperated using three categorizations: (1) Boolean REM or not, (2) SDAI REM or not and (3) SDAI REM+LDA or not. Significant variables by univariate analysis were analyzed by multivariate analysis. Cut-off values (CO) were also calculated. [Results] 998 RA patients were analyzed. (1) Boolean REM 39.4%. Not 60.6%. Valuables in relation to REM were ACPA titer (Odds ratio=0.9995, CO=42.0U/ml), stage I+II (OR=1.86) and mHAQ (OR=0.19, CO 0.0). (2) SDAI REM 51.0%. Not 49.0%. Valuables in relation to SDAI REM were stage I+II (OR=2.2), PSL doses (OR=0.86, CO=0.0mg/d), mHAQ (OR=0.26, CO=0.0) and concomitant pulmonary disease (OR=0.60). (3) SDAI REM+LDA 87.2%, Not 12.8%. Valuables in relation to SDAI REM+LDA were PSL doses (OR=0.26, CO=0.0mg/d) and concomitant pulmonary disease (OR=0.58). [Conclusions] Decreased PSL doses is likely to be results of REM or LDA. On the other hand, concomitant pulmonary disease and advanced stage are likely to be causes. ACPA titer and mHAQ have the characteristics of both causes and results.

W43-6

Lower or higher BMI could be a risk factor to exacerbate disease activity flare after discontinuation of adalimumab in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] Body mass imdex (BMI) has been reported to be a risk of RA treatment failure and bone erosion progression, but few studies have examined whether BMI is a risk factor for relapse after discontinuation of biological DMARDs. In this study, we conducted a sub-analysis of the results of the PROUD study and analyzed whether BMI is a risk factor for relapse. [Methods] The subjects were 53 cases who participated in the PROUD study. We compared BMI, other patient backgrounds, and disease activities in 20 cases that relapsed by 52 weeks and 33 cases that did not relapse. [Results] Among 53 Patients, median age was 62.0 years, females were 79.2%, and median BMI was 21.6. BMI Low (less than 20) / Normal (20 to 25 and High (25 and above) were 13, 32 and 8 patients respectively. Baseline background parameters were not significantly different between the relapsed group and the non-relapsed group. There was no significant difference in remission retention rate in both groups, but the BMI non-normal group patients tended to relapse earlier, and the period until relapse in the flare group tended to be earlier in the BMI non-normal group. [Conclusion] This study suggested that non-normal BMI was a potential risk of RA relapse and exacerbation of disease activity after cessation of ADA.

W44-1

Influence of concurrent chronic kidney disease on the treatment of rheumatoid arthritis - results from the IORRA cohort-

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Conflict of interest: None

[Objective] To examine the influence of CKD on remission and adverse clinical events in patients with RA using IORRA cohort. [Methods] CKD was defined as either eGFR<60 or the presence of proteinuria on two consecutive surveys in 2012. The severity of renal dysfunction was classified into four groups: normal, eGFR≧60; mild, 45≦eGFR<60; moderate, 30≦eGFR<45; and severe, eGFR<30. The primary outcome was time to remission. We had enrolled 2407 non-remission RA patients and had assessed them for five consecutive years. [Results] The numbers of RA patients with CKD and without CKD were 401 and 2006, respectively. The severity of kidney dysfunction was normal in 1884 (78.3%), mild in 388 (16.1%), moderate in 108 (4.5%) and severe in 27 (1.1%). The proportion of RA patients with CKD achieving remission was significantly lower than that of non-CKD patients (56% vs 70%, p<0.0001). In addition, mortality, admission rate and admission rate due to infection during the study period were significantly higher in CKD patients. In a multivariate Cox regression model, CKD was also significantly associated with remission failure

(HR: 1.21 [95% CI: 1.01-1.45]). [Conclusions] In the present study, we demonstrated that the complication of CKD was associated with remission failure for the treatment of RA.

W44-2

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

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Conflict of interest: Yes

[Objective] Little is known about the bDMARD on the risk of decreasing kidney function in RA patients. [Methods] We recruited 1058 RA pts from ASHURA database. The following background factors were analyzed: age, sex, type of bDMARD, MTX and PSL dosages, use of csDMARD and NSAIDs, BMI, smoking history, diabetes, hypertension, dyslipidemia, Cr, CRP, MMP-3 level and SDAI. We divided into two groups: bDMARD with MTX treatment group (744pts) and MTX monotherapy group (314pts). 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, 285pts 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 88.5 ± 21.8 to 86.1 ± 21.5 and 83.7 ± 21.0 at 6 months and 1 year in the combination treatment group and from 86.3 ± 37.9 to 79.5 ± 19.1 and 78.5 ± 19.5 in the MTX monotherapy group. A significant difference was observed between the groups ($p = 0.0066$) and during the treatment period ($p < 0.001$). [Conclusions] BDMARD use may lower the risk of decreasing kidney function in patients with RA.

W44-3

Assessment of the distribution of affected joints in the treatment of rheumatoid arthritis: ANSWER Cohort

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Conflict of interest: Yes

[Objective] Disease activity of rheumatoid arthritis is assessed with composite measurements, and the distribution of affected joints is not taken for consideration. This research focuses on the distribution of affected joints. [Methods] Information of swelling and tenderness of IP, PIP, MCP, wrist, shoulder, hip, knee, ankle and MTP in patients treated by biologics or JAK inhibitors was analyzed. [Results] Totally 1724 cases were analyzed. Frequent joints with swelling and/or tenderness were wrist (51% at the initiation to 26% at 6 month), 2MCP (44% to 18%), 3MCP (24% to 10%), knee (26% to 12%), 3PIP (23% to 9%), ankle (20% to 7%). At 6 month, among patients with low disease activity or remission, 17% of wrist, 6% of 2MCP, 4% of 3MCP, 8% of knee and 5% of ankle had findings. MCP tended swelling, and wrist, knee and ankle tended both swelling and tenderness. In patients with low BMI (<25), load joints with findings were knee (26% to 11%) and ankle (19% to 6%), whereas knee (30% to 16%) and ankle (26% to 9%) with high BMI (≧25). [Conclusions] Findings were often observed in wrist, 2/3MCP, 3PIP and knees. These persisted frequently even though the treatment course was good. In the cases with high BMI, the findings of knee and ankle were increased compared to the cases with low value.

W44-4

Relationship between HLA-DRB1 and therapeutic response to biological disease-modifying antirheumatic drugs in rheumatoid arthritis

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Conflict of interest: None

[Objective] HLA-DRB1 is a disease susceptibility gene for rheumatoid arthritis (RA). In this study, we analyzed the relationship between HLA-DRB1 alleles and the therapeutic response to biological disease-modifying antirheumatic drugs (bDMARDs). [Methods] We enrolled RA patients who started first bDMARDs from June 2012 to August 2018 and continued for at least three months in our hospital. HLA typing with NGS was performed by peripheral blood. Treatment response was defined as achievement of Simplified Disease Activity Index 50% improvement (SDAI50) at three months. The association between the HLA-DRB1 allele and SDAI50 was examined. [Results] The rate of SDAI50 achievement was 49% in abatacept (ABT) group (n=37), 51% in TNF inhibitor (TNFi) group (n=41) and 54% in tocilizumab (TCZ) group (n=28). In the ABT group, the nominal p-value of association between HLA-DRB1*04:05 carrier and SDAI 50 achievement was 0.22 by Fisher's exact test, but it was not significant when corrected by multiple comparison test (q=0.53). In the TNFi or TCZ groups, there was no significant association between HLA-DRB1 allele and SDAI50. [Conclusion] HLA-DRB1*04:05 carrier may be possibly related to the effectiveness of ABT. Further analysis with large population is required.

W44-5

The efficacy of TNF inhibitor without Fc portion in rheumatoid arthritis patients with high RF titers -ANSWER cohort study-

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Conflict of interest: None

[Objective] Rheumatoid factor (RF) is an antibody against the Fc portion of immunoglobulin G. There have been reported that patients with high RF titer had attenuated response to TNFi. However, these reports didn't include CZP. Our study aim is to investigate the effect of high RF titer on CZP, which is the only TNFi without Fc portion. [Methods] RA patients treated with TNFi was extracted from KANSAI consortium ANSWER cohort database. Patients were divided into 4 categories according to RF titers (RF^1: patients with RF 0-15.0 IU/mL, RF^2: 15.0-56.0, RF^3: 56.0-161.6, RF^4: 161.6-7555). SDAI after 1-year treatment (1-year SDAI) was assessed. [Results] RF^4 group included 17 IFX, 24 ADA, 33 ETN, 45 GLM, and 19 CZP cases. Baseline age, sex, disease duration, and SDAI were statistically insignificant between TNFi. 1-year SDAI were IFX 11.3±17.9, ADA 9.1±7.8, ETN 7.9±7.8, GLM 9.2±11.0, CZP 4.0±3.4. Then, we compared TNFi with Fc portion (IFX, ADA ETN, GLM) (w/ Fc)

and without Fc portion (CZP) (w/o Fc). Baseline age, sex, disease duration, and SDAI were statistically insignificant between these groups. 1-year SDAI were w/ Fc 9.2±11.0 vs. w/o Fc 4.0±3.4 (p=0.048). [Conclusions] TNFi without the Fc portion may be more effective than those with Fc portion in patients with high RF titers.

W44-6

The effect of inflammation level on the drug retention rates of biological DMARDs-ANSWER cohort study-

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Conflict of interest: None

[Objective] We aim to investigate the drug retention rate of biological DMARDs (bio) in different CRP groups. [Methods] RA patients treated with bio were extracted from KANSAI consortium ANSWER cohort database. Patients were divided into 3 categories according to CRP levels (CRP^{low}: patients with CRP 0-0.3 mg/dL, CRP^{int}: 0.3-1.9, CRP^{high}: 1.9-16.0). The 3-year drug retention rate was assessed. [Results] CRP^{low} group included 208 TNFi, 65 IL-6Ri, and 61 CTLA4-Ig cases; CRP^{int} 189, 50, 78; and CRP^{high} 157, 97, 61, irrespectively. Age (CRP^{low} TNFi 55.6±14.0, IL-6Ri 57.1±14.8, CTLA4-Ig 61.0±12.9 year-old; CRP^{int} 58.7±15.8, 56.5±14.4, 65.6±10.8; CRP^{high} 63.0±13.9, 60.3±13.1, 69.6±11.6), disease duration (CRP^{low} TNFi 6.7±7.8, IL-6Ri 10.4±10.3, CTLA4-Ig 9.6±9.5 years; CRP^{int} 7.2±9.2, 9.8±9.2, 10.9±11.8; CRP^{high} 6.5±10.6, 7.3±8.2, 10.9±10.2), bio naïve rate (CRP^{low} TNFi 51.0, IL-6Ri 21.5, CTLA4-Ig 45.9%; CRP^{int} 60.8, 24.0, 51.3; CRP^{high} 66.9, 31.8, 67.2) had statistical significance between bio in each CRP group. The results of the 3-year drug retention rate were as follows; CRP^{low} TNFi 63.8, IL-4Ri 73.9, CTLA4-Ig 69.9% (p=0.761); CRP^{int} 52.9, 80.9, 67.8 (p=0.069); CRP^{high} 37.9, 74.3, 56.0 (p=0.002). [Conclusions] IL-6Ri may have higher drug retention rate in patients with high basal CRP levels.

W45-1

Treatment response in patients with rheumatoid arthritis treated with certolizumab pegol according to determination of anticyclic citrullinated peptide antibody and rheumatoid factor levels

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Conflict of interest: None

[Objectives and Methods] We investigated the treatment response in 123 patients with rheumatoid arthritis enrolled in Tsurumai Biologics Communication Registry and who had initiated certolizumab pegol (CZP) treatment by October 2019. Our primary endpoints were the anticyclic citrullinated peptide antibody (ACPA) and rheumatoid factor (RF) levels. We focused on 69 patients treated with CZP for>52 weeks and whose DAS28-ESR could be evaluated pre- and post-treatment. We divided the data from patients according to the initial ACPA and RF levels into an low ACPA/low RF group (L/L) (ACPA ≦45/RF ≦55; n=12), a high ACPA/low group (H/L) (ACPA>100/RF≦55; n=13), and a high ACPA/high group (H/H) (ACPA>100/RF>160; n=14); and we assessed the treatment response to CZP based on DAS28-ESR results. [Results] The mean changes in DAS28-ESR were 3.86→2.85 in the L/L group; 5.04→3.73 in the H/L group, and 5.54→3.53 in the H/H group. Patients in the H/L and H/H groups had significantly improved at 52 weeks. The magnitude of improvement in ΔDAS28-ESR from the initial values was L/L group < H/L group < H/H group. [Conclusions] CZP significantly improved DAS28-ESR in patients with high ACPA and RF levels in a proportional manner. In other words, CZP showed an effect in the expected case enough as TNF high level.

W45-2

Scoring Model for Predicting Low Disease Activity in Biologic-naive Elderly Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We aimed to develop a scoring model for predicting low disease activity (LDA) in biologic-naive elderly patients with rheumatoid arthritis (RA). [Methods] This retrospective cohort study included 82 elderly patients with RA (age 65 years or older) who received initial biologic agent treatment at two hospitals of Showa University from November 2005 to December 2018. The primary endpoint was LDA (Disease activity score-28 with ESR [DAS28ESR]≦3.2) at 1 year after the treatment. A scoring model was developed using multivariable analysis. The integers score was derived from the odds ratios of these factors and divided into three groups. The scoring model accuracy was assessed. [Results] Forty-three patients (52.4%) achieved LDA. The scoring model included six factors-neutrophil-to-lymphocyte ratio (NLR), anemia, DAS28ESR, matrix metalloproteinase-3 (MMP-3), rheumatoid factor (RF), and diabetes mellitus (DM)-based on the multivariable analysis. The odds ratios of these factors were scored (NLR, RF, DM, Anemia=2 points, DAS28ESR, MMP3=1 point) and divided into three groups (0-4, 5-7, and 8-10). The high score group achieved a positive predictive value of 83%. [Conclusions] The scoring model accurately predicted LDA in biologic-naive elderly patients with RA.

W45-3

Relation between effects of targeted anti-rheumatic drugs and affected joint features: A multicenter observational study based on the NinJa (National database of rheumatic diseases in Japan)

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Conflict of interest: None

[Aim] To investigate the relation between effects of targeted anti-rheumatic drugs and affected joint features. [Methods] Patients who were serially registered in 2016 and 17 (7,315) and 17 and 18 (7,809) and treated without steroid from the first term were stratified into 5 groups, MTX (*M*), *M*+antiTNF, *M*+CTLA4Ig, *M*+antiIL6R and *M*+antiJAK. Transformation matrix of each group was computed using mean joint index vectors of stratified patients[1]. We compared transformed vectors applying transformation matrices on vectors **S** (1, 1, -1), **E** (1, 1, 0), and **L** (1, 1, 1). [Results] Vectors **S**, **E** and **L** went (0.8, 0.6, -0.3), (0.7, 0.6, 0.1) and (0.6, 0.6. 05), respectively, by transformation matrix computed from *M*. Only z component of transformed **S** vector by *M*+antiTNF was smaller than that by *M*.

All of the components of transformed **S**, **E** and **L** vector by *M*+CTLA4Ig were smaller than those by *M*. Z Components of transformed vectors from **S**, **E** and **L** by *M*+antiIL6R were smaller than those by *M*, however, y components became larger than 1. Z component of transformed **S** vector and all the components of transformed **E** and **L** by *M*+antiJAK were smaller than those by *M*. [Conclusion] Effects of the targeted anti-rheumatic drugs may depend on affected joint size and location. 1. Nishiyama S et al. J Big Data 2018;5:37

W45-4

Smoking cessation improves disease activity of rheumatoid arthritis - TOMORROW study -

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Conflict of interest: None

Objective: There is few reports of smoking on the effects of disease activity on rheumatoid arthritis (RA). In this study we analyze the effect of smoking cessation on disease activity of RA. **Methods:** We analyzed date from the TOMORROW study (UMIN000003876), which is a 10-years prospective cohort for age and sex matched RA (n=208) and volunteers (n=205). Data on smoking was self-reported on the questionnaires. We analyzed 27 RA with current smokers in 2010. We classified into 2 groups according to whether they voluntarily cease smoking during the period from 2010 to 2019, and compared for changes (Δ) in DAS28ESR, mHAQ and ACPA from 2010 to 2019. In cessation group, we also evaluated the changes in disease activity and PSL dose per day from the previous year of ceasing smoking to the following year. **Results**: In 27 RA patients, there were 12 patients in cessation group. There was no significant difference in changes in ΔDAS28ESR, ΔmHAQ and ΔACPA between 2 groups. In cessation group, there was an improvement trend in the changes of DAS28ESR (previous 3.26±1.7→following 2.86±1.5), tender joint counts (2.3±3.2→1.5±2.5), swelling joint counts (2.4±4.3→1.3±2.6), PSL (1.6±3.1→1.1±1.8), ACPA (374±357→310±378). **Conclusions:** In RA, smoking cessation may improve the disease activity.

W45-5

Changes in the circumference of the finger (P) IP Joint can be evaluated more easily and more precisely than ultrasonography

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Conflict of interest: None

[Introduction] Ultrasonography is a popular evaluation for synovial swelling of finger joints. However due to issues of human resources and time, frequent work could be a burden in daily clinics. As a simpler method, we examined measuring the circumferences of the finger (P) IP joints. [Purpose] To elucidate whether the changes of our circumferences are equivalent to the changes of ultrasonography. [Methods] Two hundred fingers in twenty RA patients required the introduction or change of biologics were included. Semi-quantitative ultrasonographic evaluation and circumference measure using the ring gauge were performed in before and 4 weeks after of the intervention. The ring gauge can measure the inner circumference every 1mm from 41mm to 71mm. We determined the cut-off value of the amount of change in the circumference for a 1 or more change in semi-quantitative score by ROC analysis. [Results] The mean age was 60.4 years. The cut-off value for the GS score change was 2 mm; however a useful cut-off value for the PD score was not determined. [Conclusions] A change of 2 mm in the circumference could be equivalent to a 1 change in the GS score. We believe that detecting changes in the circumference will help to evaluate the disease activity more easily and precisely.

W45-6

A longitudinal analysis of fatigue with Japanese patients with RA based on the IORRA cohort

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Conflict of interest: None

[Objective] To investigate fatigue longitudinally in Japanese patients with RA. [Methods] Among Japanese patients with RA in the IORRA study enrolled both in April 2015 (Baseline) and in April 2017 (2 Year), fatigue was measured by the Checklist Individual Strength 8R (CIS 8R): normal, CIS 8R≦26; heightened fatigue, 27≦CIS 8R≦34; severe fatigue, CIS 8R≧35. We performed a longitudinal investigation of the association of change in fatigue (ΔCIS 8R: 2 Year-Baseline) with background factors and changes in RA clinical factors (ΔDAS28, ΔJ-HAQ, ΔPain VAS: 2 Year-Baseline) with a multiple regression analysis. [Results] Among 3,529 RA patients, fatigue severity was normal in 1,579 (44.7%), heightened in 1,015 (28.8%) and severe in 935 (26.5%) in April 2015, and normal in 1,575 (44.6%), heightened in 1,023 (29.0%) and severe in 931 (26.4%) in April 2017, respectively. ΔCIS 8R was significantly associated with ΔDAS28 ($\beta = 0.106$, $P < 0.001$), ΔJ-HAQ ($\beta = 0.113$, $P < 0.001$) and ΔPain VAS ($\beta = 0.124$, $P < 0.001$). [Conclusions] Change in fatigue was significantly associated with changes of disease activity, functional disability and pain in patients with RA.

W46-1

The trends of the dose reduction or dose increase of 6 biological DMARDs in Japanese patients with RA by NinJa 2018 cohort

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Conflict of interest: None

[Objective] To review the dose reduction or increase of 6 biological DMARDs in patients with RA. [Methods] In 15440 Japanese RA patients registered with NinJa2018, 4127RA patients medicated biological DMARDs with or without csDMARDs were researched the dose and interval of bDMARD. [Results] The rate of dose increase of 611 RA patients medicated TCZ by subcutaneous injection is 7.2%, the rate of reduction is 16.4%. The rate of increase of 562 RA patients medicated TCZ by intravenous injection is 5.3%, the rate of reduction is 32.6%. The rate of reduction of 905 RA patients medicated ETN is 45.4%. The rate of reduction of 304 RA patients medicated ABT by subcutaneous injection is 16.4%. The rate of increase of 562 RA patients medicated ABT by intravenous injection is 2.0%, the rate of reduction is 23.8%. The rate of increase of 420 RA patients medicated GLM is 21.4%, the rate of reduction is 11.7%. The rate of increase of 304 RA patients medicated IFX is 55.9%, the rate of reduction is 10.5%. The rate of increase of 420 RA patients medicated ADA is 3.1%, the rate of reduction is 4.0%. The rate of reduction of 187 RA patients medicated CZP is 14.4%. [Conclusion] 3 bDMARDs, TCZ, ETN, ABT were widely used were selected the dose reduction, IFX and GLM were selected the dose increase.

W46-4

Clinical outcome in patients with rheumatoid arthritis switched to sarilumab after tocilizumab failure

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Conflict of interest: None

[Objective] The present study retrospectively assessed the efficacy of sarilumab in patients with rheumatoid arthritis (RA) who failed to respond to treatment with tocilizumab. [Methods] A retrospective study of 5 RA patients who did not respond to tocilizumab was conducted. Disease activity was assessed by the Disease Activity Score 28 Erythrocyte Sedimentation Rate (DAS28-ESR), the Simplified Disease Activity Index (SDAI), and the Clinical Disease Activity Index (CDAI). The effects of tocilizumab to sarilumab switch were evaluated at 4 and 12 weeks after switching. [Results] Four patients who had been treated with tocilizumab were switched to sarilumab. One patient who had been treated with tocilizumab previously were switched from JAK inhibitor to sarilumab. Treatments with disease-modifying antirheumatic drugs before the switch, especially methotrexate (MTX), was maintained. There was a reduction from baseline in DAS28-ESR, SDAI, and CDAI values at 4 and 12 weeks. [Conclusions] Switching from tocilizuma to sarilumab improved response to therapy.

W46-5

Analysis of longterm observation of patients with rheumatoid arthritis (RA) who achieved bio-free condition (BF) with adalimmab (ADA)

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Conflict of interest: Yes

[Objective] To analyze the longterm observation of patients with RA who achieved BF with ADA. [Methods] We analyzed patients who discontinued ADA with clinical remission (CR), n=25 (M 6, F 19) and with low disease activity, n=1 (F) with 19.4±7.8M of ADA treatment. Their age was 51.2±11.9 YO and disease duration was 45.1±48.4M. [Results] Four patients re-started ADA due to flare but achieved BF again with the intensification of the treatment. DAS28-CRP significantly decreased from 3.45±1.32 at base line (BL) to 1.55±0.41 ($p<0.0001$) at BF. It remained 1.59±0.59 (n=25) at 24M after BF and 1.56 ± 0.39 (n= 20) at 48M. mHAQ significantly decreased from 0.42 ±0.46 (BL, n=19) to 0.02 ±0.05 ($p<0.002$) at BF. It remained 0.03±0.07 (n=19) at 24M and 0.06 ± 0.14 (n=14) at 48M. PSL (mg/day) was 3.2±3.3 (BL) to 2.2±2.8 (p=0.105, at BF) and 2.04±2.13 (n=25) at 24M, and 1.73 ±1.9 (n=20) at 48M. MTX (mg/W) was 10.1±2.9 (BL) to 10.6±2.6 ($p< 0.78$) at BF, 10.4±3.3 (n=25) at 24M,10.7±3.4 (n=20) at 48M. The number of csDMARD significantly increased from 0.8±0.6 (BL) to 1.3±0.9 ($p<0.001$, at BF), and were 2.56 ±0.94 (n=25) at 24M, 1.6 ±1.01 (n=20) at 48M. [Conclusions] BF can be sustained with an adequate dose of MTX and combination of csDMARDs.

W46-6

Successful tumor necrosis factor inhibitor cessation among rheumatoid arthritis patients who received different types of tumor necrosis factor inhibitors as their first biologic agent

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Conflict of interest: None

[Objective] To compare the prevalence of successful tumor necrosis factor inhibitor (TNFI) cessation among rheumatoid arthritis patients who received different TNFIs as their first biologic agent. [Methods] The prevalence of TNFI cessation after achieving sustained improvement, subsequent flare and readministration of TNFI for each of the first TNFIs which was started after methotrexate failure were investigated. One-year flare- and biologic-free survivals were compared between different TNFIs and the whole molecule IgG agents and the others. [Results] In 119 patients included, infliximab (n=51), infliximab biosimilar (1), adalimumab (21), golimumab (2), etanercept (39), certolizumab pegol (5) were used as the initial biologic agent combined with methotrexate. Ninety-two (77%) stopped TNFI after sustained improvement and 24 of them required additional treatment before TNFI cessation. Over 1 year, 29 patients had a flare and 24 restarted a TNFI. Flare- and biologic-free survivals were similar between infliximab and etanercept and between the whole molecule IgG agents and the others. [Conclusions] More than half of the patients were successfully discontinued TNFI therapy over 1 year. The rate of successful discontinuation of TNFI were similar between different types of TNFIs.

W47-1

Comparison of patient background and treatment outcome by Baricitinib dose in clinical practice

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Conflict of interest: None

[Background] For rheumatoid arthritis (RA), Baricitinib (BAR) is usually taken 4mg once a day, but can be taken at 2mg depending on the patient's condition. In clinical practice, the therapeutic effect of BAR due to dose is unknown. This time, using multicenter research data, we examined the patient background and treatment effect according to the dose of BAR. [Methods] We compared 115 patients with RA who were taking BAR, and compared the patient background and disease activity in the 4 mg and 2 mg groups up to 24 weeks. [Results] The average age (74 vs 63 years, $p <0.01$), eGFR (65 vs 84 ml/ min, $p <0.01$), MTX combination rate (34.2 vs 57.1%, $p <0.01$) between 38 cases (30 females) in the 2 mg group and 77 cases (60 females) in the 4 mg group, was significantly different. DAS28-CRP improved from Week 0 (3.2 vs 3.5) to Week 24 (2.5 vs 2.4). According to the Kaplan-Meier analysis, the adverse event discontinuation rate was 15.3 vs 2.8%. [Conclusion] The 2 mg group in actual clinical practice was older age, lower renal function and lower MTX combination rate than the 4 mg group. Although the treatment effects were similar for 24 weeks, safety management was considered more important because the 2 mg group tended to have a slightly higher adverse event withdrawal rate.

W47-2

Predictors of achieving clinical remission and/or low disease activity at 12 weeks treated with baricitinib 2mg/day in rheumatoid arthritis patient

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Conflict of interest: None

[Objective] To assess the clinical characteristics of rheumatoid arthritis (RA) patients treated with baricitinib 2mg/day and achieved clinical remission and/or low disease activity (REM/LDA). [Methods] Efficacy was evaluated by CDAI. [Results] 142 (20 men, 122 women) of RA patients were treated with baricitinib 2mg/day and 69 patients who had full clinical data were enrolled in this study. Overall REM/LDA rate was 86.9%. There were no significant differences between REM/LDA achieved patient and non-achieved patient in sex, age, duration of RA, baseline CDAI and baseline ACPA. bDMARDs naive or tsDMARD naïve patients showed higher REM/LDA rate (60.0vs.22.2%, p=0.0311). Furthermore, more than 4.4 baseline improvement of CDAI at 4 weeks was the predictor of REM/LDA at 12weeks in baricitinib 2mg/day treatment (p=0.0069, AUC=0.75, ROC analysis). [Conclusions] bDMARDs naïve, tsDMARDs naïve and initial therapeutic effect in CDAI (-4.4/4weeks) are the predictor of successful achieving REM/LDA in baricitinib 2mg/day treatment in RA.

W47-3

Peficitinib (ASP015K) in Combination with Methotrexate (MTX) Inhibits Joint Destruction in Patients with Rheumatoid Arthritis (RA) and an Inadequate Response to Methotrexate: A Japanese, Randomized, Double-Blind, Placebo-Controlled Trial (RAJ4)

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Conflict of interest: Yes

[Objective] To analyze inhibition of joint destruction with peficitinib (PEF) in RA patients. [Methods] In a double-blind, PBO-controlled study in Japan, active RA patients (for <10 y) and inadequate response to MTX were randomized 1:1:1 to once-daily PEF100, 150mg/day (PEF100, 150) or PBO+MTX. Hand and foot X-rays were taken at baseline (BL), Week (W) 28, 52 or early termination (ET). Primary endpoint: mean change from BL to W28 in van der Heijde modified total Sharp score (mTSS). Mean change from BL in mTSS, proportion with rapid radiographic progression (RRP, yearly mTSS progression >5) and cumulative probabilities of change from BL in joint erosion (JE) and joint space narrowing (JSN) scores were reported. [Results] Full analysis set (PEF100, 150, PBO; n=174, 174, 170). BL demographics were similar between groups. Primary endpoint was met (previously reported). Mean change from BL to W52/ET in mTSS was significantly lower for PEF100, 150 vs PBO (2.12, 1.54 vs 6.27). The proportion of patients with RRP was significantly lower for both PEF100, 150 vs PBO (10.4%, 9.8% vs 35.3%). Changes from BL to W28/ET and 52/ET in JE and JSN scores indicate that both PEF100 and 150 inhibited joint destruction vs PBO. [Conclusions] PEF significantly inhibited joint destruction compared with PBO.

W47-4

Minimal clinically important difference (MCID) achievement in patient-reported outcomes (PRO) in RAJ4, a randomized, double-blind, placebo-controlled study of peficitinib (PEF, ASP015K) in patients with rheumatoid arthritis (RA) with an inadequate response to methotrexate (MTX)

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Conflict of interest: Yes

[Objective] To evaluate PRO MCID achievement with PEF or placebo (PBO) in Japanese patients with RA and an inadequate response to MTX. [Methods] Amulticenter, double-blind study conducted in Japan. Patients with active RA (<10 years) and inadequate MTX response were randomized 1:1:1 to PEF 100 or 150 mg/day (PEF100 or PEF150) or PBO once daily + MTX. Previously unreported PRO at Week 12/early termination, including ad-hoc assessments of MCID in Physician's Global Assessment of Disease Activity (PGA, decrease ≧10 mm), Subject's Global Assessment of Pain (SGAP, decrease ≧10 mm) and Work Productivity and Activity Impairment Questionnaire (WPAI, decrease ≧7%), were analyzed. [Results] 519 patients were treated. PGA MCID was achieved by 79.7%, 84.2% and 48.8% in the PEF100, PEF150 and PBO arms (p<0.001 vs PBO for both arms). For SGAP, 63.4%, 72.5% and 41.1% in the PEF100, PEF150 and PBO arms, achieved MCID (p<0.001 vs PBO for both arms). MCID in the WPAI parameter '% activity impairment' was achieved by 60.8%, 70.6% and 46.4% in the PEF100, PEF150 and PBO arms (p=0.009 for PEF100 and <0.001 for PEF150 vs PBO). [Conclusions] PEF100 and PEF150 were associated with significantly higher proportions of patients achieving MCID across multiple PRO.

W47-5

Comparative Efficacy and Safety of Peficitinib (ASP015K) Versus Other Janus Kinase (JAK) Inhibitors for the Treatment of Patients with Rheumatoid Arthritis (RA): A Network Meta-Analysis (NMA)

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Conflict of interest: Yes

Objective: To compare the efficacy and safety of peficitinib (PEFI) with other JAK inhibitors (JAKis) through an NMA. **Methods:** A literature review identified RCTs of PEFI, baricitinib (BARI) and tofacitinib (TOFA), which are approved in Japan for RA. Effects of JAKis on multiple efficacy outcomes and adverse events were compared by a Bayesian NMA without adjustment of baseline characteristics. 12- and 24-week (W) networks were analyzed. Interactions of concomitant methotrexate and Asian population with outcomes were analyzed by network meta-regression (NMR). **Results:** Five PEFI, 7 BARI and 9 TOFA studies were subjected to NMA. At 12W, safety and ACR20/50/70 response of PEFI 100/150mg were at least comparable to other JAKis, while PEFI 150mg was superior to BARI in DAS28≦3.2 attainment. AT 24W, PEFI 100/150mg was superior to other JAKis in ACR20/50 response and in reducing the disease progression evaluated by mTSS. Meanwhile, NMR analysis showed no evidence for an interaction between concomitant methotrexate and magnitude of JAKi treatment effect, however, indicated that ACR20/50/70 response and reduction in inflammation at 12W, and ACR50 response and reduction in inflammation at 24W may be favorable in Asian population. **Conclusion:** This NMA compared the outcomes in 21 RCTs of JAKis in RA, and demonstrated that PEFI has comparable or favorable efficacy and safety outcomes at 12 and 24W compared to other JAKis.

W47-6

Pooled Safety Findings in Japanese, Korean and Taiwanese Adult Patients with Rheumatoid Arthritis (RA) Treated with Peficitinib (ASP015K), a Janus Kinase (JAK) Inhibitor, for up to 6 Years

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Conflict of interest: Yes

[Objective] To assess the adverse event (AE) incidences in RA patients (pts) treated with peficitinib (PEF). [Methods] The AE/serious AE (SAE) were evaluated using 2 pooled safety data sets from 4 clinical studies of RA pts with PEF; 1) Phase 3 (P3) studies (RAJ3, RAJ4) and 2) P2/3 studies (P2b study RAJ1; extension study RAJ2, RAJ3, RAJ4). RAJ2 data were assessed for AEs during longer term treatment. [Results] Pooled P3 and P2/3 included 1025 and 1052 pts, respectively. In pooled P2/3, overall exposure was 2336.3 pt-years with a maximum follow up of 73.4 months. In pooled P3, AEs/SAEs and AEs/SAEs leading to discontinuation occurred in 88.5%/9.4% and 9.4%/4.3% in PEF100mg group (278 pts), 87.7%/7.6% and 6.5%/2.2% in PEF150mg group (276 pts) and 89.0%/9.0% and 6.5%/2.5% in etanercept group (200 pts), respectively. In RAJ2 (843 pts), these AEs occurred in 89.8%/16.4% and 10.3%/5.9%. In pooled P3, common AE for PEF were nasopharyngitis, upper respiratory tract infection, hepatic function abnormal, and AEs leading to discontinuation (≧2 pts) were RA, cellulitis, pneumonia, pneumocystis jirovecii pneumonia, lymphocyte count decreased, arthritis. Death for PEF was 1pt in each of RAJ1/RAJ4/RAJ2. [Conclusions] PEF is well tolerated in RA patients with no specific concerns for longer term use.

W48-1

Risk Factors and Preventive Indication for Herpes Zoster in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To clarify risk factors of herpes zoster (HZ) in patients with rheumatoid arthritis (RA), and to speculate the preventive measures against HZ. [Methods] This retrospective cohort study analyzed a total of 1094 outpatients and inpatients with RA in our hospital from 1/1/2015 to 5/9/2019. HZ diagnosis was based on medical chart. Cox regression model was used to estimate the risk factors for HZ. [Results] 64 HZ cases yielded the crude incidence rate; 17.8/1,000 patient-years. Independent risk factors for HZ included older age (HR 1.06, 95%CI 1.01-1.21 per 10 years), Steinbrocker stage II to IV compared with stage I (Stage II: HR 1.42, CI 1.16-1.74, Stage III: HR 1.56, CI 1.27-1.90, Stage IV: HR 2.07, CI 1.67-2.56), prednisolone≥4mg/day compared with 0mg/day (HR 1.18, CI 1.00-1.39), history of HZ (HR 1.63, CI 1.01-2.85). Based on each hazard ratios, we developed a scoring system as follows: 1 point for age≥60, stage II and III, prednisolone≥4mg/day, past history of HZ; 2 points for stage IV. The incidence among patients with score 3 to 5 points increased exponentially; 23.2, 70.1, 226/1,000 patient-years respectively. [Conclusions] Recombinant zoster vaccine coming soon in Japan might be recommended for RA patients with risk scores over 3 points.

W48-2

Prognostic factors of nontuberculous mycobacterial disease in rheumatoid arthritis patients

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Conflict of interest: None

[Objective] To analyze of prognostic factors of nontuberculous mycobacterial (NTM) disease in rheumatoid arthritis (RA). [Methods] We performed a retrospective analysis of the RA patients with NTM disease who were treated from 2011 to 2019 in our center. NTM disease was diagnosed based on the 2008 diagnostic criteria of pulmonary NTM disease proposed by the JST/JRS. [Results] There were 12 RA patients in the NTM disease (mean ages: 68.6 years, mean duration of RA: 14.1years). These patients had been treated with DMARDs (MTX 10, tacrolimus 3, PSL 3 and biological agent 1). The NTM species was *M. avium-intracellulare complex* (MAC) 9, *M. abscessus* 2, and *M. kansasii* 1. The features of CT imaging was nodular/bronchiectatic form 9 and fibrocavitary form 1. Preexsiting CT abnormalities were identified (interstitial pneumonia 2, COPD 2, organizing pneumonia 2). 4 patients with received anti-NTM therapy responded to the therapy. 4 of 8 patients with absence of any anti-NTM therapy showed exacerbation. Hypoalbuminemia, BMI<18, exposure to corticosteroids, and caused by *M. abscessus* were associated with the progressive risk of NTM disease. [Conclusions] We suggested that it is important to monitor the development of NTM disease in RA patients with low nutritional state and receiving corticosteroids.

W48-3

Effectiveness of pneumococcal vaccination for preventing pneumonia in patients with RA using the IORRA cohort

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Conflict of interest: None

Objective: To investigate the effectiveness of pneumococcal vaccination (PPSV23) for preventing pneumonia in patients with rheumatoid arthritis (RA). METHODS: RA patients who answered "had first PPSV23 in the last 6 months" in the IORRA survey from 2011 to 2012 were defined as vaccination group (VG). Pneumonia was defined as that requiring admission or intravenous antibiologics, which was confirmed in the medical chart. Control group (CG) was defined as RA patients who were never vaccinated in the study period. The incidences of pneumonia were evaluated for 5 years. Then, a propensity score for PPSV23 was constructed, and weighted analysis was performed using the propensity score. RESULTS: There were 320 patients in the VG (average 70 years, females 84.7%, DAS28-ESR 3.1, J-HAQ 0.78, IP 4.7%, DM 9.4%, biologic use 9.6%), and 1233 patients in the CG (average 55.3 years, females 88.1%, DAS28-ESR 2.7, J-HAQ 0.46, IP 0.7%, DM 3.8%, biologic use 16.9%). Among them, 14 (4.4%) in the VG and 41 (3.3%) in the CG developed pneumonia (p=0.46). After propensity score matching procedure, 11 (3.8%) of 293 patients in the VG and 31 (4.0%) of 767 patients in the CG developed pneumonia (p=0.76). CONCLUSIONS: The pneumonia prevention effect of PPSV23 in RA patients could not be confirmed in this study design.

W48-5

A prospective study of the influence of therapeutic agents on the standardized incidence ratio (SIR) of tuberculosis (TB) in patients with RA by NinJa cohort data for 16 years

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Conflict of interest: None

[Objective] To evaluate the incidence of therapeutic agents on the standardized incidence ratio (SIR) of tuberculosis (TB) in patients with rheumatoid arthritis (RA) prospectively. [Methods] We calculated the standardized incidence ratio (SIR) of TB from the clinical data on National Database of Rheumatic Diseases in Japan (***NinJa***) prospectively from 50 facilities for 16 years. In addition, we compared the SIR of TB between patients with and without biologics. [Results] Among 156,510 RA patients registered from 2003 to 2018, 75 patients developed TB and the SIR of TB was 1.91 (95%CI: 1.48-2.34), which was not significant increase compared with the SIR 3.98 (1.22-6.74) of TB in RA patients without anti-TNF therapy. Looking at trends every two years, it was on a downward trend with peak at 4.76 in 2007-08. 28 patients (37.3%) and 10 patients (13.3%) were treated with MTX and biologic agents, respectively. The SIR of TB in RA patients treated with biologic agents was 0.44 (0.17-0.71), and the SIR of TB in patients treated without biologic agents was 3.64 (2.79-4.52). [Conclusions] The SIR of TB of RA patients tended to decrease, and it was reconfirmed by prospective studies that there was no increase due to administration of biologic agents.

W48-6

Clinical features and HTLV-1 proviral load in HTLV-1-positive patients with rheumatoid arthritis: Chort study in a single facility

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Conflict of interest: None

[Objective] HTLV-1carrier cohort study reported that the first ATL risk factor was high values of HTLV-1 provirus (PVL). We investigated the relationships between clinical features and temporal variation of PVL. [Methods] The PVL was measured by Real-time PCR methods. PVL value of each clinical features was compared using Mann-Whitney U test. Cases

with higher PVL in the 1st year were also measured in the 2nd and 3rd years. [Results] The PVL for baseline was 19.6 (0-257) copies×1000PBMCs. Compared to RA patients without comorbidity, patients with comorbid bronchiectasis, malignant tumors, other autoimmune diseases, opportunistic infections, and diabetes mellitus were significantly higher in PVL. Patients treated with TOF showed significantly higher PVL than patients without TOF. Compared the 2nd year with 1st year values, 26 cases did not change, 6 increased and 9 decreased. If patients had recurrent infections, PVL increased, when their diseases were stable, PVL was unchanged or stable. The values decreased after discontinuation of TOF. Three of the 5 cases had complicated with herpes zoster. [Conclusions] HTLV-1seropositive patients comorbid for diseases and drugs will be a higher risk for developing ATL. Careful follow-up of these patients is necessary to detect ATL development.

W49-1

Twenty-year follow-up of radiocarpal arthrodesis for the rheumatoid wrist

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Conflict of interest: None

[Objective] The purpose of this study was to clarify the long-term outcome of radiocarpal (RC) arthrodesis in patients with rheumatoid arthritis (RA). [Methods] Twenty-three wrists in 20 patients who underwent RC arthrodesis 20 years ago were included. The mean age at the time of surgery was 46.0 years and their mean duration of RA was 9.7years. Five wrists were Larsen grade II, ten were III, and eight were IV. Pain, grip power, range of motion, CRP, ESR, mHAQ and patient's satisfaction level were investigated. In the serial X-rays, the bone union at the RC, MC, and CM joints and bone alignment at the RC joint were investigated. [Results] Pain disappeared and no recurrence in all patients. Grip power increased in19 wrists. Wrist flexion and extension decreased. Forearm rotation unchanged. CRP and ESR decreased. mHAQ unchanged. Bone union at the RC joint occurred in all patients. At the MC joint, it occurred in 22 wrists, and at the CM joint it occurred in 7. Radiographically, X-ray parameters including ulnar shift and palmer subluxation improved just after the operation and unchanged throughout the following 20 years. Eighteen patients were satisfied with this operation. [Conclusions] Painless stability was provided by the radiocarpal arthrodesis and it maintained for 20 years.

W49-2

Twenty-year follow-up of Darrach procedure or Sauvé-Kapandji operation for the rheumatoid wrist

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Conflict of interest: None

[Objective] The purpose of this study was to clarify the long-term outcome of synovectomy combined with Darrach procedure (D) or Sauvè-Kapandji operation (SK) in patients with rheumatoid arthritis (RA). [Methods] Eight wrists in 7 patients who underwent D or SK 20 years ago were included. The mean age at the time of operation was 51.9 years and their mean duration of RA was 9.0 years. One wrist was Larsen grade IV and 2 wrists had bony fusion at the radiocarpal (RC) joint in D group. In SK group, 2 wrists were Larsen grade I, 2 were grade II, and 2 were grade III. Pain, grip power, range of motion, CRP, ESR, and patient's satisfaction level were investigated. In the serial X-rays, Changes in Larsen grade and alignment at the RC joint were assessed. [Results] Pain disappeared and no recurrence was observed in all patients. Grip power increased in 7 wrists. CRP and ESR decreased. Larsen grade at the RC joint progressed in 7 wrists. Ulnar carpal shift at the RC joint progressed during the follow-up period. Three patients highly satisfied with the operation, though 4 patients were dissatisfied with loss of range of motion. [Conclusions] Pain-free wrist and increased grip power were provided by synovectomy combined with D or SK.

W49-3

Outcome of the Sauvé-Kapandji procedure in 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 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). The presence or absence of joint surface remodeling between the radio carpal joint in lateral views was also examined. [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.

W49-4

Comparison between the implant survival rate of AVANTA and Swanson in MCP joint arthroplasty for rheumatoid arthritis of the hand

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Conflict of interest: None

[Objective] MCP joint arthroplasty were corrected rheumatoid arthritis of the hand deformity. We mainly use two types of silicone implants, Sutter type AVANTA® and Swanson type Swanson® . In this study, we evaluated the survival rate of each implant. [Methods] Patients were recruited to the patients with rheumatoid arthritis who had undergone MCP joint arthroplastyonany one offingers in our hospitalbetween January 2000 and December 2018. In the case of multi-finger surgery, we assessed the inplant at fracture even if only one implant was broken. We evaluated the Implant fracture using the X-rays after operation, and examined using Kaplan-Meier method and Log-rank test. [Results] We collected 233 hand including143 hand using Sutter type and 90 hand using Swanson type. The 7.5-year survival rate of the Sutter type is 28.6% and the Swanson type is 75.1%. The survival rate of Swanson type is significantly higher than the Sutter type ($P<0.05$). [Conclusions] We found that the Sutter type was significantly more easily damaged than the Swanson type. There is no significant difference in the damage rate due to the number of fingers operated on. The further investigation is necessary regarding related factors regarding the difference in the damage rate due to the implant.

W49-5

The corrective surgery of buttonhole deformity in patients with rheumatoid arthritis in the era of biologics

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Conflict of interest: None

[Objective] We assessed the surgery of buttonhole deformity in RA patients in the era of biologics. [Methods] We assessed age, disease duration, medication, disease activity, and ROM of MCP joint in 24 RA patients (36 fingers) performed corrective surgery of buttonhole deformity in recent 10 years. The surgical procedure was advancement of EPB and rerouting of EPL tendon in case with Larsen grade 0-2 (17 patients, 24 fingers) and silastic implant in case with grade 3-5 (8 patients, 12 fingers). [Results] The mean value of age was 66.4 y.o. and the disease duration was 22.4 years. The biologics agents was taken in 11 patients. The mean CRP was 0.35 mg/dl. The improvement of extension lag on MP joint was 44.8 to 25.0 degrees in soft tissue balancing group and 33.4 to 12.6 degrees in silastic implant group. The improvement of buttonhole deformity after corrective surgery was better in silastic group than that in soft tissue balancing group. The level of pre-operative flexion contracture on MP joint was the factor of correction loss in the both groups. [Conclusions] The corrective surgery of buttonhole deformity in RA patients was effective even if with soft tissue balancing in the era of biologics. The level of pre-operative flexion contracture was important factor for the surgical result.

W50-1

Analysis of peripheral blood T cell subsets in patients with idiopathic multicentric Castleman's disease/ TAFRO syndrome

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Conflict of interest: None

[Objective] The purpose of this study is to clarify the characteristics of T cell subsets in each disease by flow cytometric analysis of peripheral blood T cells of patients with iMCD/ TAFRO syndrome that we experienced in our hospital. [Methods] We isolated peripheral blood mononuclear cells from patients with iMCD (n = 7) and TAFRO syndrome (n = 2) before induction of therapy and from patients with rheumatoid arthritis (RA) before induction of biologics (n = 7). The cells were classified into Th1, Th2, Th17, Th17.1, Treg, Tfh, and Tph using flow cytometry, and the proportion of T cell subsets in each disease was compared. [Results] The mean age of patients with iMCD, TAFRO syndrome, and RA was 57, 47, and 62 years, respectively, with no significant difference between groups. Patients with TAFRO syndrome tended to have a higher Th17 subset at the time of induction than patients with iMCD. Patients with TAFRO syndrome also tended to have a lower Tph, Tfh subset than patients with iMCD or RA. There were no significant differences between the groups for Th1, Th2, Th17.1, or Treg. [Conclusions] The proportion of Th17 and Tph, Tfh subsets differs between iMCD and TAFRO syndrome, which may contribute to the pathological differences in both diseases.

W50-2

Glucocorticoid-resistant multicentric Castleman disease with additional tocilizumab administration

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Conflict of interest: None

Objective: Approximately 50% patients with multicentric Castleman disease (MCD) are resistant to glucocorticoid (GC), but the clinical feature of GC-resistant MCDis unclear. This study aimed to evaluate the severity and clinical course of GC-resistant MCD. Methods: Patients diagnosed with MCD from August 2005 to August 2019 were evaluated using the severity classification and CHAP score proposed by Fujimoto et al. in 2018. Results: All 4 patients had multiple lymphadenopathy, and lymph node biopsy was consistent on histology. Severity assessment showed that 1 patient with severe and 3 with mild MCD. The average CHAP score was 5.3 (4-9) during initial visit and 5.0 (3-8, -1 in 2, unchanged in 1, +1 in 1) at 2 weeks after starting GC. All patients were GC-resistant and showed improved inflammatory markers and hypergammaglobulinemia after TCZ administration. The mean CHAP score 2 weeks after TCZ administration was 1.8 (0-5, -4 in 3 and -2 in 1 compared with the initial visit). Discussion: All the patients with MCD, including the ones with mild MCD, were refractory to GC monotherapy and needed TCZ administration. The CHAP score was effective in evaluating the therapeutic effects for MCD. Combined GC and TCZ therapy should be considered for the initial induction therapy of MCD.

W50-3

Exacerbation of adult-onset Still's disease by tocilizumab; a report of 2 cases

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Conflict of interest: None

Case1: A 72-year old woman was admitted because of rash with spiking fever. Laboratory examination revealed liver dysfunction, leukocytosis and hyperferritinemia (40000 ng/ml). She was diagnosed as adult-onset Still's disease (AOSD) with hemophagocytic lymphohistiocytosis because of hemophagocytosis in the bone marrow. High-dose GC and cyclosporine (CsA) were given, which improved her condition and decreased ferritin level to 3000 ng/ml. Tocilizumab (TCZ) was added on day 31. The next day, she showed elevation of ferritin levels (9719 ng/ml). Exacerbation of AOSD was diagnosed and GC-pulse therapy was added, which improved her condition. **Case2:** A 60-year old woman was admitted because of spiking fever, generalized erythema, arthritis. Laboratory examination revealed liver dysfunction, leukocytosis and elevated levels of ferritin (102190ng/ml). She was diagnosed as AOSD and treated with high dose GC therapy and CsA, which controlled fever and decreased ferritin level to 22940. TCZ was added on day19. The next day, she showed elevation of ferritin levels (79460 ng/ml). Exacerbation of AOSD was diagnosed and GC-pulse therapy was added. **Conclusion:** TCZ could induce the exacerbation of AOSD, particularly, when serum ferritin levels were elevated in spite of therapy with high GC and CsA.

W50-5

Clinical Implications of Ultrasonography (US) in Monitoring Disease Activity of Relapsing Polychondritis (RP) and Comparative Investigation by US between Auricle of RP, Repeated Trauma, cellulitis and Healthy Subject

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Conflict of interest: None

[Objective] To assess the clinical implications of ultrasonography (US) in monitoring disease activity and diagnosis of relapsing polychondritis (RP). [Methods] Firstly, auricular and nasal chondritis of patients with RP (n=6) were assessed by US before and after treatments. The relationship between US findings and serum markers were evaluated. Moreover, the comparisons of US findings between the auricle of patients with RP (n=5), repeated trauma (n=5), cellulitis (n=2) and healthy subjects (n=5) were also assessed. [Results] US finding before treatment showed

low-echoic swollen auricular and nasal cartilage with increased power Doppler signals (PDS) in all cases of RP. US findings corresponded to biopsy findings. After treatment, the swollen ear and nose completely resolved. Then, US findings also showed dramatic reductions in swollen cartilage with the decrease in PDS. Although serum markers completely improved, US finding remained in 1 of 6 cases, and this case showed flare due to PSL tapering. Finally, RP could be differentiated from the damage of repeated trauma with PDS and producing subperichondrial serous effusion. [Conclusions] US of auricular and nasal cartilage in RP possibly facilitates evaluation of auricular lesions and monitoring of disease activity.

W51-1

The role of rheumatology nurses required for implementation of T2T and optimal patient care

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Conflict of interest: None

[Objective] The concept of T2T has been widespread but not necessarily well implemented in clinical settings. This study aims to evaluate the roles of rheumatology nurses required for implementation of T2T and optimal care for RA patients in Japan. [Methods] Participants are nurses engaged in rheumatic care. Focus group interview was conducted on "the role of nurses for implementing T2T and optimizing care for RA patient", and a semi-structured interview was performed. Data analysis was used with Krippendorff's content analysis method. [Results] 24 nurses participated in this study. The result was classified into 9 categories and 37 subcategories. The categories were as follows; provide basic knowledge of RA, provide knowledge of RA drugs, provide knowledge and skills of self-monitoring, enhance self-efficacy and support self-management, support decision-making, psychological support, understand the diversity and feelings of patients and their families, and support according to individual needs, ensure the quality of care by continuing education for nurses, collaborate with multi-disciplinary teams [Conclusions] This result is all included in EULAR recommendations 2018 revised version on the role of nurses. This will be useful in considering education for nurses to support RA patients.

W51-2

Degree of recognition of rheumatic care nurse and roles required from patients with rheumatic arthritis in OMC-RMA (Osaka medical college-Rheumatic disease medical stuff association) study

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Conflict of interest: None

[Objective] To investigate the degree of recognition of rheumatic care nurse and roles required from RA patients in OMC-RMA study. [Methods] 97 RA patients in our 3-hospitals were included. A questionnaire survey was conducted to examine the awareness of rheumatic care nurses and whether doctors or nurses would like to be involved in treatment or care. [Results] 25 males, 72 females, ages 20s-90s, Patients were treated with MTX (39.1%), Biologics (44.3%) and tsDMARDs (4.1%). The degree of recognition of rheumatic care nurses was 15.5%. In the survey, explanation of diseases, therapeutic drugs, treatment goals, examination have high rate of requesting a doctor. On the other hand, explanation of rehabilitation, self-help devices and braces, and self-injection instruction have high rate of requesting a nurse. In addition, patients who had Biologics self-injection were significantly higher rate of requesting a nurse if they received infusions/injections (p=0.037). [Conclusion] The degree of recognition of rheumatic care nurses is still low. Patients who have received self-injection guidance from a nurse, trust nurses' injection techniques. For the aging society in Japan, it is important to expand the role of nurses. We need to be recognized and trusted by patients as RA expert care nurses.

W51-3

Study on the incident in patients with rheumatoid arthritis under the treatment of self-injection of the biologic DMARDs

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Conflict of interest: None

[Objective] To clarify the frequency and the types of incident/accident in patients with rheumatoid arthritis under the treatment of self-injection of the biologic DMARDs. [Methods] We retrospectively reviewed the medical charts of RA patients who started the treatment with self-injection of bDMARDs from July 2012 to May 2018. [Results] Among 188 patients under the treatment with bDMARDs, 93 cases started self-injection. During the total 144 person-years, the incidents occurred 61.1/100 person-years; 57.0 in patients under 65 years old (group A), 55.6 in those aged between 65 and 74 (B), and 137.5 in those at 75 or older (C). There were more incidents seen among auto-injector user than syringe-users (66.2 v.s. 55.2/100 py). The types of the incidents were poor compliance (18.1), technical problems (16.0) and dare injection on a sick day (12.5). Technical problems were observed at 12.0 in group A, 13.9 in B and 75.0 in C. Dare injection on sick days was most seen in group A (14.0) compared to group B (11.1) and C (0). There were no accidents or serious incidents observed. [Conclusion] While no accidents associated with fatal complications were observed by the frequent and intensive patients care, strategies of instruction on self-injection should be modified according to the age.

W51-4

Benefit of Joint Echo with Rheumatoid Care Nurses Patient satisfaction survey wth NPS® using POCUS (Point of care Ultrasound)

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Conflict of interest: None

Objective To evaluate the satisfaction of rheumatoid arthritis patients who received ultrasonography (MSKUS) in our hospital by using the net promoter score (NPS). Methods Questionnaires were performed in 81 RA patients. There were 2 points to be investigated. One was (1) Patient satisfaction and the other was (2) level of recommendation to others. There were 5 questions in 81 (1) 1. Was it good to receive the joint echo? 2. Could you receive the joint echo in peace? 3. Was the time of the joint echo appropriate? and 4. Could you understand the disease condition better after the joint echo? and 5. Would you like to the joint echo periodically? These 5 items were evaluated on a 5 point scale (high~low,1~5). Level of recommendation to others was evaluated with NPS, which is "Do you wish to recommend the joint echo to others?" . Result Questionnaires were administered to 81 RA patients and all patients responded. In (1), for the 5 items of patient satisfaction, more than 80% of patients had high scores (1 and 2) for all the questions. In (2), the NPS was high, which was 65. Conclusions It was suggested that the satisfaction may be improved by explaining symptoms instantly using POCUS. In addition, NPS® was also considered that POCUS would lead to medical management merits.

W51-5

Effect of pain catastrophizing for disease activity and achievement of clinical remission in rheumatoid arthritis

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Conflict of interest: None

[Objective] To determine the effect of pain catastrophizing (PC) for achievement of clinical remission in rheumatoid arthritis (RA). [Method] A cross-sectional study of 421 RA outpatients (mean 65 years old, bDMARDs use: 48%, DAS28 remission achieved: 56%). PC was assessed by the Pain Catastrophizing Scale (PCS, 0 to 52). The positivity of PC was defined as PCS≧30. PCS scores were compared according to presence/absence or severity of the clinical features. The relationship between positivity of PC and achievement of remission was analyzed by logistic regression analysis adjusted for age, sex, disease duration, and treatments. [Results] Twenty six percent of the patients had PC. PC positive patients showed higher PGA, pain-VAS, tender joint counts, and HAQ than PC negative patients. The odds ratio of PC for achieving DAS28 remission was 0.54 (95%CI: 0.34-0.84, p=0.007). Clinical features associated with elevated PC scores were disease activity, HAQ severity, history of falls, complications of respiratory disease, depression, anxiety, and history of zoster. [Conclusion] PC affected RA disease activity and interfered with achieving remission. Management of depression/anxiety and complications such as falls, respiratory disease, and zoster may be important for decreasing PC.

W51-6

Clinical Evaluation of Upper Limb Function Using Hand 20 in elderly patients with rheumatoid arthritis

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Conflict of interest: None

<Purpose> To evaluate upper limb function in elderly patients of rheumatoid arthritis (RA) using Hand 20. <Materials and Methods> 84 female RA patients who were over 65 years old were enrolled and Hand 20 scores were obtained from these subjects. We compared them with Hand 20 scores of elderly subjects without upper limb disorders. <Results> The total score of Hand 20 in the RA group (n=84, 72.2 ± 5.5 years old, disease duration 15.1 ± 14 years, DAS28 2.4 ± 1.0) and the elderly group (77.2 ± 6.2 years old) were 32.0 ± 23.3 and 9.1 ± 13.7 points respectively. (P <0.001) Hand 20 scores in the RA group were significantly higher for all items than those in the elderly group. (P <0.01) Items which showed significant differences (a difference in scores more than 3 points) between the RA group and the elderly group were No7 (5.2 ± 3.5 vs 0.84 ± 2 points, p <0.001), No8 (4.5 ± 3.6 vs 0.6 ± 1.7 points, p <0.001), No10 (4.1 ± 3.4 vs 0.6 ± 1.8 points, p <0.001). <Conclusions> In previous studies reported that these movements are related to the difficulty of self-injection as well as grip strength. From our finding, it is considered as an important to take care patients difficulty of self-injection in daily medical care in outpatient clinic.

W52-1

Effects of finger function training using SARAH on finger function and joint synovial blood flow in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the effects of finger function training on finger function and synovial blood flow in patients with rheumatoid arthritis (RA). [Methods] Finger function training was performed daily for 4 weeks by using strengthning and stretching for rheumatoid arthritis of hand (SARAH). Finger function was evaluated by grip and pinch strength, hand pain VAS, and Quick dash. RA disease activity was evaluated by joint ultrasonography, DAS28 and HAQ. The median and interquartile range before and after 4 weeks the intervention were calculated for each end point, and was used for the analysis the Wilcoxon signed-rank test. [Results] 17 female RA patients were studied. After 4 weeks finger function training both grip and pinch strength improved. Hand pain VAS also improved in the right hand. Quick dash did not improve. In RA disease activity assessment, 8 out of 17 patients with 21 joints were positive for synovial blood flow observed by joint ultrasonography. Synovial blood flow improved after 4 weeks. In addition, patients with negative synovial blood flow did not worsen after the intervention. DAS28 and HAQ did not change. [Conclusion] Finger function training using SARAH in RA patients with is an effective treatment for improving the finger function without worsening RA synovitis.

W52-2

Strengthening and Stretching for Rheumatoid Arthritis of the Hand (SARAH): Translation and implementation issues

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Conflict of interest: None

[Objective] The Strengthening and Stretching for Rheumatoid Arthritis of the Hand (SARAH) program is a tailored 12 week progressive exercise treatment which was shown to be clinically/cost-effective in a UK clinical trial (Lamb et al, 2015). This study investigates implementation of SARAH in Japan by examining translation and practice issues. [Methods] SARAH consists of 10 primary documents used by therapists and patients. These were translated from English into Japanese (SARAH-J) in compliance with the guidelines for translation (Inada, 2015). Issues practicing SARAH were identified by surveying therapists who attempted to implement the program. [Results] SARAH-J can be downloaded from iSARAH websight. Two main issues have been identified: 1) Therapists had difficulty obtaining items required for strength exercise and 2) Making reservations for SARAH treatment in hospital settings was sometimes difficult due to Japanese insurance regulations. [Conclusions] SARAH has clearly been shown to be an effective treatment program for RA patients with hand problems. A key to this success is the documentation which helps patients use SARAH to fulfill their treatment goals. The creation of SARAH-J brings this valuable program to Japan, although further research is needed to refine its implementation.

W52-3

A study of music therapy for patients with rheumatoid arthritis on the expansion of playing music instruments

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Conflict of interest: None

[Objectives] We previously reported that music therapy improves general health (GH) condition, positive emotion and self-efficacy of patients with RA and decreases pain, anxiety and negative emotion. In this study, we investigated the effects of music therapy on the expansion of playing music instruments. [Methods] Eight Japanese songs were sung with a piano accompaniment and 4, increased from 2, were played with two chime bars, increased from one of each, held by the both hands. GH condition, pain, positive and negative moods, and emotional relaxation were surveyed by self-rating questionnaire including 10cm GH-VAS, face pain rating scale, PANAS, PMS, and ERS. [Results] Sixteen female patients were participated. mHAQ was 0.41±0.46 (0-1.38). GH was significantly improved from 1.6 to 1.0, FS from 3.6 to 2.1, total PMS from 62.4 to 75.3, positive affect of PANAS from 25.7 to 35.0 respectively. Negative affect of PANAS was not changed. Four subscales of ERS indicated positive emotional relaxation effects. While fatigue by playing instruments was not reported, pain was by 12.5%, with similar frequency to the previous, 0-17.6%. [Conclusions] Playing music instruments may be expanded in

the music therapy for patients with RA, which increases positive emotions and emotional relaxation.

W52-4

The effect of low intensity exercise of lower extremity on the upper extremity and the lower extremity in female patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Pedersen reported that some myokines have anti-inflammatory effect. Last year, we reported that low intensity exercise was efficacious against arthritis in patients with rheumatoid arthritis (RA). We investigated the effect of low intensity exercise of lower extremity on the upper and lower extremity in patients with RA. [Methods] Twenty-eight female patients with RA were enrolled. Inclusion criteria were receipt of a stable dose of biologics, JAK inhibitorys, and conventional DMARDs more than 3months prior to the first exercise. The exercise circuits consisted of 6 different low extremity exercises. Each exercise was less than 50% of the 1-repitition maximum. [Results] Mean DAS28 (ESR) was 3.86 at base line and 3.53 at 2 months, mean lower extremity joint tenderness (JT) 5.4 and 2.1, mean lower extremity joint swelling (JS) 4.0 and 1.9, mean upper extremity JT 4.3 and 3.5, mean 10m gait speed (sec) 7.5 and 6.8, mean knee extension strength (kgf) 18.9 and 21.9, mean grip strength (kg) 13.2 and 15.1 respectively, improved significantly ($p<0.05$) at 2 months than baseline. [Conclusions] It was suspected that low intensity exercise of lower extremity was efficacious against not only lower extremity arthritis but also upper extremity joint arthritis in patients with RA.

W52-5

Characteristics of Dysphagia in Patients with Dermatomyositis (DM) Based on Autoantibody Profile

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Conflict of interest: None

[Objective] To examine whether clinical characteristics of dysphagia in DM patients can be stratified based on autoantibody profile. [Methods] Nine DM who needed dysphagia rehabilitation were extracted from 58 DM admitted to our hospital between October 2016 and September 2019. Nine were stratified into 4 groups based on antibody profile (T: anti-TIF1-γ, M: MDA-5, A: ARS, and O: others). Baseline characteristics such as tongue pressure, penetration-aspiration scale (PAS) and dysphagia severity scale (DSS) based on the findings of videofluoroscopy and/or videoendoscopy were compared. Duration of rehabilitation was also evaluated as an outcome. [Results] Of 9 cases, 3 was in Group T, 3 in M, 1 in A, and 2 in O. Mean tongue pressure (kPa) was T: 27.1, M: 30.2, A: 30.7, O: 26.2. As for PAS, PAS3 and 5 (penetrations), 8 (silent aspiration) were found in T, but no aspirations in other groups. In DSS, all patients in T were 2/food aspirators. In M, 2 cases with 3/water and one with 4/occasional aspirators, and 3 was in A. DSS4 and 6/minimum problem were involved in O. Mean duration of rehabilitation (days) was T: 125.3, M: 93.3, A: 113.0 and O: 40.5, respectively. [Conclusions] DM patients with anti-TIF1-γantibody might be more severe and need longer duration of rehabilitation than other groups.

W52-6

Do exercise therapy and occupational therapy improve patient-reported outcomes in rheumatoid arthritis treatment?

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Conflict of interest: None

[Objective] To make 2020 Japanese Guidelines for the management of rheumatoid arthritis as a clinical epidemiological study regarding the standardization of RA treatment in Japan, specified by the Ministry of Health, Labor and Welfare. [Methods] We searched from PubMed, The Cochrane Library, and Ichushi (exercise therapy from 2009 to 2018 and occupational therapy from 2003 to 2018). We selected articles evaluating patient-reported outcomes (PROs) and describing RA drug treatment. [Results] Meta-analysis of 7 RCT on exercise therapy and 3 RCT on occupational therapy were performed, which were extracted from 662 articles and 396 articles respectively. The exercise or occupational therapies analyzed were diverse and different in terms of targeted patients, intervention methods and duration, but the results were considered consistent. For exercise therapy, significant improvement was achieved in HAQ-DI (mean difference 0.28 [95% confidence interval 0.03-0.52]), pain VAS (mean difference 9.4 [95% confidence interval 0.8-19.6]), and SF-36. Also, for occupational therapy, HAQ-DI improved significantly with mean difference 0.35 (95% confidence interval 0.08-0.63). [Conclusions] The exercise therapy and occupational therapy in RA treatment improved PROs.

W53-1

Elevated expression of BAFF receptor, BR3, in peripheral monocytes is involved in B cell activation and clinical features of patients with primary Sjögren's syndrome

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Conflict of interest: None

[Objective] We reported that monocytes from primary Sjögren's syndrome (pSS) showed robust increase in IL-6 production upon the stimulation. In our present study, we investigate the possible roles of abnormal monocytes in clinical features of pSS. [Methods] The expression level of BR3 on peripheral monocytes of pSS patients (n = 67) and healthy controls (HC: n = 37) was analyzed by FACS. The serological data of the patients was collected by clinical records. Peripheral B cells were cultured with autologous monocytes with/without BAFF. The proportion of plasmablasts/plasma cells and IgG production were analyzed by FACS and ELISA, respectively. [Results] BR3 expression on pSS monocytes ($BR3^+/CD14^+$) was significantly higher than HC and was correlated with serum levels of IgG and IgM and ESSDAI score of the patients. In addition, $BR3^+/CD14^+$ was elevated in anti-Ro/SSA and/or anti-La/SSB positive patients as compared to negative patients. BAFF enhanced the proportion of plasmablasts/plasma cells and IgG production when pSS B cells were cultured with autologous monocytes. Notably, addition of anti-IL-6 receptor antibody into the culture inhibited IgG production. [Conclusions] Our data clearly indicate that accelerated BAFF-BR3 axis in monocytes is involved in the pathogenesis of pSS.

W53-2

Possible involvement of Toll-like receptor 4 in enhanced expression of BAFF receptor on peripheral monocytes from patients with primary Sjögren's syndrome

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Conflict of interest: None

[Objective] It has been reported that Toll-like receptors (TLRs) are involved in onset and/or development of primary Sjögren's syndrome (pSS) and that monocytes play a crucial role in pathogenesis of the disease. We showed that elevated expression of BAFF receptor (BR3) on peripheral monocytes contributed to B cell activation in pSS. In this study, we investigated possible involvement of TLRs in enhanced expression of BR3 on pSS monocytes. [Methods] THP-1 cells were stimulated with TLR1-9 agonists and BR3 expression on the cells and amount of IL-6 produced by the cells were analyzed by FACS and ELISA, respectively. The expression of TLR4 and MyD88 in peripheral monocytes from pSS patients (n = 26) and healthy controls (n = 15) were analyzed by qPCR. [Results] FACS analysis revealed that TLR4 and TLR5 agonists, LPS and flagellin, respectively, enhanced BR3 expression on THP-1 cells in 24h. LPS induced IL-6 production by THP-1 cells, whereas flagellin did not show the production. In addition, the expression of TLR4 and MyD88, signal transduction molecule via TLR4, in peripheral monocytes were elevated in pSS patients as compared to HC. [Conclusions] Our results collectively suggest that TLR4 is involved in the elevated expression of BR3 on peripheral monocytes from pSS patients.

W53-3

Examination of parotid gland ultrasonography (US) and serological findings in cases with dry mouth

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Conflict of interest: None

[Objective] We examined serological findings related to parotid gland US findings in dry mouth patients. [Methods] The subjects were 102 patients with dry mouth. The US grades of the parotid gland were classified into G0 to G4 (G0: 41, G1: 18, G2: 11, G3: 9, G4: 23 cases). [Results] The positive rates of ANA and RF of G0 group were significantly lower than the other groups. The positive rates of anti-Ro were no difference between the 5 groups (G0: 73%, G1: 88%, G2: 100%, G3: 100%, G4: 80%), the positive rates of anti-centromere antibody (ACA) were significantly different in the 5 groups (G0: 9%, G1: 11%, G2: 0%, G3: 44%, G4: 32% ($p < 0.05$)). Grades in 67 ACA negative cases (ACA (-) group) were G0 / G1 / G2: 73%, G3 / G4: 27%, and ACA positive 15 cases (ACA (+) group) were G0 / G1 / G2: 33% and G3 / G4: 67%. G3 / G4 was significantly higher in the ACA (+) group ($p < 0.01$). IgG (mg / dL) level was 1861 ± 594 in the ACA (-) group, which was significantly higher than 1478 ± 656 in the ACA (+) group ($p < 001$). the IgG value was a significant difference among 5 groups in the ACA (-) group, and increased in order from G0 to G3. [Conclusions] ACA was found at a high rate in G3 and G4, suggesting a relationship with echogenic bands. IgG reflected grade progression in anti-SS-A antibody positive patients.

W53-4

Clinical characteristics associated with glandular involvement evaluated by salivary gland ultrasonography in Sjögren's syndrome

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Conflict of interest: None

[Objective] To identify clinical index including disease activity associated with glandular involvement evaluated by salivary gland ultrasonography (SGUS) in patients with Sjögren's syndrome (SS). [Methods] We enrolled SS patients (n=109) and non-SS sicca subjects (n=90). SGUS and clinical index such as age, sex, focus score (FS), sicca symptom, Saxon test, Schirmer test, anti-SS-A/Ro antibody, anti-SS-B/La antibody, anti-centromere antibody (ACA), rheumatoid factor, serum IgG, and clinical ESSDAI were examined. The US score was calculated based on the SGUS imaging (hypoechoic area, hyper echoic band and irregular border). [Results] The multivariate analysis selected FS, Saxon test positivity, ACA positivity and clinical ESSDAI as the variables independently associated with US score in SS patients. The ACA positive patients had significantly higher the US score compared to ACA negative patients, whereas the FS was not significantly high. In addition, the ACA positive patients had significantly greater the positivity of hyperechoic bands compared to ACA negative patients. [Conclusions] These results suggest that glandular involvement was associated with systemic disease activity, and US findings of ACA positive patients might show specific change of salivary glands not only sialadenitis.

W54-1

Quantification of AC13, a novel serum biomarker candidate for microscopic polyangiitis

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Conflict of interest: None

[Objective] We previously found that a peptide fragment of the C-terminal 13 amino acid residues of apolipoprotein A-I, AC13, was specifically increased in sera from patients with microscopic polyangiitis. In this study, we tried to quantify serum AC13 concentration using an internal control peptide (stable isotope labeled, SIL-AC13) and mass spectrometry (MALDI-TOF/MS). [Methods] Peptides were extracted from 20 pmol/μL SIL-AC13-added serum samples, and ion intensity of the extracted peptides were measured using MALDI-TOF/MS. Concentration of serum AC13 was calculated from the ratio of its ion intensity to the intensity of SIL-AC13. [Results] Serum AC13 was significantly increased in MPA (6.2±4.2 pmol/mL, $p<0.05$; n=12) compared to GPA (2.3±0.9 pmol/mL, n=5), RA (2.0±0.6 pmol/mL, n=12), and healthy condition (2.0±0.9 pmol/mL, n=12). Serum AC13 concentration was correlated with CRP values at a moderate level ($r=0.596$, $p<0.05$). [Conclusions] Serum AC13 concentration was quantified using an internal control peptide and mass spectrometry. The MPA-specific increase of AC13 suggested the usefulness of AC13 as a biomarker for MPA.

W54-2

Investigating the clinical relevance of serum immune complexes in ANCA-associated vasculitis (AAV)

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Conflict of interest: None

[Objective] To investigate the clinical relevance of serum immune

complexes in AAV patients. [Methods] We developed a novel proteomic strategy for identifying and profiling antigens in immune complexes in the serum of microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) patients. The serum was collected from the cohort of Japan Research Committee of the Ministry of Health Labour, Welfare for Intractable Vasculitis (JPVAS) before treatment and 6 months after initiation of treatment. The serum from healthy individuals was used for control samples. [Results] We were able to examine 91 AAV patients (52 MPA patients and 39 GPA patients). We identified auto antigen of EGF-containing fibulin-like extracellular matrix protein 1 (EFEMP1) in 43 of MPA (82.6%) and 16 of GPA (41.0%). The clinical features of EFEMP1 positive in AAV patients were higher age at onset ($p < 0.01$), less ear, nose and throat symptoms at initiation of treatment ($p < 0.05$), higher serum Cr at initiation of treatment ($p < 0.01$), higher BVAS renal component at 12 and 24 months after initiation of treatment (both $p < 0.05$). [Conclusions] Our findings indicate that an autoantigen as immune complexes of EFEMP1 were involved in the pathogenesis of AAV patients and may predict renal prognosis.

W54-3

Analysis of biomarkers associated with interstitial pneumonia in patients with microscopic polyangiitis

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Conflict of interest: None

[Objective] This study aims to identify serum biomarkers for interstitial pneumonia (IP) in patients with microscopic polyangiitis (MPA) using the results of chest high-resolution CT (HRCT) analysis (AJR Am J Roentgenol. 2019;11:1) and serum proteome analysis in the Remission Induction Therapy in Japanese Patients With ANCA-Associated Vasculitis and Rapidly Progressive Glomerulonephritis (the RemIT-JAV-RPGN) study. [Methods] The subjects were 64 MPA patients. Serum levels of TIMP1, Tenascin C (TNC), CD93, Transketolase, LRG1, S100A8/A9, MMP9, Multimerin 1 (MMRN1), CRP and MPO-ANCA were measured by ELISA using samples collected before treatment. The relationship between each biomarker and HRCT findings was analyzed. [Results] The serum levels of TNC, MMP9 and KL-6 were significantly higher in patients with IP than in those without. The following positive correlations were found: between ground-glass opacity score and KL-6; honeycombing score and MMRN1 or KL-6; and reticulation score and TNC. The level of MMRN1 was significantly higher in the UIP group (median 395 ng/mL), compared with those in the Possible UIP (117 ng/mL) or Inconsistent with UIP group (165 ng/mL). [Conclusions] We identified MMRN1 as a novel biomarker for MPA patients with UIP pattern.

W54-5

Association of a variant upstream of HLA-DRA with MPO-ANCA positive vasculitis

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Conflict of interest: None

[Objective] We previously reported the association of *HLA-DRB1*09:01* with MPO-ANCA positive ANCA-associated vasculitis (MPO-AAV) in the Japanese population. We recently conducted genome-wide association study (GWAS) in AAV and detected a tendency for association of single nucleotide variant (SNV) upstream of *HLA-DRA* with MPO-AAV. In this study, we validated the association of the *HLA-DRA* SNV. [Methods] Association of *HLA-DRA* SNV with MPO-AAV was tested using 556 AAV, including 441 MPO-AAV, and 5557 controls. Meta-analysis was conducted by Mantel-Haenszel method. [Results] In our GWAS, a tendency for association of *HLA-DRA* SNV with MPO-AAV was detected ($P=1.3\times10^{-5}$). In replication study, significant association of the *HLA-DRA* SNV was detected ($P=5.0\times10^{-4}$) and the association reached genome-wide significance ($P=4.1\times10^{-8}$) by meta-analysis. To examine whether the *HLA-DRA* SNV and *DRB1*09:01* are independently associated with MPO-AAV, we conducted conditional logistic regression analysis. The association of the *HLA-DRA* SNV remained significant after conditioning by *DRB1*09:01* ($P=0.039$), while that of *DRB1*09:01* disappeared after conditioning ($P=0.42$). [Conclusions] Our observations suggested that SNV upstream of *HLA-DRA* may be primarily associated with MPO-AAV in the Japanese population.

W54-6

Venous thromboembolism and clinically important bleeding during remission induction therapy for ANCA-associated vasculitis

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Conflict of interest: None

[Background] ANCA-associated vasculitis (AAV) is a systemic inflammatory disease, and thromboembolism and bleeding due to persistent small vessel inflammation are problematic. In addition, hypercoagulability due to corticosteroids used for induction therapy and bleeding tendency due to anticoagulant therapy may be involved in their pathology. [Method] Between January 2010 and December 2018, we examined all patients who had received remission induction therapy for newly diagnosed AAV in our department. We examined venous thromboembolism and bleeding events during hospitalization. [Results] There were 78 AAV cases, 48 MPA cases, 16 GPA cases, and 14 EGPA cases. Deep venous thrombosis and PE (DVT/PE) occurred in 14 cases, and clinically important bleeding occurred in 19 cases. Patients with DVT / PE tended to be older; their average age was 77 years. Although bleedings occurred in 14 of 48 cases of MPA and 5 of 16 cases of GPA, there was no clinically important bleeding in patients with EGPA. In the group with bleeding, the rate of patients who received methylprednisolone (mPSL) pulse therapy was higher; 9 of 19 patients with bleeding received mPSL pulse, while 15 of 59 patients without bleeding received it.

W55-1

Usage of biologics in RA patients complicated with pulmonary lesions and chronic infections

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patients often have the complications of pulmonary lesions and chronic infections. Here we have determined whether these complications affect the usage of biologics in our hospital. [Methods] One hundred and twenty-six patients with RA (ETN n=13; ADA n=14; IFX n=12; GLM n=12; CZP n=9; ABA n=23; TCZ n=43) were analyzed for the complication rate of lung lesions and chronic infections at baseline. The exacerbation of complications, new infections, and treatment response after initiation of biologics was also analyzed. [Result] Lung lesions/chronic infections were observed in 5/2 (ETN), 4/0 (ADA), 1/0 (IFX), 2/0 (GLM), 1/0 (CZP), 9/4 (ABA), and 10/1 (TCZ) patients at baseline. Upon initiation of biologics, exacerbation of lung lesions was noted in 1 (ETN), 3 (ABA) and 1 (TCZ) patients, while that of chronic infections was noted only in 1 (ABA) patient. However, only 2 patients (TCZ and ABA) discontinued the therapy. New infections led to discontinuation of therapies in 1 (ETN) and 3 (TCZ) patients. These complications did not affect the treatment response to biologics in patients. [Conclusions] These results suggest that biologics be an effective therapeutic option for RA patients complicated with pulmonary lesions and chronic infections.

W55-2

Efficacy and safety of abatacept for rheumatoid arthritis complicated with interstitial lung disease in our department

Akinori Okada, Chisato Ashida, Fusayo Ikeda, Atsuhiro Yamamoto, Daisuke Tomita, Tetsu Itami, Kenji Sakai, Shinkai Ri, Toshihiko Shiga, Kazuya Kishimoto, Yuji Nozaki, Koji Kinoshita, Masanori Funauchi, Itaru Matsumura
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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) occur in approximately 20% of patients with rheumatoid arthritis (RA). For RA with ILD, standard treatment including methotrexate is often difficult, and biologics are also carefully administered, so there is no established therapeutic guideline. In this study, we examined the efficacy and safety of 18 patients with abatacept (ABT) for RA with ILD. [Methods] RA patients with ILD who had visited our department were retrospectively examined in 18 patients who received ABT. [Results] The average age was 70.4 ± 11.2 years, the average disease duration was 51.1 ± 73.7 months, the average DAS28-ESR was 5.2 ± 1.0, the ABT duration was 21.9 ± 15.9 months, and corticosteroid (PSL) was combined 16 cases (89%), PSL dose 7.3 ± 4.3 mg/day, ABT withdrawal cases 7 cases (6 cases due to inadequate effect, 1 case due to malignant lymphoma development), ILD acute exacerbation cases 2 cases, There were 2 cases of clinical improvement of ILD. Adverse events (AE) were shingles in 1 case and pneumonia requiring hospitalization in 2 cases. There were no discontinuation due to AE. [Conclusion] In RA with ILD, there were 2 cases of exacerbation, but 16 could be administered without exacerbation. We report on ABT for RA patients with ILD, with literature review.

W55-3

Abatacept therapy in rheumatoid arthritis with interstitial lung disease

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the clinical outcomes of abatacept (ABT) therapy in RA patients with interstitial lung disease (ILD). [Methods] Subjects were 17 RA patients with ILD treated with ABT. We investigated the patient background, treatment retention rate and reason for discontinuation. The changes in disease activity, serum biomarkers, PSL dose, and respiratory function were also investigated. (0/24 weeks/1 year/2 years/last observation) [Results] Mean age was 72.4 years, 12 women (70%), disease duration was 10.1 years, retention rate was 77% at 6 years, and the reason for discontinuation were 2 cases with insufficient responses, 1 case with malignant lymphoma, and 1 case with ILD exacerbation. DAS28-CRP: 5.0/2.8/2.7/2.5/2.5, CRP (mg/dl): 3.0/1.3/1.0/0.9/0.8, MMP-3 (ng/ml): 281/149/138/125/126. There were significant decrease after 24 weeks compared with the baseline. PSL (mg/day): 4.6/3.3/3.3/1.9/2.4. PSL dose at 2 years and at the last observation were significantly lower than baseline. There was no significant deterioration in respiratory function compared with the baseline. [Conclusions] Many reports suggest the safety of ABT for RA patients with ILD. However, ILD itself is a poor prognostic factor for RA, so it should be treated carefully.

W55-4

Sarilumab in rheumatoid arthritis with Interstitial Lung Disease

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Conflict of interest: None

[Objective] We aimed to analyze about actual usage of sarilumab for rheumatoid arthritis (RA) and the cases complicated with interstitial lung disease (ILD). [Methods] Our study enrolled consecutive RA patients administered sarilumab from October 2018 to May 2019. We evaluated the clinical data and HRCT, and prognosis. [Results] A total of 25 RA patients who had initiated sarilumab were extracted and 21 cases that could be analyzed (7 males, 14 females, median age 71 (60-78)). MTX naive 9 cases (43%), MTX dose 8mg (6-9.5), csDMARD naive 6 cases (29%), bio naive 14 cases (67%), steroid use 4 cases (19%), and complicating ILD in 4 cases (19%). Disease activity at the start of sarilumab was high (DAS28-CRP 4.8 (4.2-5.5), DAS28-ESR 6.1 (5.0-6.6), CDAI 25 (18-34), SDAI 26.0 (19.2-40.1), CRP 1.15mg/dL, ESR 69/mm). After starting sarilumab the value of CRP was dramatically decreased in 2 weeks. The continuation rate after 24 weeks was 90%, and the overall continuation rate was 81%, and 4 cases were discontinued. The reasons for discontinuation were cellulitis, epigastric pain, upper respiratory tract infection, and self-interruption. All ILD were continued without any deterioration. [Conclusions] RA treated with sarilumab was effective and well tolerated from an early stage.

W55-5

The effectiveness of anti-IL-6 therapy to elderly-onset rheumatoid arthritis

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Conflict of interest: Yes

Objective To evaluate the efficacy and safety of tocilizumab (TCZ) in elderly-onset rheumatoid arthritis (EORA) patients. ***Methods*** We retrospectively investigated EORA patients who were treated with TCZ (TCZ-EO) or TNFi (TNFi-EO). We also studied patients with younger-onset RA (YORA) treated with TCZ (TCZ-YO). DAS28-ESR (3) was used for the evaluation of disease activity. Drug survival rates and adverse events (AE) seen in the first 1 year from the initiation of these biologics were also analyzed. And the reasons for discontinuation of the biologics was collected. ***Results*** Total number of patients was follow: TCZ-EO 40, TCZ-YO 67, TNFi-EO 70. DAS28-ESR (3) from baseline to week 24 was significantly decleased in TCZ-EO than that of TNFi-EO (3.3 vs 2.5). In each component of DAS28-ESR (3), only ESR was significantly decreased in TCZ-EO than that of TNFi-EO ($p<0.05$). 456 patients (TCZ-EO: 91, TCZ-YO: 141, TNFi-EO: 224) were enrolled the analysis in AE and drug survival. AE were not different between 3 groups. The drug survival rate was significant longer in TCZ-EO than TNFi-EO group (175 vs 126 weeks). About reasons of discontinuation, insufficient effect was significantly small in TCZ-EO than the other groups (11 vs 33 vs 69). ***Conclusion*** TCZ could be effective to EORA patients.

W55-6

Elderly rheumatoid arthritis patients and selection of biologics

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Conflict of interest: None

[Objective] To analyze the use of biologics in elderly patients with rheumatoid arthritis (RA) [Methods] From July to September 2019, 622 RA patients who were administered biologics in our hospital were examined for the status of administration, dosage, and self-injection of biologics. [Results] Of 622 RA patients treated with biologics in our hospital, 47% were under 65 years of age, 33% from 65 to 75, 16% from 75 to 85, and 4% over 85. All types of biologics were administered to every RA patient regardless of age. There was no difference in the ratio of intravenous and subcutaneous injection formulations among ages. Under 65, anti-TNF antibody preparations were mainly used. On the other hand, non-anti-TNFα antibodies were the majority over the age of 85. Intravenous injection formulations were often used for the elderly. With the exception of IFX and ETN, no difference was observed between age and dosage. The proportion of self-injection decreased with age. 87 was the oldest who performed self-injection. [Conclusions] All types of biologics were administered to the elderly RA patients. No difference was observed between age and injection dose. Proportion of self-injection decreased with age. Elderly patients who have difficulty in frequent hospital visits seemed to choose self-injection.

W56-1

Therapeutic effect of certolizumab pegol on methotrexate doses in rheumatoid arthritis

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Conflict of interest: Yes

[Objective] There have been few reports comparing the therapeutic effects of certolizumab pegol (CZP) according to MTX dose, and we investigated the therapeutic effects of CZP treatment according to MTX dose. [Method] RA cases treated with CZP (N = 54) were observed retrospectively. RA cases treated with ADA (N = 30) as a control group, we compared the continuation rate, disease activity (DAS28-ESR), and treatment response (EULAR response) for patients with MTX high dose (H group: 8 mg / week or more) and low-medium dose group (L group: less than 8 mg / week). [Results] In the continuation rate after 1 year of CZP and ADA treatment, there was no significant difference between H group (89.5% vs 78.9%) and L group (87.5% vs 85.7%). DAS28-ESR changes were significantly different in the L group (H group: -2.9 ± 0.3 vs -3.0 ± 0.3, L group: -2.8 ± 0.5 vs -0.5 ± 0.6). The good response group (Good + Moderate response) was significantly increased by CZP treatment in the L group (H group: 89.5% vs 76.5%, L group: 81.3% vs 33.3%). [Conclusion] We examined the continuation rate, DAS28 and EULAR treatment responsiveness of CZP and ADA treatment in H group and L group, and showed that CZP treatment effect was higher at low-medium doses of MTX.

W56-2

Loading effect of TNF inhibitors on disease activity in patients with rheumatoid arthritis -ANSWER cohort study-

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Conflict of interest: None

[Objective] TNF inhibitors (TNFi) for rheumatoid arthritis (RA) are categorized into two groups: loading TNFi (L-TNFi) and non-loading TNFi (NL-TNFi). The purpose of this study is to investigate the loading effect of TNFi treatment on disease activity in RA patients. [Methods] Three hundred sixty-one RA patients who started TNFi treatment with DAS28-ESR ≧ 2.6 in ANSWER Cohort were included. L-TNFi (IFX, CZP) group and NL-TNFi (ETN, ADA, GLM) group were compared with DAS improvement (ΔDAS) and retention rate of TNFi. Stratified analysis was performed in the high disease activity (HDA) group and the moderate disease activity (MDA) group. [Results] There were significant differences between L-TNFi group (n=129) and NL-TNFi group (n=232) in disease duration (1.00 vs 2.00 years), DAS28-ESR (4.86 vs 4.59) and HAQ-DI (1.00 vs 0.88). The cumulative retention at one year after starting TNFi was 48.1% vs 46.8% (p=0.62). ΔDAS for 3, 6 and 12 months was -1.92 vs -1.68 (p=0.16), -2.42 vs, -1.93 (p=0.01), -2.87 vs -2.48 (p=0.03). In HDA group, L-TNFi use was associated with ΔDAS for 3 months (β=-1.14, p=0.04) in multiple linear regression model adjusted for potential confounders. [Conclusions] The loading effect of TNFi on the improvement of disease activity was seen early in the HDA group.

W56-3

The efficacy of treatment to rheumatoid arthritis (RA) after inadequate response to two bDMARDs or JAK inhibitor (Difficult to treat RA (DT-RA))

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Conflict of interest: None

Objective: If a bDMARD (Bio) or JAK inhibitor (JAKi) failed for rheumatoid arthritis (RA) patients, treatment with another Bio or Jaki (another mode of action (MOA)) should be considered. However, difficult to treat RA (DT-RA) patients with inadequate response to at least two Bio or JAKi exist in daily clinical practice. The aim of study is to assess the treatment to DT-RA. Method: In this retrospective study, we evaluated 45 DT-RA patients about the background with introduction of Bio and treatment after failure of two Bio or JAKi. Result: We classified DT-RA (80% of women, average age 59.7 years old, and average disease duration 7.4 years) to treatment with only TNF inhibitor (TNFi cycler) group and MOA group. In TNFi cycler group, MTX combination rate was high (84.2% (TNFi cycler) vs 61.5% (MOA)), and prednisolone combination rate was low (57.9% (TNFi cycler) vs. 76.9% (MOA)). However, CDAI remission rate after the treatment to switch to MOA did not differ (68.4% (TNFi cycler) vs 61.5% (MOA)). Moreover, CDAI remission rate by switching to JAKi was 87.5% of the whole DT-RA (TNFi cycler (n=2): 50%, MOA (n=6): 100%, and switching to over fourth Bio or JAKi (n=4) group: 100%). Conclusion: JAKi is regarded as effective treatment to DT-RA.

W56-4

Difference of bDMARDs and tsDMARDs usage in real-world

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Conflict of interest: None

[Objective] 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 and Methods] We used clini-

cal data obtained from ***NinJa 2016*** and ***2017***, which had been gathered from about 70 hospitals all over Japan. The **669** cases, which were treated some bDMARD or tsDMARD in 2017 and treated without any bDMARD or tsDMARD or treated with not the same medicine in 2016 were selected. [Results] Number of patients with each drugs were as follows (%: 1st bio ratio); a ETN: 74 (80), b IFX: 14 (79), c TCZ: 169 (62), d ADA: 43 (79), e ABT: 122 (68), f GLM: 84 (73) g CZP: 34 (44), h TOF: 90 (47), i BAR: 24 (63), j IFXBS 15 (20). Age; a 56.5, b 57.8, c 60.4, d 57.9, e 70.1, f 67.4, g 57.1, h 65.5, i 59.2, j 57.3, CRP (2016/2017); a 0.9/0.44, b 1.85/0.25, c 1.68/0.27, d 0.43/0.23, e 1.64/0.79, f 1.26/0.33, g 1.27/0.33, h 1.53/0.39, i 0.35/0.36, j 0.43/0.2 DAS-ESR (2016/2017); a 3.42/2.98, b 3.45/3.06, c 3.82/2.31, d 3.31/2.76, e 4.17/3.77, f 4.11/3.55, g 3.69/3.13, h 4.41/2.93, i 2.41/2.6, j 2.85/2.3. [Conclusions] This study revealed the difference in the bDMARDs and tsDMARDs usage in the real world. The detailed analysis would explain a proper treatment.

W56-5

Current status of JAK inhibitor users in our facility

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Conflict of interest: None

[Objective] Janus kinase inhibitors (JAKi) are the one of the new strategy of rheumatoid arthritis (RA) treatment. JAKi may effective with refractory RA cases. However, there are few reports on the study of switching from JAKi to JAKi. We clarified the reality of situation about the cases which were switched from JAKi to JAKi. [Methods] The subjects were 67 cases with RA treated with JAKi from July 2015 to September 2019. We investigated the proportion of cases who switched from JAKi to JAKi, the reasons for switching to JAKi, and the disease activity of RA before and after the switch. [Results] There were 33 cases of tofacitinib, 38 cases of baricitinib, and 3 cases peficitinib in our hospital. Seven patients (10.4%) switched from JAKi to JAKi. All cases were switched from tofacitinib to baricitinib. The reason for switching was ineffective in 5 cases (71.4%) and 2 cases (28.6%) for dose reduction. The disease activity of RA after switching achieved remission or low disease activity in all cases. In addition, 2 patients developed lymphoproliferative disorder (LPD) during JAKi administration. [Conclusions] We suggested that the strategy of switching from JAKi to JAKi is effective for refractory RA patients. In addition, we consider about the relationship JAKi and LPD.

W56-6

Comparison of Patient Perceptions and Satisfaction of Pen-type Autoinjectors for Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Pen-type autoinjectors for self-injection are widely used in treatment of rheumatoid arthritis (RA), but there are some differences among preparations in their shapes, button positions. The aim of this study was to investigate patient perceptions and satisfaction of sarilumab (SAR), etanercept biosimilar [MA] (MA) and golimumab (GOL) in RA patients. [Methods] Using demo devices (SAR, MAand GOL) for 102 patients with RA, we investigated "ease of grip" during the self-injection procedure and "satisfaction" . Patients rated the "ease of grip" and "satisfaction" of each injector by visual analog scale (VAS, 0-10points) [Results] Mean age of the patient was 60.5 ± 15.6 years old, DAS28-CRP was 2.1 ± 0.9, Rates of patients who were able to complete the self-injection procedure were 99% in SAR, 94% in MA, 95% in GOL respectively. The average of VAS of "easy to grip" were 8.0 cm in SAR, 7.3 cm in MA, 7.0 cm in GOL "Satisfaction" after usage were 8.2 cm in SAR, 7.3 cm in MA, 6.6 cm in MA [Conclusions] Despite highly rate of patients completed the self-injection procedure with all the three preparations, the degree of satisfaction differed among the preparations. SAR is considered to be highly satisfactory due to its fitting shape for the hand and the buttonless specification.

W57-1

Outcome of patients with rheumatoid arthritis in the intensive care unit: a single-center retrospective study in Japan

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Conflict of interest: None

[Objective] The aim of this study is to examine the outcome and the risk of mortality in the patients with rheumatoid arthritis (RA) in the ICU. [Methods] We included all patients with RA who were admitted in the ICU between January 1, 2017 and December 31, 2018. We compared the patient backgrounds, length of ICU-stay, medications and Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores between non-survivor and survivor. [Result] Seventy admission in the ICU were identified in 65 patients. Of 65 patients who were admitted in the ICU, 15 patients died during study period. The mortality in the ICU and 30-day mortality were 10.8% and 13.8%, respectively. Between two groups, there were no differences in the age, sex, disease duration, length of ICU-stay. The non-survivor group had higher SOFA and APACHE II score than the survivor group (5.0 [0-17] vs 2.0 [0-11] and 18.0 [11-50] vs 14.5 [9-36], respectively). There were no differences in CDAI and DAS28-ESR. The glucocorticoid dosage was higher among the non-survivor group. There were no differences in the usage of MTX and biologics between two groups. [Conclusions] The non-survivor group had higher SOFA and APACHE II score and glucocorticoid dosage than survivor group.

W57-2

Investigation of comorbidities affecting disease activity in rheumatoid arthritis: a register-based study

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Conflict of interest: None

[Objective] The aim of this study to investigate the association between RA activity and comorbidities in the registry. [Methods] In the cross-sectional observational multicenter study AORA in 2017, consecutive 2175 patients were enrolled, 1838 (male 365: female 1473) were analyzed. Patients were divided into two groups, remission or low disease activity and moderate or high disease activity by DAS28, and each group's demographics, treatment, and comorbidities were investigated. [Results] The prevalence of comorbidities were hypertension (33.2%), renal failure, (18.8%), respiratory disease (12.1%), diabetes mellitus (8.6%), heart disease (8.0%), malignant tumor (6.4%), cerebrovascular disease (4.9%). Univariate analysis showed significant differences in age, sex, use of MTX and biologics, and comorbidities other than malignant tumors. Multivariate logistic regression analysis showed an odds ratio of 1.97 ($p = 0.0069$) for cerebrovascular disease and 1.68 ($p = 0.0009$) for respiratory disease. The patients with these comorbidities, MTX usage was low and PSL usage was high. [Conclusions] The high disease activity group of rheumatoid arthritis had a high odds ratio for cerebrovascular disease and respiratory disease and a low rate of MTX usage

W57-4

Risk factors of the fall in patients with aged rheumatoid arthritis

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Conflict of interest: Yes

[Objective] Improvement of disease activity was obsereved by biologis treatment in aged patients with rheumatoid arthritis, ADL of those patient often deteriorate after the fall. The risk factors of the severe fall were examined. [Methods] In aged RA patients over 70 years old, 8 patients who needed admission due to the fall were the fall group and 16 patients without admission were no fall group. The difference of height, weight, skeletal muscle volume, skeletal muscle index, body fat index, MTX treatment, glucocorticoid treatment, DAS28, mHAQ and bone density by DXA mehod in two groups were investigated. [Results] In two groups, height, weight, MTX treatment, DAS28 showed no difference. In the fall group, glucocorticoid treatment and mHAQ showed high. Skeletal muscle volume and skeletal muscle index show low, but no difference in two groups. Body fat index were high in the fall group. Bone density showed no differences. [Conclusions] The risk factors of the fall in patients with aged RA were assumed high mHAQ, glucocorticoid treatment and sarcopenia obesity. Approach to the patients with those risks factor though to be necessary.

W57-5

RA patients with high disease activity and treated with high dose glucocorticoid frequently fall: nine years of the TOMORROW study

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Conflict of interest: None

[Objective] This prospective study compares the incidence of falls and risk factors influencing falls between patients with RA and Co based on the findings of the TOMORROW study. [Methods] We compared the incidence of falls by self-administered questionnaire every year in 202 patients with RA and in 202 Co over 9 years period. [Results] The rate of individuals who fell did not differ between two groups (RA: 66.9%, Co: 59.2%, p=0.19). However, the incidence of falls was higher in RA than Co (0.35 vs 0.21/person-year, p=0.03). Multivariate logistic regression analysis adjusted for age, sex and BMI, revealed that RA was not a risk factor for the incidence of falls (OR: 1.36, 95%CI: 0.80-2.32, p=0.26) and the history of falls was a risk factor for the incidence of falls (OR: 3.27, 95%CI: 1.78-6.0, p<0.01). Multivariate linear regression analysis adjusted for age, sex and BMI, revealed that mHAQ (β=0.17, p=0.04), mean DAS28-CRP over 9 years (β=0.19, p=0.02) and mean dosage of glucocorticoid over 9 years (β=0.18, p=0.03) were the risk factors for the incidence of falls. [Conclusions] The incidence of falls was significantly higher in RA group. High disease activity and higher dosage of glucocorticoid were the risk factors for the incidence of falls among RA patients.

W57-6

The factors associated with muscle mass recovery after diet and exercise treatment in rheumatoid arthritis patients

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Conflict of interest: None

Background: Rheumatoid arthritis (RA) is inflammatory joint disease and frequently accompanies low muscle mass (sarcopenia). However, the treatment is not well studied. Objectives: To identify factors that associated with muscle mass recovery after diet and exercise treatment in rheumatoid arthritis patients. Methods and Patients: 141 RA outpatients with RA who visited Osaka Minami Medical Center was conducted DXA (Dual Energy X-Ray Absorptiometry). We use 5.4 kg/m2 for women, and 7.0 kg/m2 as a cut-off point of low SMI (Skeletal Muscle Mass Index). 49 patients were identified as muscle decrease. We added diet and exercise treatment and followed low SMI patients and repeated DXA 6 month after from 24 RA patients who we obtained consent. Results: SMI increased 2% after 6 month on average. Age, gender, serum LDL-Chol, lymphocyte count, induction of bioligics during the period (TNF inhibitor 5, IL6 inhibitor 1) are identified as correlator of muscle mass change. Conclusion: Diet and exercise treatment increased muscle mass in RA patients. However, higher age, sex female was identified as inhibitor of muscle mass recovery. Low SMI is associated with female Sex, and low BMI in RA patients. Induction of biologics might help recovering skeletal muscle mass in RA patients.

W58-1

Risk factors of cardiovascular disease in patients with systemic lupus erythematosus using Japanese health insurance database

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Conflict of interest: Yes

[Objective] To identify risk factors of cardiovascular disease (CVD) 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 April 2008 and July 2017, and were ≥16 years old (n=17,730). Patients were followed from the first month in which cases met the above criteria until the earliest of the month of the first CVD, the month of loss of follow-up, or June 2018. CVD was defined using ICD10 code and treatments during hospitalization. We calculated incidence rate (IR) and adjusted hazard ratio (HR) for CVD using a time-dependent Cox proportional hazard model. [Results] IR/1,000 patient-years of CVD, angina, myocardial infarction, cerebral infarction, and cerebral hemorrhage were 5.3, 0.9, 0.7, 3.7, and 0.3, respectively. Significant adjusted HR for CVD were 1.3 for age by decade, 2.1 for hypertension, 1.7 for atrial fibrillation, 1.6 for chronic kidney disease, 1.9 for antiphospholipid syndrome, 5.8 for steroid pulse therapy, 1.6 for oral corticosteroids (CS), and 0.7 for immunosuppressants. [Conclusions] Older age, CS use, and comorbidities were identified as significant risk factors of CVD in SLE.

W58-2

Outcome of collagen and rheumatic disease-associated secondary thrombotic microangiopathy (TMA) in our facility, 2009-2019

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Conflict of interest: None

[Purpose] We present the outcome of a collagen and rheumatic disease-associated secondary Thrombotic microangiopathy (TMA) experienced in our facility over the last decade. [Methods] From April 2009 to November 2019, 32 cases were summarized. [Results] SLE, scleroderma, and MCTD were the most common underlying diseases. Patients were divided into two groups: those with Thrombotic Thrombocytopenic Purpura (TTP) group, in which ADAMTS 13 activity was markedly decreased and ADAMTS13 inhibitors were positive; and those with non-TTP group, in which ADAMTS 13 activity was slightly decreased or remained within the normal range and ADAMTS13 inhibitors were negative. TTP type was observed in 8 patients and non-TTP type in 24 cases. Plasma exchange was performed in all cases. All 8 patients with TTP type were alive at 1 year after, but 3 had recurrence. Of the 24 cases of non-TTP type, 11 died within 1-year despite the multimodal therapy. The age distribution tended to be high for the dead cases. [Conclusion] In non-TTP cases, plasma exchange is often urgently performed while aiming for underlying disease control,

but its long-term effectiveness has not been established. Understanding the secondary TMA mechanism for each case and the corresponding treatment strategies are challenging issues.

W58-3

Study of the characteristics and the novel risk factor of steroid-induced osteonecrosis

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Conflict of interest: None

[Objective] We define the novel risk factors for the steroid-induced osteonecrosis in patients with collagen disease. [Methods] All osteonecrosis patients and patients who received steroid pulse therapy or prednisolone ≧50 mg (or 1 mg/kg)/day from April 2013 to September 2019 were retrospectively evaluated. [Results] Osteonecrosis developed in 57 cases (43 bilateral, 75%). Thirty-two patients (56%) underwent total hip replacement. The median time from commencement of steroid treatment to disease onset was 3.0 years (range 1 month to 21 years). Twenty-four cases had systemic lupus erythematosus (SLE), and 12 dermatomyositis (DM). Since April 2013, osteonecrosis developed in eight of 35 SLE patients. The total observation period was 53.7 years, thus, 13.7/100 person-years; the figure for pulsed cases was 21.4/100 person-years, thus, which significantly greater than that for non-pulsed cases ($p<0.001$). When patients older and younger than 40 years were compared, the observation periods were 6.3 vs. 22.8 ($p=0.02$) per 100 person-years. Disease was predominant in younger people. The observation periods were 21.7 vs. 10.0 for males and females ($p=0.07$); disease was more common in males. [Conclusion] Steroid-induced osteonecrosis is more prevalent in patients younger than 40 years.

W58-4

Characteristics of protein-losing gastroenteropathy associated with collagen-vascular disease

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Conflict of interest: None

[Objective] To investigate the clinical features of protein-losing gastroenteropathy (PLGE) associated with collagen-vascular disease (CVD). [Methods] The clinical records of 8 patients with CVD (mean age, 58.75years; 4women and 4men), who were diagnosed with PLGE in our department, were reviewed. [Results] As for the underlying diseases, systemic lupus erythematosus was involved in 3 patients, rheumatoid arthritis in 3, mixed connective tissue disease in one, and eosinophilic polyangiitis granulomatosis in one. The manifestations related to PLEG included edema, fatigue, diarrhea, abdominal pain and distension as well as hypoalbuminemia. Two patients demonstrated PLGE as the initial episode of CVD. Meanwhile, PLGE occurred within 1 year since the onset of CVD in 3 patients, and more than 2 years later in others. Increases in the activities of underlying diseases were shown at the onset of PLGE. Monotherapy with corticosteroid (CS) was given in one patient, and immunosuppressant was concomitantly administered with CS in 6, achieving in remission. [Conclusions] PLEG might occur in the active phase of underlying CVD. Meanwhile, treatment based on the underlying disease may be suitable for achieving remission in PLEG related to CVD.

W58-5

Clinical evaluation of suffered and affected to the patients of rheumatoid arthritis at the disasters of twice Chiba-Bousou typhoons

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Conflict of interest: None

[Objective] To evaluate the clinical affect to the patients with rheumatoid arthritis (RA) at the twice typhoons. [Methods] After 9, September typhoon No 15 and 19, October 2019 typhoon No 19 at Chiba prefecture, 154 patients were clinical estimated. We evaluated on the change of number of tenderness joints, patient VAS (pVAS) score, CRP, RF, drug therapy and the difference of reaction between the patients who had or not meteoropathy after these typhoons. [Results] 12 patients (7.8%) had to live with no water and electric outage condition more than one day. 3 patients (2.0%) had to live in shelter house due to destruction of their houses. Before and at the disaster time, the number of tenderness joints were 1.9 ± 2.8, 2.1 ± 3.0 ($p=0.126$) respectively. pVAS were 12.8 ± 10.4, 13.6 ± 12.7 (mm, $p=0.369$), CRP were 0.9 ± 1.5, 0.9 ± 2.1 (mg/dl, $p=0.767$), and RF were 45.2 ± 34.9 and 50.9 ± 48.1 (U/dl, $p=0.093$). Total 24.6% had been suffered bad condition, among of them, 31 patients (81.6%) did not use any drug to relief pain, 5 patients (13.1%) used NSAID, 2 patients (5.3%) used steroid, and no patients used csDMARD or bDMARD that with doze up. [Conclusion] One of four patients were worsening temporary. The stress of the typhoon will influence the patients' condition and therapy.

W58-6

Outcome of patients with rheumatic diseases in the intensive care unit: a single-center retrospective study in Japan

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Conflict of interest: None

[Objective] The aim of this study is to examine the outcome and characteristics of the patients with rheumatic diseases in the intensive care unit (ICU). [Methods] We included all patients with rheumatic diseases who were admitted in the ICU between January 1, 2017 and December 31, 2018. We extracted the patient backgrounds, the cause of admission, mortality in ICU, 30-day mortality, and Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores. [Result] One hundred forty admission in the ICU were identified in 130 patients (median age, 74.9 years [range: 15-94], 73.6% female). The median APACHE II and SOFA scores were 16 [3-50] and 2.8 [0-17], respectively. The leading causes of ICU admission were cardiac diseases (30.7%), infection (22.1%), and cerebrovascular disease (17.9%). The underlying diseases of the patients were rheumatoid arthritis (50%), vasculitides (14.3%), SLE (11.4%), inflammatory muscle diseases (5.7%) and systemic sclerosis (4.3%). The mortality in the ICU and 30-day mortality were 10% and 11%, respectively. [Conclusion] The patients with rheumatic diseases were admitted in the ICU for various complications. The mortality in our study was lower than previous reports.

W59-1

Efficacy of iguratimod and salazosulfapyridine (IGU and SASP) combination therapy as a 2nd anti-rheumatic drug (csDMARDs) combination therapy for methotrexate ineadequate response (MTX-IR) in rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] IGU are csDMARDs approved since 2012, and MTX combination therapy is recommended in the 2016 methotrexate (MTX) clinical practice guidelines, but there is currently no evidence for the effectiveness. In this study, we compared IGU and SASP as an additional therapy in MTX-IR in the clinical treatment effects and side effects. [Method] MTX was treated as 1st csDMARDs from 2012, but MTX + IGU group (n

= 53) and MTX + SASP (n = 40) combined were observed for 6 months. We evaluated clinical treatment effects (DAS28-CRP), disease activity, corticosteroid (PSL) dose, and side effects. [Results] 3 months after treatment with MTX + IGU and MTX + SASP were ΔDAS28-CRP (-1.1 vs. -0.7), DAS remission rate (51.4% vs. 23.5%). The results were significantly improved in the MTX + IGU group. PSL reduction (-0.3 vs. +0.4 mg/day) was observed in the MTX + IGU group. The above significant difference disappeared 6 months after the start of treatment. After 3 months of treatment, side effects were similar in liver disorder as ΔAST/ALT in both groups, but renal injury as ΔeGFR was significantly decreased in MTX + IGU group (-8.4 vs. -2.2 mL/min/1.73m2). [Conclusion] In MTX-IR, IGU has the synergistic effects earlier than SASP, but it is necessary to pay attention to kidney damage.

W59-2

Iguratimod for treating rheumatoid arthritis: A Systematic Review and Meta-analysis

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Conflict of interest: None

[Objective] Iguratimod (IGU) is commonly used to treat rheumatoid arthritis mainly in Asia and a lot of RCT studies relevant to IGU have been reported since 2007. We conducted the systematic review and meta-analysis to assess the efficacy of iguratimod for rheumatoid arthritis patients. [Methods] A comprehensive electronic literature search using CENTRAL, Pubmed and Ichu-shi web from 2007 to 2019 was conducted to identify studies evaluating IGU efficacy. A meta-analysis was performed using the random-effects models to calculate relative risk (RR) with 95% confidence intervals (CI). [Results] Seven studies were included in this meta-analysis. In csDMARDs-naïve patients, ACR50 achievement at 24 weeks was significantly better in IGU than in placebo (RR 2.72: 95%CI 1.11-6.66, p=0.03). ACR50 achievements between IGU and csDMARDs (MTX or SASP) are comparable (RR 0.82: 95%CI 0.66-1.03, p=0.09). ACR50 achievement was significantly better in IGU-MTX combination than in MTX (RR 1.84: 95%CI 1.10-3.08, p=0.02). Furthermore, ACR50 achievement was significantly better in IGU-MTX combination than in MTX for csDMARDs-IR patients (RR 2.23: 95%CI 1.67-2.98, p<0.01). [Conclusions] It is suggested that IGU is effective for csDMARDs-naïve or csDMARDs-IR patients from the results of this meta-analysis.

W59-4

An effect of iguratimod as add-on therapy to patients with rheumatoid arthritis inadequately responding to biological DMARDs: (A retrospective study)

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Conflict of interest: None

[Purpose] We investigated the efficacy of rheumatoid arthritis (RA), which was inadequate for bDMARDs, by adding iguratimod (IGU). [Methods] We added IGU to the RA patients being treated with bDMARDs, and analyzed effects on the 44 patients who were able to continue for 12weeks. We examined CDAI, DAS28-ESR, LDA achievement rate. [Results] At baseline; age 66.9, disease duration 14.4, MTX had used 61.3%, PSL had used 43.1%, TNFi 17, CTLA-Ig 16, IL-6Ri 8, JAKi 3. For all bDMARDs, CDAI before add on IGU was 15.6±7.5, at 12 Weeks 8.5±9.6, 24 weeks of 7.9±9.5. Before administration of IGU, LDA was 24%, but after 24 weeks it was 79.5%. As the LDA achievement predictor, the cut-off value at the start of IGU combination was CDAI 21.4 or less, sensitivity 97.1%, specificity 74.9%. Among the bDMARDs, ΔCDAI before start and at 24 weeks showed a significant IGU combination effect in CTLA-Ig: -3.6, TNF inhibitor: -9.2, and IL-6 receptor inhibitor: -13.1. Regarding safety, no cases were discontinued until 24 weeks after the start of IGU combination. [Conclusions] In cases where the bDMARDs effect is insufficient, IGU addition can be expected to improve disease activity. Furthermore, IGU combination is effective as an additional therapy for IL-6 receptor inhibitors compared to CTLA-Ig.

W59-6

Inhibition of joint destruction by Iguratimod in patients with rheumatoid arthritis inadequate response to Disease-modifying antirheumatic drugs

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Conflict of interest: None

[Objective] In 93 RA patients resistant to DMARDs, Iguratimod was additionally used for 1 year to evaluate the efficacy (clinical effects, joint destruction suppression effect by X-ray) and safety. [Methods] The clinical effects were examined by DAS28-ESR and the X-ray evaluation by mTSS by radiographs of hands and feet, and the safety by adverse events. [Results] The subjects were 93 DMARDs IR (DAS28-ESR≧3.2) RA patients (23 male / 70 female), age (mean) 63.4 yrs, disease duration 8.1 year. MTX was used weekly (8.8mg/w, 65 cases, 69.8%), and cs DMARDs were used as BUC 35 cases, SASP 11 cases, TAC 4 cases, and LEF 2 cases. Biological DMARDs were used even in 9 cases (9.7%), and steroids were used in 3.9 mg (56 cases, 60 %). Complications were observed in 55cases (59.1%). DAS28-ESR were significantly improved from 4.62 (baseline) to 3.82 (6 months), 3.81 (12 months), respectively (P<0.0001). Joint destruction measured by mTSS was significantly suppressed from 7.81 before administration, to 0.37 at 1 year (P<0.0001). CRRRP (5>mTSS>3) was observed in 4 cases (4.3%), and RRP (mTSS≧5) was not recognized. Adverse events were observed in 19 cases (20.4 %). The annual continuation rate was 82.8%. [Conclusion] Iguratimod suppressed joint destruction in RA patients resistant to DMARDs therapy.

W60-1

Impact of belimumab on renal outcomes in patients with systemic lupus erythematosus (SLE) located in North-East Asia (China, Japan and South Korea)

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Conflict of interest: Yes

[Objective] Evaluate the renal impact of belimumab (BEL) in pts with SLE in North East Asia (NEA). [Methods] This Phase 3 study randomized NEA pts with SLE aged ≧18 years to standard therapy plus BEL 10 mg/kg IV or placebo (PBO) on Days 0, 14 and 28, then every 28 days until Week 48. Renal outcomes over 52 weeks were: renal flares, SELENA-SLEDAI and BILAG renal-item improvements, proteinuria change, and creatinine (Cr). [Results] Renal flares were reduced with BEL (n=57/451; 12.6%) vs PBO (n=40/226; 17.7%) (BEL HR [95% CI] vs PBO: 0.68 [0.45-1.02]; p=0.0637). At baseline, 31.6% (BEL 30.2%; PBO 34.5%) pts had SELENA-SLEDAI renal involvement, and 25.0% (BEL 24.2%; PBO 26.5%) had BILAG A/B renal involvement. Of these pts, 61.8% and 41.0% (SELENA-SLEDAI), and 61.5% and 51.7% (BILAG A/B) had renal improvements with BEL and PBO, respectively. Pts with baseline proteinuria >0.5 g/24 h had a median proteinuria reduction of 58.8% for BEL and 58.3% for PBO. Proteinuria shift to ≦0.5 g/24 h was seen in 45.6% and 33.8% of pts with high baseline proteinuria for BEL and PBO, respectively. Baseline Cr was similar between treatments; few pts (≦1.5%) exhibited doubling at any visit. [Conclusions] The renal outcome improvement trend with BEL vs PBO is consistent with prior Phase 3 studies. [Funding] GSK

W60-2

Across-Trial Comparison of Intravenous Belimumab Efficacy and Safety in Children and Adults With Systemic Lupus Erythematosus

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Conflict of interest: Yes

[Objective] An across-trial comparison of belimumab (BEL) safety and efficacy in children and adults with active systemic lupus erythematosus (SLE). [Methods] Patients (5-17 years PLUTO [NCT01649765]; ≧18 years BLISS-52/76 [NCT00424476/NCT00410384], NEA [NCT01345253], and LBSL02 [safety comparison only; NCT00071487]) were randomized to intravenous (IV) BEL or placebo (PBO) + standard therapy. Primary efficacy endpoint: SLE Responder Index (SRI) 4 at Week (Wk) 52. Other endpoints: SRI6 at Wk 52 (*post hoc*: BLISS) and time to first severe flare over 52 wks. Adverse events (AEs), serious AEs (SAEs), and AEs of special interest (AESI) were recorded. Comparisons are descriptive. [Results] BEL vs PBO showed improved SRI4 (OR [95% CI] 1.49 [0.64, 3.46]) and SRI6 (1.35 [0.56, 3.22]) in PLUTO, aligning with the adult trials (not shown). Risk of severe flare was reduced in BEL vs PBO for PLUTO (HR [95% CI] 0.38 [0.18, 0.82]) and adult trials (not shown). Patients with ≧1 AE, ≧1 SAE, and malignant neoplasm and postinfusion systemic reaction AESI were similar across trials, except for infection and herpes zoster AESI, which were higher in PLUTO. [Conclusions] Safety and efficacy of IV BEL in children with SLE were consistent with adult studies supporting a favorable BEL benefit/risk profile. [Funding] GSK

W60-3

Effectiveness and safety of belimumab in the treatment of SLE patients in clinical practice

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Conflict of interest: None

[Objective] Belimumab (BLM), a human anti-BAFF monoclonal antibody, is currently a sole biologic agent for SLE patients, however our experience with BLM in clinical practice was still relatively limited. [Methods] SLE patients in our hospital were analyzed for a chronological change in clinical symptoms and laboratory findings prior to and following BLM treatment. [Result] Sixteen SLE patients (1 male, 15 females) were enrolled in this study. Their median age was 34 years, median disease duration 10 years, median PSL dose 12 mg, and concomitant drugs were HCQ 56%, CyA 50%, TAC 25%, MMF 38%, MZR 19%, and IVCY 13%. The median disease activity was 5 (2-10) for SLEDAI-2K, and BILAG category B or higher was 19% (mucocutaneous), 6% (musculoskeletal), 6% (ocular), 25% (renal) and 6% (hematology). Upon BLM therapy there was a tendency towards improvement in disease activity scores, complement levels and autoantibody titers. Skin improvement was particularly noted in patients. Therapy was aborted due to infections (n=2) and self-discontinuation (n=1). [Conclusions] These results suggest that BLM exert a therapeutic effect on SLE when added to conventional therapies. We will also present a chronological change in immunocompetent cells prior to and following treatment in the meeting.

W60-4

Efficacy of belimumab for Systemic Lupus Erythematosus-comparison of corticosteroid reduction between anti-ds-DNA antibody positive and negative patients-

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Conflict of interest: None

[Objective] We examined the clinical course of Systemic Lupus Erythematosus (SLE) patients treated with belimumab and the effect of corticosteroid reduction in SLE patients with stable disease activity. [Methods] We retrospectively examined medical records of 35 SLE patients administered belimumab in our institution. Among 19 patients continuing belimumab more than 6 months, we classified anti-ds-DNA antibody (aDNA Ab)-positive and -negative groups. Between 2 groups, we compared patient background and the dose of corticosteroid at 24 weeks. [Results] Among 35 patients, mean age was 41 years old, mean disease duration was 14 years, female rate was 86%, median using duration of belimumab was 7 months and adherence rate of belimumab was 71%. There were 11 aDNA Ab-positive patients and 8 -negative patients. The mean age, female rate and serum C3 were not significantly different. The disease duration, serum IgG, and dose of corticosteroid were significantly different. Although corticosteroid at 24 weeks was significantly lower in negative group (-1.6±5.7 vs -4.6±5.0 mg/day, p=0.04). [Conclusions] Belimumab seems to be effective even in the serologically inactive SLE patients.

W60-5

Efficacy and Predictive Factor of Belimumab

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Conflict of interest: None

[Objective] Belimumab has been shown to improve disease activity, hypocomplementemia, anti-dsDNA antibody titers and reduce PSL dosage in patients with systemic lupus erythematosus (SLE). We took the observational study to assess the efficacy and predictive factor of belimumab (BLM). [Methods] Seventeen SLE patients who received maintenance therapy and started BLM between February 2018 and June 2019 were studied. Efficacy of BLM was evaluated at baseline and 24 weeks by anti-dsDNA antibody, PSL dosage, SLEDAI-2K, along with BILAG. [Results] Female was 96%, disease duration was 12.7 years. Positivity of anti-dsDNA antibody, anti-RNP antibody, anti-Sm antibody, anti-SS-A antibody, anti-APS antibody were 83%, 56%, 56%, 61%, 55%, respectively. Lupus Nephritis and CNS lupus rates were 26% and 26%. SLEDAI-2K score, anti dsDNA antibody, PSL dosage were significantly decreased. C3 and C4 levels were remarkably increased. Patients receiving hydroxychloroquine (HCQ) significantly achieved PSL dosage reduction of more than 25% and experienced increased C3 and C4 levels and decreased anti-dsDNA antibody. [Conclusions] In clinical practice, BLM significantly improved serological marker and disease activity score, reduced PSL dosage and showed the effectiveness of combination therapy with HCQ.

W60-6

The Effect And Safety Of Belimumab In Clinical Practice

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Conflict of interest: None

[Objective] Belimumab is a drug that has recently become available for systemic lupus erythematosus (SLE) treatment, but has not been used efficiently in clinical practice. Therefore, we investigated the effect and safety of belimumab in clinical practice. [Methods] We extracted the patients with SLE prescribed with belimumab from September 2017 to No-

vember 2019, and analyzed the adverse events. In addition, changes in prednisolone (PSL) dose, anti-ds-DNA antibody, C3, C4 and IgG were examined. [Results] Thirteen patients were extracted during the period, with average administration duration of 490 days. One of the 13 patients discontinued due to inadequate effect, and one discontinued because of arrhythmia; but arrhythmia continued even after discontinuation. There was no serious infection in all patients during the period. SDI did not increase except for one case with angina. PSL was reduced from 6.8 mg/day to 4.9 mg/day on average, and not increased in any patients. C3, C4 and IgG were significantly improved, but there was no significant decrease in anti-ds-DNA antibody. [Conclusions] It was proved that belimumab can safely reduce serological activity and PSL dose. In addition, belimumab may have a clinically significant effect in about 1 to 2 years.

W61-1

Changes of platelet counts in rheumatic disease patients affected by cytomegalovirus infection

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Conflict of interest: None

[Objective] Based on mechanisms that human hematopoietic stem cell and stromal cell in bone marrow are infected by cytomegalovirus (CMV), patient comes to thrombocytopenia. But there are several competing risks of thrombocytopenia as for CMV infection, for example, ganciclovir (GCV). Thus, We aimed to study the changes of platelet counts in patients affected by CMV. [Methods] Patients were chosen from hospitalized to be under treatment of rheumatic disease in our hospital, diagnosed with CMV infection and started the GCV treatment. We included 15 patients have adequate data and excluded 8 patients not so. Platelet counts data were collected and allocated by period, and we carried out Wilcoxon signed-rank test. [Results] 73% (11/15) of patients recovered from thrombocytopenia within first week (average increasing rate 12%; p=0.02). Over two weeks later, platelet counts of three patients delayed recovery, then increasing after finishing GCV. It is suggested that risk factor of delayed of recovery is the rate of thrombocytopenia before treatment (p=0.04), on the other hand, lymphocyte count and antigen level of CMV is not the risk. [Conclusions] Thrombocytopenia due to CMV infection generally recover within first week after starting GCV. We should consider other cause of thrombocytopenia.

W61-2

Incidence and risk factors of herpes zoster in patients with systemic lupus erythematosus using Japanese health insurance database

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Conflict of interest: None

[Objective] To calculate identify incidence andidentifyrisk factors of herpes zoster (HZ) 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 April 2008 and January 2018, and were >16 years old (n=21,374). 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. HZ was defined using ICD10 code and one prescription of antiviral drugs. We calculated incidence rate (IR) and adjusted hazard ratio (HR) for risk factors of HZ using a Cox proportional hazard model. [Results] Mean age in years was 54 and 81.2% were female. IR of HZ was 20.3 /1,000 patient-years. Significant adjusted HR for HZ were 1.15 [1.01-1.30] for hypertension, 1.38 [1.16-1.63] for diabetes mellitus, 1.27 [1.10-1.46] for chronic obstructive pulmonary disease (COPD) or asthma, 1.40 [1.07-1.82] for depression, 2.95 [2.32-3.75] for malignancy, 1.91 [1.59-2.29] for steroid pulse therapy, and 1.26 [1.12-1.41] for immunosuppressants. [Conclusions] Comorbidities, steroid pulse therapy, and immunosuppressants were identified as significant risk factors of HZ in SLE.

W61-3

Clinical features of nocardiosis as a complication of connective tissue disease

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Conflict of interest: None

<Objectives> To investigate the clinical features of nocardiosis as a complication of connective tissue disease. <Methods> We examined patients diagnosed with nocardiosis from October 2004 to October 2019. We retrospectively investigated 1) patient characteristics, 2) therapeutic course and 3) comparison between survivors and non-survivors. <Results> 1) Fourteen patients (4 male/10 females,60.0±19.9 years old) were examined. Underlying disease were SLE (n=4), vasculitis syndrome (n=4), rheumatoid arthritis (n=3), adult still disease (n=2) and dermatomyositis (n=1). Infection sites were lung (n=12), brain (n=6), skin (n=4) and muscle (n=1). Multi-site infections were seen in 8 patients, and blood cultures were positive in 4 patients. At the onset of nocardiosis, all patients were given PSL (23.2±11.9mg/day). Only 2 patients were given TMP-SMX for prophylaxis. 2) Nine patients were given TMP-SMX, and 7 of them were reduced or changed to other antibiotics (IPM, MINO) due to adverse event. Relapse was occurred in a patient, and 4 patients died. 3) In a comparison of survivors (n=10) and non-survivors (n=4), cutaneous infections were significantly more frequent in the later (10% vs 75%, p=0.04). <Conclusion> Cutaneous infections were significantly more frequent in non-survivors than survivors.

W61-4

Whether biologics use or low nutritional status increase the risk of surgical site infection?

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Conflict of interest: None

[Objective] We examined whether biologics use or low nutritional status increase the risk of surgical site infection or not. [Methods] We evaluated 372 patients data who was performed orthopaedic surgery in 2017 (Rheumatoid arthritis (RA): 100; others: 272). We evaluated weight, height, sex, duration of operation, implant use, type of surgery, total volume of bleeding, use of MTX, biologics, prednisolone, blood albumin, CRP, total protein, cholesterol, lymphocyte, and nutritional status using Geriatric nutritional risk index and Controlling Nutrition Status. [Results] Six patients affect surgical site infection, 1 patients was RA and 5 patients were others. There was no statistical differences of rate of surgical site infection between RA patients and others. Use of biologics did not increase the rate of surgical site infection. Only male and higher height increased the rate of surgical site infection in all patients. Nutritional status did not affect the rate of surgical site infection. [Conclusions] In this study, only 6 patients were affected surgical site infection, because we examined only 1 year data. Now we are evaluating further number of patients in several years to improve the knowledge of the risk factors for surgical site infection in patients with biologics use.

W61-5

Does prophylaxis with trimethoprim-sulfamethoxazole against pneumocystis pneumonia suppresses the development of bacteremia in immunosuppressed patients?

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Center

Conflict of interest: None

[Objective] To investigate whether trimethoprim-sulfamethoxazole (TMP/SMX) suppresses the development of bacteremia in patients with high-dose glucocorticoid for rheumatic diseases. [Methods] We includes all patients who were admitted in our hospital between October 1, 2003 and March 31, 2018 and started high-dose glucocorticoids for rheumatic diseases. The incidence of bacteremia were assessed for 120 days after commence of high-dose glucocorticoid regimen. The predictors of bacteremia were evaluated by multivariate analysis. [Results] Total of 455 patients were enrolled. There were 138 cases of primary vasculitis, 110 cases of lupus, 98 cases of myositis, 42 cases of rheumatoid arthritis, and 67 cases of other rheumatic diseases. Of 392 patients who were given TMP/SMX prophylaxis, TMP/SMX was discontinued in 87 patients. A total of 19 bloodstream infections were found: 12 in patients with TMP/SMX and 7 in patients without. Predictors of bacteremia were TMP/SMX (odds ratio (OR): 0.32 (95%CI: 0.1-0.9)), glucocorticoid pulse therapy (OR: 4.29 (95%CI: 1.2-15.6)), central venous catheter (OR: 6.75 (95%CI: 2.4-18.7)). [Conclusion] Prophylaxis with TMP/SMX may reduce the risk of bacteremia in patients with rheumatic diseases undergoing high-dose glucocorticoid therapy.

W61-6

The risk of infection in patients with ANCA vasculitis treated by Rituximab

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Conflict of interest: None

[Objective] Discovering of risk factors for infection in rituximab (RTX) treatment to ANCA vasculitis (AAV). [Methods] Target: AAV patients used RTX in our department (Jan. 2015-Nov. 2019). They were devided 2 groups (Inf+/-) by getting infection or not 6 months after RTX. They were retrospectively checked. [Results] Inf+: 10 (M6, F4), Inf-: 10 (M7, F3). Age: Inf+: 77.0 (69-85), Inf-: 73.9 (29-91) (p=0.61). AAV type: Inf+ (MPA: 9, GPA: 1), Inf-(MPA 4, GPA 5, EGPA 1). 3 deaths were in Inf+ and 2 were pneumonia. RTX was used 1-4 times, NSD in frequency (p=0.71). Days to infection: 46.4 (6-104). Infection type: bacterial pneumonia: 4, deep fungal infection: 2, PCP: 2, FN: 1, pulmonary abscess: 1, tuberculosis: 1, Herpes Zoster: 1. Premedication: Inf+ (TAC: 2, AZA: 2), Inf- (AZA: 2, CY: 1); concomitant medications at onset: TAC: 5 (1.6; 0.5-2.5), AZA: 2 (75; 50 -100). Total PSL dose (mg) before RTX was NSD (p=0.85). IgG (mg/dL), segmented cell, Lymphocytes (/μl) before RTX were NSD (p=0.36,0.82,0.67). CD4+ (/μl): Inf+: 467 (185-677), Inf-: 869 (361-1160), sinificant difference (p=0.006). By ROC curve, CD3+ (/μl) cut-off was 1107.7 (SS 71.4%, SP 71.4%, AUC 0.694), CD4+ (/μl) cut-off was 697.5 (SS 100, SP 85.7, AUC 0.898). [Conclusion] The number of CD3+ and CD4+ lymphocytes before RTX is effective for predicting infection.

W62-1

Investigation of the optimal tibial posterior slope angle in cruciate-retaining total knee arthroplasty in rheumatoid arthritis

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Conflict of interest: None

[Objective] The goal of the study was to investigate a surgical procedure to determine the optimal tibial posterior slope angle in cruciate-retaining total knee arthroplasty (CR-TKA) in rheumatoid arthritis (RA). [Methods] The subjects were 30 knees with RA knee. The femoral component size was determined based on the anterior reference. Then, tibial osteotomy vertical to the tibial axis was applied using a medullary rod, and the extension gap and flexion gap were measured with a femoral trial setting. The difference between the extension and flexion gaps was defined as Δ gap. In the normal knee, the contact point between the femur and tibia at 90° flexion is located about 70% from the anterior tibial joint surface toward posterior. Thus, using 70% of the anteroposterior diameter of the tibia as the base and Δ gap as the height, and the angle was calculated from the base and height using an inverse trigonometric function. The calculated angle was defined as the optimum tibial posterior slope angle. [Results] Δ gap was 2.7 mm, and the tibial posterior slope angle added was 5.2°. Partial dissociation of the PCL was not used in any case. [Conclusions] Using this surgical procedure, the optimum tibial posterior slope angle in CR-TKA can be determined in RA.

W62-2

Perioperative Transition of C-Reactive Protein in Rheumatoid Arthritis and Osteoarthritis for Total Knee Arthritis

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Nagoya University Medical Hospital

Conflict of interest: None

[Objective] It is important to know perioperative transition of CRP in patients with RA because postoperative CRP is not only an index of a perioperative infection but also disease activity of RA. We investigate transition of CRP in RA for TKA and verify whether anti-rheumatic drug have an effect on postoperative CRP. We compare transition of CRP after TKA between RA and OA patients. [Methods] We examined transition of CRP in 104 patients with RA and 124 patients with OA for TKA at our hospital between 2006 and 2017. We collected blood test data before surgery,1day,3or4day,1week and 2week after surgery. [Results] The median age was 66 years,88 patients was female, and the median disease duration was 13.2 years. Postoperative CRP peaked at 3 or 4 days after surgery. Patients who treated with TCZ had lower CRP at any time compared to patients who did not treat with biologics and those who treated with non-TCZ biologics. Patients who treated with MTX also had lower CRP at 3 or 4 days after surgery compared to patients who did not treat with MTX. RA patients had lower CRP at 3 or 4 days after surgery than OA. [Conclusions] MTX and TCZ may influence CRP after TKA in RA patients.

W62-3

Comparison of clinical outcomes of total knee arthroplasty between patients with rheumatoid arthritis and osteoarthritis using patient-reported questionnare

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Conflict of interest: None

[Objective] total knee arthroplasty (TKA) was widely performed for patients with rheumatoid arthritis (RA) and osteoarthritis (OA) in the word, however there are some patients who do not satisfy the clinical outcomes of TKA. We investigated clinical outcomes of TKA between patients with RA and OA using patient-reported questionnaire (J-KKOS). [Methods] We included 13 RA knees and 27 OA knees we can collect the pre-op and post-op 1-year data of J-KOOS from April 2017 to April 2018. We analyzed the data with WZR. [Results] Each domain of J-KOOS were significantly improved from pre-op to post-op situations among RA group and OA group (P<0.05. RA group significantly had lower score in the domains of pre-op symptom (RA: OA=44:58) and pre-op pain (RA: OA=35:45) (P<0.05). On the other hand, in the post-op situation, symptom and pain were improved in the same level between both groups. There was no difference between both groups in the post-op ADL, sport and quality of life. Each domain had ceiling effect as 80-85 peak points, and the items which did not adequately improve were deep flexion, heavy labor and lifestyle. [Conclusions] RA group improved symptom and pain at the same level compared to OA group although RA group had lower symptom and pain score before TKA.

W62-4

TKA Outcomes in Hemodialysis Patients: Comparative Study with Non-Hemodialysis Patients

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Conflict of interest: None

[Objective] We compared the outcomes after total knee arthroplasty (TKA) between hemodialysis (HD) patients and non-HD patients. [Methods] We compared 14 HD patients 20 knees (male 4 female 10) with a matched cohot of 14 non-HD patients 20 knees. The average age was 71.6 years. The average HD duration was 9.1 years. Clinical outcomes were evaluated preoperatively and 1 year postoperatively by JOA, Lysholm and Oxford scores. [Results] Total JOA scores in HD/non-HD groups were 48/56 preoperatively and 68/76 postoperatively, respectively, with significant differences. Although JOA-pain/walk subscores in HD/non-HD groups were 12/17 preoperatively and 18/25 postoperatively, respectively, with significant differences, there were no significant differences in the other JOA subscores. Preoperatively and postoperatively, there were no significant differences in Lysholm (preop 49/50 and postop 71.5/76.5) and Oxford scores (49/50 and 72/77), but postoperative Oxford-walk subscores were significantly lower in the HD group (2.1/2.9). [Conclusions] Depsite poorer long-distnace walking ability in HD patients compared to non-HD patients, TKA in HD patients is expected to bring good short-term outcomes largely comparable to those in non-HD patients.

W62-5

Annual changes in age of patients with osteoarthritis and rheumatoid arthritis undergoing total knee and hip arthroplasty

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Conflict of interest: None

[Objective] This study aimed to compare the annual changes in the age of the surgery in the case of artificial knee and hip replacement (TKA, THA) for RA patients and osteoarthritis (OA) patients. [Methods] At two facilities from 2004 to 2018, TKA 1406 cases (RA 479 cases, OA 927 cases) and THA 1362 cases (RA 186 cases, OA 1176 cases) were implemented. The annual change of the age of surgery and the age of RA onset was investigated. The three period (04-08 years: first period, 09-13 years: mid period, 14-18years: late period) was divided by the surgery date. [Results] Although the age at the time of surgery of TKA increased significantly in RA patients ($P<0.001$), there was no significant annual change in OA patients ($P=0.026$), and there was significantly younger in RA patients in all periods. The age of surgery in THA has increased significantly in RA and OA patients (both $P<0.001$), which was significantly lower in RA patients in the first period, but in mid period and late was not significantly different in RA and OA patients. [Conclusions] The increase in the age at the time of surgery in total joint arthroplasty is a characteristic change in RA patients compared to OA patients, and is considered to be one of the causes of the increase in the age of RA onset.

W62-6

Radiographic analysis of the primary fixation of cementless stems after total hip arthroplasty -RA v.s. other hip arthritis-

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Conflict of interest: None

[Objective] To compare radiographically the primary fixation of cementless stems in total hip arthroplasty between patients with rheumatoid arthritis and other hip arthritis. [Methods] Sixty-two primary cementless THAs including 9 hips with RA were subjected to this study. All hips were followed for minimum 3 years after surgery. Using the Gruen classification, spot welds and reactive/radiolucent lines were analyzed in each zone, and the points of total 14 zones were defined as the total score (TS). In addition, the points of the porous area were defined as the porous score (PS). TS and PS were compared between patients with RA and other hip arthritis at 6-month, 1-year, 2-year, and 3-year after surgery. [Results] Both TS and PS were not significantly different at any time-points between patients with RA and other hip arthritis. [Discussion] In this study, there were no significant differences in the primary fixation of cementless stems between patients with RA and other hip arthritis. When the stem size is fitted with the proximal canal shape and the stem alignment is optimal, the primary fixation of cementless stems for RA is considered stable.

W63-1

Analysis of clinical manifestations of Adult-onset Still's disease patients

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Conflict of interest: None

[Objective] We aimed to classify AOSD patients into the latent class, and reveal the risk factors for relapse in AOSD. [Methods] A total of 216 AOSD patients (52 men and 164 women) diagnosed between 2000 and 2019 were identified from medical records in 9 hospitals. Baseline characteristics, treatments, relapses, and death were evaluated by retrospective chart review. Classification was performed using latent class analysis. [Results] The median age of disease onset was 51.6 years old. At the disease onset, 99.5% of the patients had fever, 79.5% had arthralgia, 90.7% had eruption, and 63.6% had a sore throat. The median WBC at diagnosis was 12600/mL, serum ferritin value was 7230ng/mL, and CRP was 10.8mg/dL. The median starting dosage of prednisolone was 40mg/day. During the follow-up period, 13 cases died of infectious disease. Seventy-six cases experienced recurrences, and the cumulative 5-year relapse-free survival probability was 58.0%. As a result of the analysis, patients were divided into two groups: a typical group and an elderly-onset group. The risk factor for relapse of Adult-onset Still's disease is the high erythrocyte sedimentation rate. [Conclusions] AOSD patients are divided into the typical group and the elderly-onset group. The risk factor for relapse is the high ESR.

W63-2

Clinical features and prognosis of arthritis in 3 cases of adult onset stills disease showed synovitis by musculoskeletal ultrasonography

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Conflict of interest: None

[Background] It is known that arthritis of adult onset still's disease (AOSD) don't cause joint erosion, but in some cases cause joint erosion and destruction. We investigated the clinical features and prognosis of arthritis in three cases of AOSD showed synovitis by musculoskeletal ultrasonography (MSKUS). [case 1] A 30-year-old female with fever, joint pain, rash, lymphadenopathy and liver damage, ferritin 4039U/l, CRP 5.8mg/dl. Moderate articular synovitis of only the left PIP3 joint were observed by MSKUS. [case 2] A 67-year old female with fever, joint pain, and liver damage, ferritin 28506U/l, CRP 31mg/dl. Severe articular synovial thickening and high doppler signal reached bone surface of MCP and wrist joints were observed by MSKUS. [case 3] A 74-year old female, with fever, swelling in both legs, rash, and liver damage, ferritin 15522U/l, CRP

16mg/dl and hemophagocytosis in bone marrow. She showed moderate articular synovitis, tenosynovitis of fingers and wrist and baker cysts by MSKUS. They achieved remission by the combination of high-dose corticosteroids (CS) and tocilizumab (TCZ). Case 2 maintained by CS, and showed ulnar deviation and swan neck deformity half a year later. [Conclusion] MSKUS may be available to predictive prognostic of arthritis with AOSD.

W63-3

Clinical features in refractory Adult onset Still's disease

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Conflict of interest: None

[Objective] In Adult onset Still's disease (AOSD), corticosteroid (CS) is first-line therapy. However, some patients are resistant to monotherapy with CS. We aim to clarify the clinical features of refractory AOSD. [Methods] The clinical records of 42 patients with AOSD who had admitted in our hospital were reviewed; consequently, 37 patients (54 ± 18 years) were recruited. Of those, patients who required an additional treatment with another immunosuppressant and/or increase in corticosteroid after the initial treatment were categorized into "refractory group" . Clinical background including Pouchot score, treatments, complications and prognosis were analyzed. [Results] Mean period of hospitalization was 57 ± 30 days. Refractory group was classified in 23 patients. Body weight was lower in refractory group than that in non-refractory group. Patients in refractory group significantly indicated sore throat; moreover, percent frequency of neutrophil, Pouchot score, and initial dose of CS were significantly higher in refractory group than those in non-refractory group. [Conclusions] Our study, in which some clinical factors implicated in refractory AOSD development were demonstrated, may contribute to improving prognosis of patients with AOSD.

W63-4

Clinical features of elderly onset adult-onset Still's disease

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Conflict of interest: None

[Objective] To clarify the characteristics of elderly onset adult-onset Still's disease (AOSD). [Methods] By a retrospective multicenter study, we collected clinical information on 131 patients with AOSD. Clinical features were compared between the elderly onset group (older than 60 years) and younger onset group. [Results] The age of onset was bimodal with peaks at 26-40 and 61-70. Elderly onset group had fewer typical skin lesions and sore throat, and more pleuritis and disseminated intravascular coagulation. The severity score, LDH and ferritin was higher in elderly onset group. Cyclosporine was more frequently used, and biologics were less frequently used. Prognosis was poor and drug-free remission was less frequent in elderly onset group. [Conclusions] Various characteristics of clinical features and prognosis were observed in elderly onset AOSD.

W63-5

Clinical features of adult Still's disease complicated with Sjöegren syndrome

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Conflict of interest: None

[Objective] About 30% of Sjögren's syndrome (SS) is secondary SS. Most of secondary SS is associated with rheumatoid arthritis and systemic lupus erythematosus; however, there are few reports about secondary SS complicated by adult Still's disease (AOSD). The aim of this study was to investigate the characteristics of SS complicated by AOSD. [Methods] Consecutive patients, who were diagnosed with SS and AOSD were retrospectively examined. Clinical and laboratory features were compared between the groups of SS with and without AOSD. [Results] We identified 550 SS patients without AOSD (SS group), 16 AOSD patients without SS (AOSD group) and 6 SS patients with AOSD (SS+AOSD group). The rate of drug eruption in the SS+AOSD group (66.7%) was higher than in the SS group (24.6%) and the AOSD group (38.5%). The mean levels of ferritin were 9791.83 ng/mL in the SS+AOSD, and 399.7 ng/mL in the SS group. While we noticed fever in 83%, rash in 83%, joint pain in 67% of the SS+AOSD group, extraglandular manifestations were observed more frequently in the SS+AOSD group than in the SS group. [Conclusions] Among patients diagnosed with SS, high ferritin levels and extraglandular manifestations may be associated with AOSD. In addition, patients with SS complicated by AOSD had frequent drug eruptions.

W63-6

Clinical features and efficacy of tocilizumab in adult onset Still's disease patients

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Conflict of interest: None

[Objective] To clarify the clinical features of patients with adult onset Still's disease (AOSD) treated with TCZ, and its efficacy. [Methods] 26 cases with AOSD in University of Tsukuba hospital in 2015-2019 were included in this study. We divided into 2 groups of patients whether treated with TCZ and not, and retrospectively evaluated and compared 1) characteristics, 2) clinical course, 3) adverse events. [Results] 1) We identified 5 cases with TCZ and 21 cases without TCZ. Mean severity score of AOSD in research group of Ministry of Health, Labour and Welfare is 4.4±1.9 and 2.8±1.3 in cases treated with or without TCZ, respectively, and there were statistically significant difference between them (p=0.03). 2) Dose of predonisolone (PSL) and levels of CRP and ferritin were significantly decreased since 12 weeks after the therapeutic intervention in both cases treated with or without TCZ, and there were no significant differences between them. 3) Liver injury was reported as TCZ-related adverse events in 2 cases. [Conclusions] These results suggested that TCZ was effective for PSL reduction and improvement of disease activity even in more severe cases with AOSD.

W64-1

Investigation of characteristics of immune checkpoint inhibitor-induced rheumatic and musculoskeltal immune-related adverse events

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Conflict of interest: None

[Objective] To investigate characteristics of immune checkpoint inhibitor (ICI)-induced rheumatic and musculoskeltal immune-related adverse events (irAE). [Methods] We investigated medical reports of patients who had rheumatic and musculoskeltal irAE induced by ICI in the department of rheumatology in Kyoto Prefectural University of Medicine from 2018 Jan to 2019 Oct retrospectively. [Results] Number of patients; 4, age; 75.3±2.5 years old, 4 male, period from administration to onset; 3.5±2.6 months, amount of corticosteroid (predonisolone-adjusted); 13.8±6.3 mg/

day. Two patients had renal cell carcinoma, 1 lung adenocarcinoma, and 1 lung squamous cell carcinoma. Two patients received nivolumab and 2 received pembrolizumab. Three of 4 patients were examined with ultrasonography and 3 exhibited wrist tenosynovitis, 2 bicipital tendinitis, and 1 wrist synovitis. Autoantibodies were negative for all patients. One patient continued ICI but 3 discontinued. Three patients showed partial response but 1 stable disease. One patient complicated hypoadrenocorticism and 1 showed eosinophilia. [Conclusions] Rheumatic and musculoskeltal irAE were induced by PD-1 inhibitors, associated with good anti-tumor effect. Adrenocortical hormone test might be useful to treat rheumatic and musculoskeltal irAE.

W64-2

Retrospective analysis of the risk of severe infections caused by immunosuppressants

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Conflict of interest: None

[Objective] Although the frequency of complications of infection during the use of immunosuppressants and biologics has been reported as part of drug information, the actual clinical risk of infection is not clear. The purpose of this study is to clarify the risk of developing severe infections caused by the use of immunosuppressants and biologics in patients with regular visits to internal medicine in collagen disease. [Methods] From March 1996 to August 2019, patients who visited the Tokyo Medical Center's Collagen Disease Department outpatient department for more than two months were included. Multivariate analysis assessed the risk contribution of age, sex, and treatments. [Results] A total of 3647 patients who visited the hospital for two months or more from March 1996 to August 2019 were included. 204 patients were hospitalized for infectious diseases. Risk factors for hospitalization due to infection are elderly ($p = 0.0006$), female ($p = 0.008$), Infliximab ($p = 0.005$), Abatacept ($p = 0.0181$) Golimumab ($p = 0.0131$), MTX ($p = 0.0431$), Azathioprine ($P = 0.0186$) and Cyclosporine ($p = 0.042$). [Conclusions] Elderly, female, MTX, Azathioprine, Cyclosporine and some biologics correlated significantly with hospitalization due to infection.

W64-3

A Rapid ATP Bioluminescence-based Antimicrobial Susceptibility Test Starting from Positive Blood Culture Bottles

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Conflict of interest: None

Administering appropriate antimicrobial therapy as early as possible is important for rescuing bacteremic patients. Therefore, rapid antimicrobial susceptibility tests in positive blood culture specimens have been diligently sought. Adenosine triphosphate (ATP) bioluminescence-based methods have been used for rapid antimicrobial susceptibility tests. However, blood culture specimens have not been examined in many studies, possibly due to abundant intracellular ATP in blood corpuscles resulting in false-susceptible results. In this study, we developed a rapid ATP bioluminescence-based method for detecting antibiotic resistance starting from positive blood culture. To minimize background ATP originating from blood corpuscles, specimens were centrifuged and the supernatant diluted with broth, and an ATP-eliminating reagent was then added to the bacterial suspension at the beginning of incubation. This newly devised procedure reduced the background ATP by more than five orders of magnitude. In a pilot study using levofloxacin, no false-susceptible results were observed in 15 clinical specimens. Therefore, our approach will contribute to the treatment of infectious diseases as a rapid antimicrobial susceptibility test.

W64-4

Rapid diagnosis of septic arthritis with synovial fluid presepsin compared to crystal arthritis

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Conflict of interest: None

[Objective] Therapeutic outcomes for septic arthritis vary greatly depending on the span of time between disease-onset and surgery. However, some cases may be difficult to diagnose against crytal arthritis. We investigated presepsin, a biomarker of sepsis, to determine whether or not presepsin in synovial fluid would be useful for the diagnosis of septic arthritis. [Methods] We selected 98 patients with septic arthritis, crystal arthritis and osteoarthritis. We measured the concentrations of synovial fluid presepsin and blood C-reactive protein (CRP) in the three groups. And we compared the value of synovial fluid presepsin, blood CRP in the groups. [Results] Synovial fluid presepsin were significantly higher in septic arthritis and crystal arthritis compared to osteoarthritis. Crystal arthritis was significantly lower than septic arthritis. And blood CRP were significantly higher in septic arthritis and crystal arthritis as well as synovial fluid presepsin. However, there were not significant difference in blood CRP between septic and crystal arthritis. [Conculusion] We found that synovial fluid presepsin is markedly elevated in case of septic arthritis compared to crystal arthritis, and therefore it has potential as a new biomarker of septic arthritis.

W64-6

MSU Deposition in Gout Patients and Their Disease History

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Conflict of interest: None

[Objective] Monosodium urate deposition is detectable on musculoskeletal ultrasonography (US) in gouty arthritis patients, but it remains fully understood whether this finding is associated with the patient's gout history. [Methods] We searched for eligible gout patients who undertook timely US during the years 2007-2018. We then examined their medical history, serum uric acid, uric acid excretion index, eGFR and US findings. Double contour sign (DCS) was defined as an abnormal hyperechoic band over the superficial margin of the cartilage. [Results] A total of 28 patients (4 female, 24 male) were selected to be eligible for this study. DCS was found in 23 patients (82%). 16 of them showed this finding in an MTP joint of their big toes. First episode of a gout flare occurred in 4 (17%) of DCS-showing patients, whereas 4 (80%) of non-DCS patients, suggested that DCS was associated with multiple gout flares ($p=0.0148$). Anti-hypertension drug was given to DCS-showing patients less frequently than non-DCS patients (21.7% vs 80%, $p=0.0256$), but the serum uric acid level, uric acid excretion index and eGFR were similar between two groups. [Conclusions] DCS suggested a history of multiple gout attack and was important for the patient education to engage in the treat-to-target treatment.

W65-1

Galectin-9 as a biomarker for disease activity in systematic lupus erythematosus

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Conflict of interest: None

<Objective>SLE is an autoimmune disease characterized by elevated

interferon (IFN) signature genes. Recent study demonstrated that galectin-9 (Gal-9) is an useful biomarker for IFN signature. <Methods>This study included 58 patients with recent-onset SLE and 26 SLE patients obtained cerebrospinal fluid (CSF) samples. All patients underwent physical examination, laborarory test, and review of medical records. Gal-9 and IFN-α were measured using ELISA. <Results>The serum levels of Gal-9 were significantly higher in SLE patients compared to healthy controls. Serum levels of Gal-9 in SLE patients showed positive correlation with SLEDAI and serum levels of ds-DNA antibody titer, CXCL-10, M2BPGi, and negative correlation with C3. Serum levels of Gal-9 were significantly higher in SLE patients with detectable serum IFN-α compared to those without detectable INF-α. Serum levels of Gal-9 were significantly higher in SLE patients with active renal involvement determined by BILAG score compared to those without renal involvement. CSF levels of Gal-9 were significantly higher in SLE patients with NPSLE compared to those without NPSLE as well as non-SLE controls. <Conclusion>Serum and CSF Gal-9 could be an useful biomarker for SLE-mediated organ involvement including lupus nephritis and NPSLE.

W65-2

Clinical and Immunological Analysis of Deep Remission During Induction Therapy for Lupus Nephritis

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Conflict of interest: Yes

[Methods] We prospectively enrolled the patients with active LN who started IT in our hospital from 2015. We divided them by complete remission (CR) (stabilization in serum Cr with UPCR≦0.5 g/gCr) and DR. We compared renal flare (persistent UPCR>0.5g/gCr or active urinary sediment associated with renal dysfunction), increase in SLICC damage index (ΔSDI) and peripheral immunophenotyping. [Results] Forty-one patients were enrolled. Mean observational period was 31.3±11.3 months. Cumulative renal flare and ΔSDI were significantly lower in patients with DR than CR (p=0.036 and p=0.035). The patients with DR had higher SLEDAI at baseline (p=0.021). The proportions of NKT-like cells and CD19+B cells were higher in patients with DR than those with CR (p=0.021, p=0.043). [Conclusions] Achievement of DR within 12 months after IT had lower prevalence of renal flare and lower progression of SDI compared with CR. Higher SLEDAI, the proportions of NKT-like cells and CD19+B cells before starting IT may distinguish the patients with DR and CR.

W65-3

Monocyte CD64 (Fc gamma RI) for disease activity marker in systemic lupus erythematosus

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Conflict of interest: Yes

[Objective] Systemic lupus erythematosus (SLE) is one of the typical autoimmune diseases that cause a variety of organ lesions with Interferon (IFN)-alpha as key cytokines. Focusing on monocyte CD64 molecular (mCD64) to enhance expression by IFN-alpha, we have reported the possibility of measuring mCD64 of SLE (n=40) and becoming a disease activity marker. The number of cases was increased only to SLE which exhibited a variety of pathologies, and a more detailed study was carried out. Methods] mCD64 of SLE of 128 cases was measured by flow cytometry. SLEDAI (SLE disease activity), which is an SLE activity marker, anti-ds DNA antibody and complements were compared with mCD64. Results] Mean (±SD) of mCD64 is 28154 (±13874) molecules/cell in active SLE (SLEDAI≧6). The mCD64 of active SLE is significantly higher than the inactive SLE (p<0.000), it showed a positive correlation with SLEDAI (r=0.38, p<0.000). The correlation was observed compared to other active markers. mCD64 was not correlated with IFN-alpha, it was correlated with macrophage-colony stimulating factor (M-CSF). Conclusion] mCD64 may be an activity marker for SLE, but it not only reflects IFN-alpha, but it has also been suggested that it may be highly expressed under the influence of various cytokines such as M-CSF.

W65-4

Detection of characteristic immune subpopulations by mass cytometry in systemic lupus erythematosus

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Conflict of interest: None

[Objective] Cytometry by time-of-flight (CyTOF) is a mass cytometry that can simultaneously analyze more than 40 antigens using metal-labeled antibodies. In this study, we attempted to identify new cell populations related to pathological mechanisms in SLE by the analysis of peripheral blood mononuclear cells (PBMC) in untreated SLE using CyTOF. [Methods] PBMCs from untreated SLE patients and healthy individuals were stained with 36 kinds of metal-labeled antibodies, and expression markers were evaluated by CyTOF analysis using viSNE and FlowSOM. [Results] $CD19^+$B cells increased in SLE, among which $CXCR5^-$HLA-$DR^+Ki\text{-}67^+$ B cells were positively correlated with SLE disease activity score (SLEDAI). There was no difference between regulatory T cells and follicular T cells (Tfh), but $CXCR5^-PD\text{-}1^+$ peripheral helper T cells (Tph) increased in SLE. In addition, $CD14^+$ monocytes and $CD11c^+$ $HLA\text{-}DR^+$ dendritic cells decreased, while $Ki\text{-}67^+$ $CD14^+$ cells increased. [Conclusions] The increase in $CXCR5^-$HLA-DR^+ $Ki\text{-}67^{high}$ B cells might have contributed to the pathogenesis of SLE based on the increase of Tph and $Ki\text{-}67^+CD14^+$ cells.

W65-5

The usefulness and the potential of a new SLE disease activity measure, SLE Disease Activity Score (SLE-DAS)

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Conflict of interest: None

[Objective] The accurate evaluation of SLE disease activity is of great importance for adopting a treat-to-target strategy. In this study, we exam-

ined the efficacy of SLE Disease Activity Score (SLE-DAS), a newly proposed measure of SLE disease activity. [Methods] We studied 224 patients with SLE from our hospital. Data from March 2019 to September 2019 was collected. [Results] The mean score of SLEDAI-2K, SLE-DAS, and Physician's Global Assessment (PGA) was 3.1±4.6, 4.2±6.1, and 0.54±0.50, respectively. SLEDAI-2K and SLE-DAS significantly correlated with PGA (r = 0.49 and 0.56). Correlation between SLE-DAS and SLEDAI-2K was 0.66. A cut-off value of 4.0 in the SLE-DAS was identified as the optimal discriminant for either SLEDAI-2K≦4 or >4 (sensitivity 85%, specificity 84%). Besides, SLEDAI-2K and SLE-DAS highly correlated with PGA (r = 0.41 and 0.49) in patients with no proteinuria. The correlation was, however, reduced to 0.16 for SLEDAI-2K. On the contrary, the correlation of SLE-DAS with PGA remained as high as 0.42 in patients with proteinuria≧500mg/day. [Conclusions] SLE-DAS demonstrated a high correlation with PGA and SLEDAI-2K. Furthermore, SLE-DAS may have the potential to show superior performance, especially in patients with increased proteinuria compared with SLEDAI-2K.

W65-6

A new systemic lupus erythematosus disease activity index SLEDAS correlates with disease activity assessment by patients

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Conflict of interest: None

[Objective] There is a discrepancy between physician's evaluation and patient's evaluation. Recently, SLEDAS has been developed, but there are many unclear points such as correlation with patient's evaluation. [Methods] This study was conducted for SLE patients who visited our hospital from July to October 2019 with the approval of our ethics committee. We measured SLEDAI-2K, physical global assessment (PhGA), SLEDAS, patient global assessment (PtGA), and SLAQ. Spearman's rank correlation method was used to analyze. [Results] Analysis was performed on 164 subjects who were obtained consent and responses. The subjects were 87.9% female, the median age (interquartile range) was 45 [34.5-60.5], and LLDAS was 50.5% (n=107). The median (interquartile range) of SLEDAI-2K was 2.5 [2-4], and the median (interquartile range) of SLEDAS was 2.07 [1.12-3.82]. The correlation between SLEDAS and SLEDAI was 0.598. The correlation between SLEDAI-2K and PhGA, PtGA, and SLAQ was 0.322, -0.126 (p> 0.05), and 0.092 (p> 0.05). The correlation between SLEDAS and PhGA, PtGA, and SLAQ was 0.569, 0.453, and 0.455. [Conclusions] SLEDAS was correlated with PtGA, although it does not include patient evaluation items.

W66-2

Long-term use of golimumab at Niigata Rheumatic Center

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Conflict of interest: Yes

[Objective] The purpose of this study is to evaluate the effectiveness and safety of Golimumab (GLM) every 4 weeks in daily practice at single institution. [Methods] Sixty-five patients started GLM therapy from 2011 October to 2016 March at our institution with a minimum follow-up period of 52 weeks. Sixteen patients discontinued GLM therapy. Mean follow-up period was 129±48 weeks. Rheumatoid arthritis (RA) status was evaluated at 0, 52 weeks and final follow-up using following valuables; Disease activity score, J-HAQ, grip power and treatment continuation rate. Patients were divided into the naïve group and the switch group based on prior use of bDMARDs. Patients' background was analyzed between the continue group and the discontinue group. [Results] Mean DAS28-ESR value improved from 4.4 ± 1.2 to 3.0 ± 1.0 in the naïve group and from 4.2 ±1.3 to 3.3 ± 1.2 in the switch group (p<0.01). J-HAQ did not improve in each group. Grip power improved in both groups. Continuation rate at 52/104/156 weeks were 85.6/81.1/76.3% in the naïve group and 75.7/75.7/71.5% in the switch group, respectively. In the discontinue group, DAS-28 ESR was higher and dose of MTX was less than that in the continue group. [Conclusions] GLM showed high continuation rate, effectiveness and safety by the long-term use.

W66-3

A study focusing on anti-drug antibodies in patients with rheumatoid arthritis who switched from the original infliximab to biosimilar

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Conflict of interest: None

[Purpose] We focused on anti-drug antibodies in RA patients who switched from infliximab to BS. [Methods] The subjects were 29 RA patients (7 males and 22 females) who switched to the infliximab brand or BS. The average age was 69 years old, the average disease duration was 12.1 years, the average MTX use/use amount was 5.6 mg/week, and the PSL usage rate was 45%. The treatment period with the original infliximab was an average of 112 months and an average of 345 mg per dose. Anti-infliximab antibody (ADA) measurement at the time of switching from the original to BS and at the start of treatment 1 year and ESR, CRP, MMP-3, rheumatoid factor, and anti-CCP antibody were examined. [Results] Eight cases (27.6%) were positive for ADA at the start of BS, and one case (3.4%) was newly positive for ADA one year later. Two of the ADA positive cases at the start of BS became negative one year later. The ADA positive group showed significantly higher ESR and rheumatoid factor values than the ADA negative group. [Conclusion] There was no increase in ADA by switching from infliximab brand to BS. ADA-positive cases have high laboratory inflammatory responses and high rheumatoid factors, which may result in poor control of disease activity.

W66-4

Discontinuation of concomitant methotrexate in patients with rheumatoid arthritis treated with tocilizumab: 64-week results from the T-ReX study

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Conflict of interest: Yes

[Objective] To evaluate the efficacy of methotrexate (MTX) discontinuation in Japanese rheumatoid arthritis (RA) patients with sustained low disease activity (LDA) undergoing combination therapy with tocilizumab (TCZ) plus MTX, and to investigate predictors of maintaining LDA. [Methods] This multicenter, open-label, uncontrolled, prospective study included RA patients maintaining LDA (CDAI ≦10) for ≧12 weeks with TCZ plus MTX. MTX was discontinued following 12 weeks of biweekly administration while continuing tocilizumab therapy. [Results] A total of 49 patients completed 64 weeks. Of the 49 patients, 6 received TCZ at a longer dosing interval than that described in the drug label (i.e., intravenously every 4 weeks, or subcutaneously every 2 weeks). According to Kaplan-Meier estimates, the cumulative rate of maintaining of LDA was 69.4% at week 64 (52 weeks after MTX discontinuation). Multivariate logistic regression analysis revealed that female (OR: 18.0, 95% CI: 2.80-115.56) and extended dosing interval of TCZ (OR: 0.08, 95% CI: 0.01-0.58) were independently predict maintaining LDA at week 64. [Conclusions] Our findings suggest that it is necessary to pay attention to the dosing interval of TCZ when discontinuing concomitant MTX in RA patients maintaining LDA.

W66-5

IL-6 monotherapy for rheumatoid arthritis

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Conflict of interest: None

[Purpose] To investigate the therapeutic results of IL-6 monotherapy in patients with rheumatoid arthritis (RA). [Subjects and Methods] The subjects were 48 RA patients who had been treated with tocilizumab (TCZ) in August 2019 and continued for more than 6 months. Their average age was 78.9 years and the average duration of RA was 14.6 years. There were 8 males and 44 females. There were 21 patients in the TCZ monotherapy group (M group) and 27 patients in the csDMRDS combination treatment group (group c). The patient background, disease activity and complications were examined. [Results] There were no significant differences in age, disease duration, duration, or Steinblocker's class stage in the M and C groups. There was no significant difference in disease activity among VAS, CRP, ESR, MMP-3, DAS28, and CDAI. Both groups had low remission rates but high rates of low disease activity. There were 5 complications in group M, 10 in group C. Although there was no significant difference, the group C tended to be more infected. [Conclusion] IL-6 Monotherapy achieved the same therapeutic results as the csDMARDS combination group, and there was a tendency for fewer complications of infection. IL-6 monotherapy can be a treatment option.

W66-6

Abatacept directly suppresses inflammatory cytokine production from monocytes

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Conflict of interest: Yes

[Objective] Our demonstration that abatacept (ABT) engaged CD86 and directly down-regulated expression of Fc gamma receptor I on monocytes leads to hypothesis that ABT potentially suppresses immune complex (IC), which comprised of anti citrullinated peptide antibody (ACPA), mediated inflammatory cytokine production from monocytes. Our examination in vitro aimed to confirm the hypothesis. [Methods] Peripheral monocytes were isolated from patients with rheumatoid arthritis and cultured with citrullinated fibrinogen and IgG either from ACPA positive RA patients or healthy individuals (HI), and concentrations of IL-1β, IL-6 and TNFα in the supernatants were determined by multiplex assay. We examined effects of the presence of ABT or CD28-Ig on cytokine production in the culture. [Results] IC formed with ACPA-IgG induced production of IL-1β, IL-6, TNFα from monocytes compared to HI-IgG. ABT was able to decrease in cytokine production (IL-1β 14.8±6.9→12.5±6.1 pg/mL; IL-6 352.1±204.3→229.1±175.5 pg/mL; TNFα 88.0±34.1→45.5±6.4 pg/mL), although CD28-Ig failed to show a consistent change. [Conclusions] ABT directly affects peripheral monocytes and suppresses ACPA-IC mediated inflammatory cytokine production.

W67-1

Investigation of the association of cardiovascular events and anti-SS-A antibodies as risk of development in patients with lupus nephritis from the LUNA registry: A cross-sectional study

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Conflict of interest: None

[Objective] Cardiovascular disease (CVD) is the most common cause of death in patients with lupus nephritis (LN). Recently, there have been reports that suggest the association between CVD and anti-SS-A antibody (Ab) in adult systemic lupus erythematosus (SLE). So far, no studies have not been reported to evaluate the relationship between anti-SS-A Ab and the risk of developing CVD in LN in a large cohort of patients with SLE in Japan. Because of that, we investigated this. [Methods] Of 931 patients diagnosed with SLE included in the Lupus registry of nationwide institution (LUNA), 275 LN patients with known the presence or absence of both onset of CVD and anti-SS-A Ab were included. The exposure factor was anti-SS-A Ab, and the outcome was CVD. SLEDAI (at diagnosis), eGFR <60%, HbA1c, BMI, and steroid pulse therapy history were used as confounding factors and analyzed using logistic regression analysis. [Results] In univariate analysis, there was no significant difference in the occurrence of CVD depending on the anti-SS-A Ab ($p = 0.3151$), and the multivariate analysis showed no significant difference in anti-SS-A Ab [$p = 0.2298$, odds: 0.4087, 95% confidence interval (0.089-1.886)]. [Conclusions] The association between anti-SS-A Ab and the onset of CVD in LN in Japan has not been identified.

W67-2

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 corticosteroid 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 steroid and at 1 month thereafter. [Results] By 3 months after the start of corticosteroid treatment, ION was diagnosed by MRI in 33 patients (25.9 %) 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. [Conclusions] A high TG level and proteinuria are important risk factors for ION in patients with SLE, and large-scale epidemiologic surveys of such early events are needed in this patient population.

W67-3

Outcome of chronic kidney disease in connective tissue disease associated pulmonary hypertension: a possible association with cardiorenal syndorome

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Conflict of interest: None

[Objective] To investigate the association of chronic kidney disease (CKD) with right heart catheter findings and survival in connective tissue disease associated pulmonary hypertension (CTD-PH). [Methods] We examined the CTD patients diagnosed with PH by right heart catheter in our hospital from 2000 to 2018. We divided them into 2 groups according to the progression of CKD and compared baseline clinical characteristics, right heart catheter findings after the treatment and survival. [Results] Forty patients were enrolled. Mean observational period was 7.1±3.0 years and 24 (60%) patients progressed to CKD. At baseline, patients with CKD had a lower level of eGFR (p<0.01) and a higher level of urine NGAL (p=0.05). Although no significant difference was observed in mean pulmonary arterial pressure (mPAP) and cardiac index (CI) at baseline, their improvement after the treatment was poor in patients with CKD than those without (p=0.05 and p=0.03). Early exposure of pulmonary vasodilator combination therapy was less frequently observed in patients with CKD (p=0.05). Cumulative survival rate was higher in patients with CKD than those without (p=0.03). [Conclusions] CKD may contribute to PH progression and lead to poor prognosis in patients with CTD-PH.

W67-4

Risk of malignancy in patients with systemic lupus erythematosus receiving calcineurin inhibitors: a retrospective observational study in LUNA registry

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Conflict of interest: None

[Objective] The incidence of malignancy in patients with systemic lupus erythematosus (SLE) is known to be higher than that in healthy individuals. However the effects of exposure to calcineurin inhibitors (CNIs) have not been well investigated in SLE. [Methods] We investigated the cohort of Lupus registry of the nationwide institution (LUNA) registry. We analyzed the standardized incidence rate of patients with SLE based on the age-adjusted incidence rate of malignancy reported by Ministry of Health, Labour and Welfare. Multivariate analysis was performed to determine whether CNIs could be a risk factor for malignancy. [Results] We enrolled 714 patients and 663 women (88.9%). The median age at registry was 44 years. The median past maximum steroid dose was 40 mg/day, and SDI at registry was 1. Two hundred forty-eight patients (34.9%) had smoking history and 53 patients (7.4%) had a malignancy. The standardized incidence rate was 1.46 (95 % CI: 1.07-1.85) (p <0.01) in SLE patients. The multivariate analysis showed that treatment history of CNIs was not risk factors for development of malignancy. [Conclusions] In the LUNA cohort, the incidence of malignancy in SLE was higher than that in the general population. The CNIs treatment is not a risk factor for the development of malignancy.

W67-5

Clinical features and cytokine profiles of CTD patients with macrophage activation syndrome

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Conflict of interest: None

Purpose: To clarify the differences in clinical features and cytokine profiles of macrophage activating syndrome (MAS) among underlying connective tissue diseases (CTDs). **Methods:** Medical records of CTD patients who admitted our hospital were reviewed and selected those who had MAS for analysis. MAS was diagnosed according to modified sJIA-MAS criteria by Ravelli et al. **Results:** Subjects were 44 patients (male/female: 13/21, mean age: 44.2 years, underlying diseases: adult-onset Still's disease (AOSD): 16, SLE: 21, DM: 4, pSS3). Demographic features were similar among the 4 groups. One-year mortality rate was high in DM (50%). WBC number was larger in AOSD, particularly of neutrophils, although differences were not found in Hb and platelet numbers among groups. The results of liver function tests and coagulation tests, and levels of LDH, TG, and sIL2R were similar among 4 groups. However, CRP and ferritin levels were high in AOSD compared to other diseases. Additionally, IL-18 and IL-6 levels were elevated in AOSD. Multiplex cytokine profile analysis is in progress. **Conclusion:** Cytokine profiles were differed by underlying diseases, which might cause differences and similarities in the clinical features of MAS.

W67-6

Clinical profile and risk of recurrence in patients with lupus enteritis

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Conflict of interest: None

Objective: The aim of this study was to clarify their clinical profile and to explore risk factors for the recurrence of Lupus enteritis (LE). **Methods**: This retrospective study enrolled LE patients diagnosed as LE for the first time between 2001 and 2018. The event was defined as the first recurrence of LE. Risk factors for recurrence of LE were analyzed by Cox regression model. **Results**: Among 25 patients enrolled in this study, 23 (92.0%) were female and the median age at enrollment was 33 years old (interquartile range [IQR] 21.5-40.0). The median observation period was 1.5 years (IQR 0.3-5.6). Lupus cystitis (24.0%) were recorded in those patients at enrollment. Eighteen patients (72.0%) were treated with glucocorticoid (GC) plus immunosuppressive agents and 7 (28.0%) with GC

alone. LE recurred in 14 patients (56.0%) during the observation period. In multivariate analysis, lupus cystitis (p=0.027), elevated serum IgA levels (p=0.001), and severe bowel wall thickness (> 8 mm) (p=0.011) at the baseline were identified as risk for the recurrence. **Conclusions**: The recurrence of LE was frequent, and the presence of lupus cystitis, elevated serum IgA levels, and severe bowel wall thickness would serve as predictors of the recurrence in patients with LE.

W68-1

Anti-TNF Treatments for Women with Chronic Rheumatic Diseases: A Comparison of Attitudes and Perceptions of Clinicians in Japan and Australia

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Conflict of interest: Yes

The objective wasto understand clinicians' attitudes and perceptions towards treating women with anti-tumour necrosis factor (TNF) around pregnancy. Surveys were completed by Japanese (JPN) and Australian (AUS) rheumatologists (RH), obstetricians (OB) and orthopaedic surgeons (OR) who medically manage chronic rheumatic diseases (e.g. rheumatoid arthritis).103 JPN-RH, 44 JPN-OB, 77 JPN-OR, 30 AUS-RH and 30 AUS-OB participated. JPN-OR managed the fewest women (28% vs others: 41-80%); of which, only 19% were prescribed an anti-TNF (others: 26-34%). Similar to AUS clinicians, >60% of JPN-RH considered maintaining disease control during pregnancy their primary goal. Comfort levels were low with prescribing anti-TNFs in women actively planning pregnancy (JPN clinicians, AUS-OB: 5-13%; AUS RH: 43%) or in pregnant women (JPN clinicians, AUS-OB: 4-11%; AUS RH: 37%). The proportion of clinicians who did not feel women should avoid anti-TNFs until after pregnancy varied (JPN-OR: 13%-AUS-RH: 80%). Safety data during pregnancy (reported by AUS-OB: 97% vs others: 75-82%) and for the child 5 years post-delivery (reported by 60-70% of JPN-OB, JPN-OR, AUS-RH, AUS-OB) would increase comfort with anti-TNFs. There is a need for improved clinician information on the safe use of anti-TNFs.

W68-2

Assessment of physical dysfunction in patients with rheumatoid arthritis who planned pregnancy from the IORRA cohort

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Conflict of interest: None

[Objective] To investigate disease activity and quality of life in patients with rheumatoid arthritis (RA) who planned and didn't plan pregnancy. [Methods] We identified RA patients aged 20-49 years who answered 'pregnant' or 'delivered' in the IORRA survey in 2010-15 and whose pregnancy and the pregnancy planning time were confirmed in the medical records, and defined them as the pregnancy planning (PP) group. Patients with RA who matched for entry time, age, J-HAQ, disease duration, DAS28-CRP, and complications, and had no pregnancy plan were extracted at 1:3 and defined as the control group. The date of the IORRA survey before the pregnancy plan was used as the baseline and the primary endpoint was J-HAQ score 3 years after the baseline. The mixed effect model was used to compare with the control group. [Results] There were 40 patients in the PP group (average 32.2 years, disease duration 5.7 years, DAS28-CRP 1.7, J-HAQ 0.26), and 120 patients in the control group. DAS28-CRP at year 3 of the PP group elevated and was higher than the control group (PP, 2.3, control, 1.7; p<0.01), while J-HAQ was stable and didn't differ between the two groups (PP, 0.21, control, 0.22; p=0.92). [Conclusions] Relatively favorable disease control was obtained even in PP patients with RA in clinical settings.

W68-3

Survey and examination of treatment content, disease activity and maternal-child outcome during perinatal period in patients with rheumatoid arthritis who became pregnant / delivery ~ Analysis by Kansai Multicenter ANSWER cohort ~

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Conflict of interest: None

[Objective] To investigate the content of treatment, disease activity, and maternal outcomes of RA patients who became pregnant or delivered. [Method] From the Kansai Multicenter ANSWER cohort database, pre-pregnancy, during pregnancy and postpartum treatment, disease activity, and maternal and child status of RA women who were pregnant and delivered between 2013 and 2019 Outcomes were extracted. [Results] Values are shown as median. The age at delivery was 35 years. There are 75 cases of pregnancy, had 63 live births and 38 weeks of average delivery. The treatment contents before and during pregnancy were 50% and 39% for csDMARD, 30% and 41% for corticosteroids, and 48% and 39% for bDMARD, respectively. Mean pre-pregnancy DAS28-CRP: 1.76, and disease activity increased during pregnancy and postpartum in 62% of cases. In the increased disease activity group, DAS28-CRP in the early pregnancy was significantly higher (1.78 vs 1.47) (P = 0.005) than in the remission maintenance group, and the use of bDMARD in the early pregnancy was significantly less (19 % Vs 47%) (P = 0.028). [Conclusion] In RA combined pregnancy, disease activity before and during pregnancy is related to activity during pregnancy and postpartum, and it is important to control disease activity before and during pregnancy.

W68-4

Preventive Approach to Congenital Heart Block with Hydroxychloroquine: an investigator-initiated, multi-center clinical trial in Japan (J-PATCH)

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Conflict of interest: None

[Objective] Pregnant women with anti-SSA antibodies carry 2% risk of fetuses with cardiac neonatal lupus (cNL), typically congenital heart block (CHB). The risk of recurrence in a subsequent pregnancy was 16-18%. Hydroxychloroquine (HCQ) reduced the risk to 7-8% due to the recent clinical trial. [Methods] This is an investigator-initiated open-label single-arm trial. This trial was originally started in 9/2017 as a single center study utilizing telemedicine and now shifted to a multi-center study since 9/2019. The subjects were pregnant (<10 weeks) women with anti-SS-A antibody who had a previous child with cNL. HCQ 400mg/day were given during pregnancy. Fetal echocardiography is performed every 2 weeks from 18 to 26 weeks. The primary endpoint is the rate of advanced atrioventricular block (II and III) in fetal period or at birth. The mother will follow up until 6 months after the delivery and the child will follow up until 1 year after birth. Maternal HCQ blood concentration is measured. [Results] As of 11/2019, 8 mothers were included. By adding the collaborative centers nearby, all mothers who are willing to participate successfully joined in this study. [Conclusions] An investigator-initiated, multi-center clinical trial is ongoing for the mothers who had previous child with cNL.

W68-5

Three cases of successful pregnancy with continuous administration of tocilizumab

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Conflict of interest: None

Introduction: There are few cases of using tocilizumab (TCZ) during pregnancy. We reported here three cases of successful pregnancy with continuous administration of TCZ. Case1: The patient was a 38 years old woman with Castleman disease who treated with TCZ 400mg/4w div. Although she withdrew TCZ after pregnancy, she resumed TCZ due to relapse of the disease on gestational week 10. She delivered an infant on gestational week 40, day 2. Case 2: The patient was a 32 years old woman with Takayasu arteritis who initially treated with 30mg PSL, and combined with TCZ 162mg/w sc. due to the repeated relapses. She continued TCZ during pregnancy, considering the high risk of relapse. She delivered an infant on gestational week 36, day 5. Case 3: The patient was a 25 years old woman with juvenile idiopathic arthritis who treated with TCZ 162mg/2w sc. Although she withdrew TCZ after pregnancy, she resumed TCZ due to the relapsed disease activity. She underwent caesarean section on gestational week 40, day 2. All cases had no developmental abnormalities with their infant. Discussion: Primary disease activity should be controlled during pregnancy for successful delivery. TCZ might be one of the therapeutic options to avoid disease relapse and lead to favorable outcome of pregnancy.

W68-6

Importance of pediatric rheumatologists and transitional care for juvenile idiopathic arthritis-associated uveitis: A retrospective series of 9 cases

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Conflict of interest: None

[Objective] Juvenile idiopathic arthritis-associated uveitis (JIA-U) is a serious condition associated with the risk of blindness. However, pediatric rheumatologists rarely encounter cases of blindness. Here, we report the progress of 9 patients with JIA-U including 2 patients who became blind after the transition period. We aimed to highlight the importance of the role of pediatric rheumatologists and transitional care. [Results] We conducted a retrospective analysis of the case records of 9 JIA-U patients. All patients presented with oligo-JIA (one patient presented with extended oligo-JIA); the median age of uveitis onset was 5.0 years (3.0-13.0 years). The median disease duration was 12.5 years (3.5-24.7 years). Two patients developed blindness after the transition period. Medical examination by pediatric rheumatologists and use of biologics had been delayed for both these patients. One patient developed depression after transition and -interrupted her treatment herself. [Conclusions] For good prognosis, specialized treatment with the involvement of pediatric rheumatologists is desirable early on, and consideration for transitional medicine is important. Therefore, this report reaffirms the importance of planned transitional care that has been advocated globally.

W69-1

Combination of genome-wide association study and whole genome sequencing in a Japanese population revealed novel candidate genes for antineutrophil cytoplasmic antibody-associated vasculitis

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Conflict of interest: Yes

Objective: To identify common and rare variants associated with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in the Japanese population. **Methods:** Genome-wide association study (GWAS) was performed using samples from 374 Japanese patients with AAV. The data were compared with those of 2,994 healthy Japanese persons. The four-digit *HLA* alleles were imputed by the HIBAG algorithm. Whole genome sequencing (WGS) was performed on a HiSeq X platform for 50 patients with AAV. **Results**: A single nucleotide variant (SNV) rs2858331 in a region between *HLA-DQB1* and *HLA-DQA2* was associated with MPO-ANCA (odds ratio (OR)=1.649, P=9.504E-09) at the genome-wide significance level. HLA imputation test revealed a significant association of *HLA-B*51:01-C*14:02* haplotype in addition to the previously reported *HLA-DRB1*09:01-DQB1*03:03* haplotype with MPA and MPO-ANCA. An SNV rs749873 in a region near *CXCR4* showed a trend for association with GPA (OR=8.058, P=6.755E-08). WGS identified 86 rare variants in 55 genes. **Conclusions**: GWAS demonstrated multiple AAV-associated signals in *MHC class I* and *class II* regions, not previously reported from European populations. In addition, GWAS and WGS identified multiple novel candidate non-*MHC* variants in patients with AAV.

W69-2

The pathogenic CSF biomarkers in ANCA-related hypertrophic pachymeningitis

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Conflict of interest: None

[Objective] To investigate the pathogenic biomarkers associated with ANCA-related hypertrophic pachymeningitis (ANCA-HP). [Methods] The levels of B-cell activation factor of the tumor necrosis factor family (BAFF), a proliferation-inducing ligand (APRIL), and transforming growth factor beta 1 (TGF-β1) in the CSF were analyzed among 22 patients with ANCA-HP or other types of immune-mediated HP (other HP), as well as those with multiple sclerosis (MS) and non-inflammatory neurological disorders (NIND). [Results] CSF levels of BAFF, APRIL, and TGF-β1 were significantly increased in ANCA-HP and other HP. BAFF and APRIL levels were significantly correlated with the IgG index in ANCA-HP. In other HP, BAFF and APRIL levels were significantly correlated with cell counts and protein levels in CSF. Of 12 patients with ANCA-HP, the CSF of 7 patients (58%) tested positive for MPO- or PR3-ANCA, while none of the CSF samples from HP, MS, or NIND patients tested positive. [Conclusions] CSF levels of BAFF and APRIL may be implicated in disease activity in immune-mediated HP. Furthermore, BAFF and APRIL may impact on developing ANCA-HP by promoting autoreactive B cells, while detecting MPO- or PR3-ANCA in the CSF may be useful as disease specific validation of ANCA-HP.

W69-3

Comparison of Various ANCA Detection Methods in Predominantly MPO ANCA-associated Vasculitis Cohort

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Conflict of interest: None

[Objective] We aimed to compare various ANCA detection methods in predominantly MPO ANCA-associated vasculitis cohort. [Methods] Stored sera from 162 patients with newly diagnosed and untreated AAV, from 124 disease controls, and from 50 unmatched healthy controls were tested for the presence of P-ANCA and C-ANCA by standard IIF, and for the presence of MPO-ANCA and PR3-ANCA by 4 different antigen-specific immunoassays: ELISA, CLEIA, FEIA, and LA. Sensitivities and specificities for AAV diagnoses and concordance of each AAV tests were evaluated. [Results] P-ANCA and MPO-ANCA was detected in 82% and 61-82% of the AAV patients, respectively. The sensitivities and specificities for AAV diagnoses were 90% & 94% with the IIF, 82% & 98%, 89% & 95%, 88% & 97%, and 65% & 91% with 4 different antigen-specific immunoassays. K coefficients between P-ANCA and MPO-ANCA were 0.64-0.96. Screening for ANCA with the CLEIA and FEIA and confirming by IIF strategy increased the diagnostic accuracy only minimally (from 0.92 to 0.93 with CLEIA/IIF and from 0.93 to 0.94 with FEIA/IIF). [Conclusions] The present study demonstrated a high diagnostic performance by antigen-specific immunoassays to discriminate AAV from controls in predominantly MPO-ANCA-associated vasculitis cohort.

W69-4

Production mechanism of anti-glomerular basement membrane (GBM) antibody subsequent to anti-neutrophil cytoplasmic antibody (ANCA)

Yuka Nishibata[1], Sakiko Masuda[1], Daigo Nakazawa[2], Utano Tomaru[3], Akihiro Ishizu[1]
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Conflict of interest: None

[Objective] ANCA sometimes precedes in the production of anti-GBM antibody. The GBM epitopes are present in the cryptic region of type IV collagen that constitutes the glomerular and alveolar basement membranes. This study aimed to determine the production mechanism of anti-GBM antibody subsequent to ANCA. [Methods] Immunostaining for the GBM epitope, α3 (IV)NC1, and the M1 macrophage marker, CD11c, was performed on the kidney sections of microscopic polyangiits (MPA). IgA nephritis (IgAN) and arteriosclerotic glomerular sclerosis were employed as controls. We modified the method to induce ANCA-associated vasculitis (AAV) in rats and monitored the production of ANCA and anti-GBM antibody. [Results] In the affected glomeruli of MPA, the expression of α3 (IV)NC1 accompanied by CD11c-positive M1 macrophage infiltration was observed. In contrast, there were few M1 macrophages though α3 (IV)NC1 was expressed in the sclerotic glomeruli of IgAN or arteriosclerosis. In some AAV rats, anti-GBM antibody was produced subsequent to ANCA. The expression of α3 (IV)NC1 was observed in the affected kidneys. [Conclusions] ANCA-mediated expression of the GBM epitopes and antigen presentation by M1 macrophages can contribute to the production of anti-GBM antibody subsequent to ANCA.

W69-5

Serum concentrations of S100A12 in patients with ANCA associated vasculitis

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Conflict of interest: None

[Objective] S100A12 is a member of the S100 family of proteins, expressed in neutrophil, and binds to RAGE (Receptor for Advenced Glycation End product) on endothelium, mononuclear phagocytes, and lymphocytes with generation of proinflammatory mediators. There are some reports that S100A12 is associated with disease activity of autoimmune diseases, but there are still few reports about the correlation between S100A12 and ANCA associated vasculitis (AAV). [Methods] Serum concentrations of S100A12 were measured by ELISA in sixteen active AAV patients and fifteen healthy controls. Unpaired t-test, One way-ANOVA with Tukey's correction, Pearson correlation coefficient were used for statistical analyses. [Results] Serum concentrations fS100A12 were elevated in active AAV patients than healthy controls (405.9±321.7 ng/ml vs 112.6±48.0 ng/ml, p=0.0024), especially in patients with microscopic polyangitis (MPA: n=5, 666.7±445.7 ng/ml) than healthy controls (p=0.000067) and patients with granulomatosis with polyangitis (GPA: n=7, 271.4±173.9 ng/ml, p=0.012). [Conclusions] Serum concentrations of S100A12 were elevated in active AAV patients, especially MPA patiens than healthy controls with statistical significance. This result may imply the association of S100A12 with the pathogenesis of MPA.

W69-6

Association of Work Productivity Assessed by Absenteeism and Presenteeism with Disease Activity, Damage and Health-related Quality of Life in Patients with ANCA-associated Vasculitis: A Crosssectional Study in 3 University Hospitals

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Conflict of interest: None

[Objective] Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) substantially affects patients' ability to work. Many patients still have to take sick leave or even stop working because of their diseases (i.e., absenteeism) and may experience problems due to AAV resulting in productivity loss while at work (i.e., presenteeism). We aimed to investigate the absenteeism and presenteeism in patients with AAV and associated factors. [Methods] Patients were approached in the 3 hospitals from November 2017 through February 2018. Patients were asked to complete the WPAI, EQ-5D-5L, and other related demographic questionnaires. Physicians completed the BVAS and the VDI simultaneously and recorded other medical information. [Results] A total of 92 patients with AAV participated. Of the 25 patients working for pay, 11 reported missing work due to their health problem. WPAI absenteeism was correlated with the BVAS and EQ-5D-5L scores. WPAI presenteeism was correlated with the BVAS, VDI, and EQ-5D-5L scores. Patients with lower HRQoL status had significantly higher absenteeism, and presenteeism than those with higher HRQoL status. [Conclusions] Work productivity assessed by absenteeism and presenteeism are associated with disease activity, damage, and HRQoL in patients with AAV.

W70-1

A single center retrospective analysis of efficacy and safety between low-dose versus high-dose rituximab as remission induction therapy in patients with ANCA-associated vasculitis

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Conflict of interest: None

[Objective] To compare the efficacy and safety between low-dose versus high-dose RTX therapy as remission induction in Japanese patients with AAV. [Methods] A single center retrospective analysis of 34 AAV patients had been performed from 2013 to 2019. 25 patients were treated with low-dose RTX infusions, while 9 with high-dose RTX infusions. Outcomes between the two groups were compared by complete remission (CR) rates, survival rates (SR), and severe adverse effects (sAEs) at 6 months. [Results] The low-dose group included more elderly and female patients than the high-dose group, with hospitalization being shorter. The high-dose group included more smokers than the low-dose group, and their ANCA levels and initial PSL doses employed were higher. There were no significant differences in CR rates, SR, and sAEs. Severe infections occurred similarly, regardless of decreased RTX infusions. [Conclusions] Our retrospective study showed that low-dose RTX therapy may be effective for CR induction, as well as high-dose RTX therapy, but be not associated with reduced infections.

W70-3

Usefulness of Rituximab administered to ANCA-associated vasculitis (AAV) as remission induction therapy in our hospital

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Conflict of interest: None

[Objective] According to Japanese AAV guidelines, CY has priority over RTX as remission induction therapy in AAV in terms of safety. In this study, we compared RTX with CY for efficacy and safety. [Method] We performed retrospective analysis of 46 cases (25 cases received CY and 21 cases received RTX) in our hospital between January 2016 and August 2019. [Result] Of 46 patients, mean age was 72.8±9.4 years (6 males and 40 females). The mean BVAS were 14.2 in CY group and 13.6 in RTX group (p=0.78). There was no difference of remission rate at 3 months between 92.0% in CY group and 95.2% in RTX group (p=0.66). All 8 cases of relapsed disease in RTX group had achieved remission at 3 months. By the end of follow up, 2 cases in CY group and 1 case in RTX group had had a relapse. 11 infections occurred in CY group (2 severe infections) and 8 infections occurred in RTX group (7 severe infections), severe infections were significantly more in RTX group (p=0.03). 2 cases in RTX group had died due to scleroderma renal crisis and pancreatic cancer progression. [Conclusion] There was no difference of remission rate between CY and RTX. More cases of relapsed disease had received RTX than CY and there were effective. We should be careful about severe infections when RTX is selected.

W70-4

Characteristics of elderly-onset ANCA associated vasculitis in our hospital

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Conflict of interest: None

[Purpose] The features of ANCA-associated vasculitis (AAV) of the elderly onset are not yet clear. [Method] We retrospectively analyzed 123 patients diagnosed with AAV between April 2000 and January 2017 in our department. Patients were divided into two groups according to the age of onset: an elderly onset group (65 years or older) and a non-elderly onset group (Under 65 years of age). [Result] The mean age of the subjects was 69.2 years, 79 cases of MPA, 31 cases of GPA, and 13 cases of EGPA. The elderly onset group consisted of 93 cases, and the non-elderly onset group consisted of 30 cases. The incidence of interstitial lung disease was 74% and that of kidney 70% in the elderly group. In the non-elderly crisis group, the kidney was limited to 37%. IVCY was given to 18% of the elderly patients and 26% of the nonelderly patients. Steroid monotherapy accounted for 44% of the elderly patients and 20% of the non-elderly patients. The rates of relapse during the first 1 year and 2 years were 18% and 31% in the elderly group and 10% and 26% in the non-elderly group, respectively. [Conclusion] The elderly group had a lower rate of IVCY, a higher rate of steroid monotherapy, and a higher rate of relapse.

W70-5

Clinical investigation of otitis media with anti-neutrophil cytoplasmic antibody associated vasculitis (OMAAV)

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Conflict of interest: None

[Objective] To clarify the clinical characteristic of OMAAV with better hearing outcome. [Subjects and Methods] Patients with OMAAV, who were hospitalized in our department between 2009 to 2019, were consecutively involved. Hearing disturbance was analyzed by the audiogram. Clinical information was compared between improved (group A) and non-improved cases (group B) after the treatment. [Results] Thirteen patients were included. Male was 5 (38.5%) and the mean age was 66.2±9.3 years. Eighty-five percent had bilateral otitis media, 5 (38.5%) were with lung lesions, 3 (23.1%) with renal lesions, and 5 (38.5%) with mononeuritis multiplex. Nine (69.2%) were with MPO-ANCA and 4 (30.8%) with PR3-ANCA. The mean duration from onset of otitis media to diagnosis of OMAAV was 4.8±13.8 months. All patients were treated with glucocorticoid and the mean PSL dose was 44.2±13.8 mg/day. Immunosuppressants were used in 11 (84.6%). No difference in hearing loss at baseline and in initial PSL dose were observed between groups. IVCY was more frequently administered in group A ($p < 0.01$). Interestingly, all in group A was treated with IVCY within 7 days from the start of glucocorticoid. [Conclusion] Early diagnosis and treatment especially using IVCY may improve hearing outcomes of OMAAV.

W70-6

Characteristics of the patients with polyarteritis nodosa in Japan

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Conflict of interest: None

[Objective] This study aimed to describe the epidemiological and clinical features of the patients with polyarteritis nodosa (PAN) in Japan. [Methods] We used the database of the Ministry of Health, Labour and Welfare (MHLW) in 2013 and 2014. Data of 178 patients who fulfilled the diagnostic criteria by MHLW and had registered within a year after onset of PAN was analyzed. [Results] The analysis included 75 males and 103 females, with a mean age of 64.5 ± 20.3. As a systemic symptom, fever was observed in 55.2% of cases. As organ symptoms, muscle and joint symptoms (74.7%), skin symptoms (73.0%), neuropsychiatric symptoms (50.0%), respiratory symptoms (32.6%), and renal symptoms (19.7%) were common. MPO- and/or p-ANCA positive rate was 30.5% and PR3- and/or c-ANCA positive rate was 11.0%. Angiography was performed in 20.7%. Glucocorticoids were used for treatment in all cases. Concomitant immunosuppressants were used in 28.7%, half of which was cyclophosphamide. Cyclophosphamide tends to be used for patients with higher CRP or patients with respiratory symptoms. [Conclusions] PAN developed in middle-aged and elderly people and exhibited various clinical symptoms. The treatment options were determined depending on the types of organ symptoms and severity.

W71-2

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 document and evaluate the long-term safety and efficacy of mepolizumab in patients with eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] The target subjects were patients who received mepolizumab for the treatment of EGPA in Japan. The surveillance period was from May 2018 to the lifting of approval condition and the follow-up period per patient was from the starting day of drug administration to a maximum of 96 weeks (2 years). The safety endpoint was the occurrence of adverse events, and the efficacy endpoint was the overall efficacy assessment, clinical symptoms, and the number of asthma exacerbations. [Results] As of March 23, 2019, 367 patients were enrolled. With 33 patients in the safety analysis (median observation period: 86 days), 54.5% were male, the average age was 55.7 years, the average duration of disease was 3.7 years, and 93.9% of patients had a comorbidity. No adverse events or side effects were reported. The effective rate at 3 months after the start of administration of this drug was 100.0% (33/33 cases). [Conclusions] Initial interim data on safety and efficacy endpoints in the post-marketing surveillance of Mepolizumab for EGPA was reported. (Funding: GSK, 208505 survey)

W71-3

Study of 16 cases of mepolizumab use in 33 cases of eosinophilic polyangiitis granulomatosis

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Conflict of interest: None

[Objective] There are few studies on the clinical use of mepolizumab in patients with eosinophilic polyangiitis granulomatosis (EGPA). [Methods] We retrospectively examined cases in which mepolizumab was used in EGPA patients going to our department. [RESULTS] Mepolizumab was used in 16 out of 33 patients with EGPA who were in the hospital as of November 2019. There were 3 cases in the induction period, 7 cases at the time of relapse, and 6 cases in the maintenance period. The observation period was 3 to 24 months, the continuation rate was 100%. The starting dose was 100 mg in 8. Eight patients started with 300 mg, and one patient was reduced to 200 mg. The internal dose was 21.9 ± 15.6 mg (prednisolone equivalent) at the start of treatment and 7.1 ± 5.8 mg at the end of observation. Six of seven patients who failed to reduce steroids without mepolizumab were able to reduce steroids after introduction of mepolizumab. Eleven patients used other concomitant medications. [Conclusions] In clinical practice, meprizumab was used according to the patient's condition from the induction period to the maintenance period. There is no discontinuation due to side effects, and concomitant use may reduce corticosteroid doses.

W71-4

Study on the onset of eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

Objective: Eosinophilic granulomatosis with polyangiitis (EGPA) is generally considered to have no seasonal onset. However, there were few reports that investigated the time of onset, and we investigated and examined our cases. Methods: The patients diagnosed as EGPA at Kyoto Prefectural University of Medicine and Japanese Red Cross Kyoto Daiichi Hospital from January 2007 to August 2019 with clear onset time were set to target of this study. Results: There were a total of 32 cases. Month with the highest incidence were June and December (5 cases each), with clear onset peaks in summer and winter. All cases were divided into summer onset group (group S, all 12 cases), winter onset group (group W, all 10 cases), and the others (group O, all 10 cases). Compared with the other groups, the group S has a lower IgE (group S 792±1318 IU/mL, group W 1826±1717 IU/mL, group O 954±961 IU/mL), and a lower positive rate of ANCA (group S 16.7%, group W 30%, group O 60%), and the frequency of peripheral neuropathy tended to be low (group S 58.3%, group W 70%, group O 100%). Conclusions: It was suggested that EGPA occurs frequently in summer and winter, and the phenotype may vary depending on the month of onset. This differences may help elucidate the onset mechanism.

W71-6

The Efficacy of Immunosuppressive Therapy for Each Organ Involvement in Granulomatosis With Polyangiitis

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Machiyama[2], Tomomi Tsutsumi[1], Tomoki Takeda[1], Yumiko Oka[1], Takao Kodera[1], Ryo Kuwata[3], Tomonori Ishii[2], Hideo Harigae[2], Junichi Kameoka[1]
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Conflict of interest: None

[Objective] We assessed the efficacy of immunosuppressants for each organ involvement in GPA. [Methods] We retrospectively studied 80 patients referred between 2000 and 2019. The severe cases were treated with PSL and IVCY or RTX as induction. Mild cases were treated with AZA, MTX, TAC. We analyzed the efficacy of immunosuppressants for each organ, 1) upper airway, 2) lung, 3) nephritis, 4) other vasculitis. [Results] The frequencies of each organ were ENT 80%, orbital mass 13%, ocular vasculitis 19%, pneumonia 48%, subglottic stenosis 6%, bronchial stenosis 9%, nephritis 31%, cerebral and peripheral neuritis 31%, heart 8%, and skin 5%. Among 19 cases of ocular and cerebrovascular lesions, 13 cases were treated with IVCY, but 11 cases flared, then RTX were effective. A 70-year-old patient, treated with only one cycle of RTX, had kept in remission for 5 years. 4 cases of RPGN treated with IVCY worked. A case of orbital mass and sinusitis was inactivated with immunosuppressants, flared with complete obstruction of left main bronchus. [Conclusions] We found that ocular and cerebral involvements had better outcome treating with RTX compared to IVCY. IVCY was effective for nephritis. Practitioners need to be aware of bronchial stenosis, independently of any other active organ involvements.

W72-1

Clinical study of 63 cases of rheumatic polymyalgia in the past 7 and half years

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Conflict of interest: None

[Objective/Methods] Japan became an aging society, and many rheumatic polymyalgia (PMR) are being diagnosed. We investigated clinical analysis of PMR since the establishment of outpatient clinic for rheumatoid arthritis (RA) (2012/4-2019/10) retrospectively. The purpose was to improve PMR. [Results] N=63, male/female ratio is 17:46, period: 31.4±25.2 months, age: 71.9±9.86 years, ESR (1hr) 66.6±43.9mm, CRP 6.50±7.20, MMP-3 (male) 304.9 ±180.1, MMP-3 (female) 324.5±322.5. As treatment, initial prednisolone (PSL) 18.1±8.8mg/d, relapse 15.2±6.0mg/d, withdrawal 19/57: (33.3%). Initial immunosuppressant: 4/58 (6.9%), relapse 31/58 (53.4%), (MTX: 20, TAC: 14, MZB: 11, AZA: 11, TCZ: 5, IFX: 1, CY: 1). With giant cell arteritis: 3/63 (4.76%) and malignant tumors: 7/63 (11.1%) (thyroid, bladder, breast, bile duct, hematopoiesis). Remission is 19/58 (32.7%), Inactivity is 17/58 (29.3%), maintain PSL is 6.0±1.9 mg/dl, Activity is 21/58 (36.2%), PSL is 3.2± 2.6. Transition to RA (including co-occurrence cases) were 16/57 (28.1%) and the time was 9.3 ± 27.0 months. [Conclusions] The PMR remission rate was about 30%, and immunosuppressive drugs were often used. Giant cell arteritis and malignant tumors was relatively low. To improve PMR, further analysis is required to define remission and characteristics of RA transition.

W72-2

Analysis of clinical features of refractory polymyalgia rheumatica

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Conflict of interest: None

[Objective] To reveal mechanisms of refractory polymyalgia rheumatica (PMR). [Methods] In 2008-2018, we retrospectively analyzed PMR which met Bird criteria. We defined “refractory” as cases which were required prednisolone (PSL) more than 6 mg/day or DMARDs at two years after starting treatment. [Results] A cohort of 106 patients was identified, comparing 43 refractories with 63 non-refractories. In univariable analysis, refractories had high CRP level (8.47 vs 5.54 mg/dl, *P*=0.02), high MCV≧90 fl proportion (58.1% vs 34.9%, *P*=0.02) and low lymphocyte counts (1,380 vs 1,630 /μl, *P*=0.05). In logistic regression analysis, CRP≧5 mg/dl (OR=3.50, 95% CI 1.37, 9.75, *P*=0.008) and MCV≧90 fl (OR=2.81, 95% CI 1.29, 6.86, *P*=0.02) were identified as significance predictor of refractories. High MCV (≧90 fl) group required more PSL dosage over two years after starting treatment and relapsed over two years than low MCV group (34% vs 17%, *P*=0.04). In our study, two refractory PMR cases with macrocytic anemia which were caused by myelodysplastic syndrome (MDS) with isolated 5q-. [Conclusions] We identified high MCV as a noble prognostic factor for refractory PMR. Because macrocytic anemia suggests an indication of early MDS, pathogenesis of MDS may associate with treatment resistance for PMR.

W72-3

The examination in the risk of relapsing and the prednisolone (PSL) tapering and methotrexate (MTX) tapering in patients with polymyalgia rheumatica (PMR)

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Conflict of interest: None

[Objective] We often experience that PMR is relapsed during PSL taper. And we examined the clinical background of the cases which remitted only with PSL and relapsed during PSL taper. [method] 56 patients were diagnosed with PMR by 2012 EULAR/ACR provisional classification criteria. We examined 35 cases that remitted only with PSL or relapsed during PSL taper. 17 cases (group remission) was remitted only with PSL and 18 cases (group relapse) was relapsed during PSL taper. We analyzed both group for background factors, PSL tapering and MTX tapering. [results] In group remission, 13 cases introduced MTX. In these, 7cases was PSL-free, 3 of 7 cases was MTX-free. Regarding both clinical background factors, their CRP and ESR have a statically significant difference. But we could find no difference in their gender, onset-Age, RF, IgG, MMP-3, maximum dose of PSL. The receiver-operating characteristic (ROC) analysis of CRP showed the AUC value was 0.742 and the cut-off value was 6.24mg/dl. [conclusions] We suggest that reducing of dose of MTX is possible by patients with PMR who using MTX, and we showed that the higher risk of relapsing, the higher CRP in patients with PMR.

W72-4

Two cases of onset of remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome with exacerbation of type 2 diabetes administrated with DPP4 inhibitors

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Conflict of interest: None

[Case 1] A 54-year-old female had visited our hospital because of type 2 diabetes and rheumatoid arthritis (RA) for 8 years. Disease activity of her arthritis had controlled with salazosulfapyridine. She had been treated with sitagliptin for 6 years. She was hospitalized complaining of pitting edema of the dorsum of both hands with pain. HbA1C was increased (8.2 %) and VEGF level elevated. She was diagnosed with RS3PE syndrome. Sitagliptin was stopped and her symptoms were improved treated with prednisolone. [Case 2] A 76-year-old male had a 13-year history of type 2 diabetes. He had been prescribed teneligliptin for 5 months. He admitted to our hospital for bilateral edema of the hands and feet and arthralgia. Blood examination revealed elevated levels of HbA1C (8.1%) and VEGF. He was diagnosed with RS3PE syndrome. Teneligliptin was stopped and his symptoms disappeared treated with prednisolone. [Discussion] Recently, there have been reports that RS3PE syndrome was complicated by diabetes after administrating DPP4 inhibitors and VEGF was related to the pathological condition. It is suggested that onset of RS3PE syndrome in our cases may be associated with aggravation of daibetes and increase of VEGF under the treatment of DPP4 inhibitors.

W72-6

Inflammatory arthritis associated immune check point inhibitors: a case series

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Conflict of interest: None

Background: Although immune checkpoint inhibitors (ICI) are effective for various cancer, immune related adverse events (irAEs) have been reported. There are few reports of inflammatory arthritis (IA) in irAEs. Objectives: To investigate the clinical features and treatment for IA associated ICI. Methods: The clinical characteristics and treatment of patients who developed IA during ICI treatment were evaluated retrospectively. Results: A total of 11 patients were identified. The median age (IQR) was 70 (69-76) years. They were all treated with anti-PD-1 antibodies. The period from initial ICI treatment to the onset of IA was 102 (52-394) days. The affected joints were mainly in the finger and wrist (82%), shoulder (73%) and knee (45%). RF and anti-CCP antibodies positivity were 18% respectively. Musculoskeletal ultrasound showed synovitis (73%), tenosynovitis (56%), bursitis (18%), and enthesitis (9%). The 82% of patients were treated with prednisolone (median (IQR) 10 (10-18) mg), and 18% needed additional MTX treatment (8 (7-9) mg/week). The 64% of patients had clinical improvements and 18% of whom continued ICI treatment. Conclusion: The clinical symptoms of IA varied. We need to accumulate additional cases to elucidate IA treatment and ICI re-administration.

W73-2

Effects of rheumatoid arthritis treatment on osteoporosis

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Conflict of interest: None

[Objective] To investigate the prevalence of osteoporosis and vertebral fractures in patients with rheumatoid arthritis (RA) by age group, and to investigate the effects of RA drugs. [Methods] Of the 901 RA patients who were treated with methotrexate (MTX) or biologics (Bio) from August 2015 to March 2016 at our hospital, 792 patients were included. We investigated the prevalence of osteoporosis and the presence or absence of vertebral fractures by age group. We compared the disease duration, DAS-28CRP, CRP value, use of Bio, MTX, steroid, and osteoporosis treatment in the osteoporosis group group P) and non-osteoporosis group (group N). [Results] The prevalence of osteoporosis is 6% in the 40s (5% women), 28% in the 50s (28%), 41% in the 60s (46%), 63% in the 70s (70%), It was 67% (77%) over 80 years old. Bio and MTX use had no effect on osteoporosis or vertebral fractures at any age. The disease activity was low in women without vertebral fractures in the 70s. The group using osteoporosis treatment was more common in group N, but there was no difference between group P and group N except for the RA duration in the 80s. [Conclusions] In elderly patients with RA, in addition to osteoporosis treatment, control of disease activity without PSL may be useful for prevention of osteoporosis.

W73-3

The bone strength of proximal tibia and femoral head is reduced by deterioration of bone quality demonstrated as randomization of apatite orientation in rheumatoid arthritis

Satoshi Kamura[1], Ryosuke Ozasa[2], Takuya Ishimoto[2], Aira Matsugaki[2], Hiroto Yoshida[3], Mayu Magi[3], Yoshihiro Matsumoto[3], Kenjiro Fujimura[1], Koji Sakuraba[1], Hisaaki Miyahara[1], Takayoshi Nakano[2]

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Conflict of interest: Yes

[Objective] RA is a disease that induces the secondary osteoporosis and the risk of fractures. Bone strength is controlled not only by BMD but also by bone quality. However, the relationship between bone strength and bone quality in RA patients is not clear. One of the bone quality elements is the orientation of apatite. In this study, we investigated the relationship between bone strength and the apatite orientation as bone quality in RA patients. [Methods] Bone volume, BMD, apatite orientation, and bone strength were analyzed using the proximal tibia and femoral head isolated from RA or OA patients at joint replacement. [Results] In the subchondral bone of proximal tibia and femoral head, RA had a lower BMD and thickness than OA, and the apatite orientation was more randomized in RA. In addition, bone strength was lower in RA. Both of BMD and apatite orientation were positively correlated with bone strength at the proximal tibia, but at the femoral head, only the apatite orientation was positively correlated with bone strength. [Conclusions] In this study, RA patients had lower bone quality and bone strength than OA patients, and that bone strength may be affected by bone quality than BMD. Therefore, we may need to consider the improvement of bone quality in RA patients.

W73-4

Acute phase reaction after initial use of 5 mg zoledronic acid hydrate injection in patients with rheumatoid arthritis (RA) during use of biologic DMARDs. Comparison with non-RA patients

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Conflict of interest: None

[Objective] To investigate the onset of acute phase response after the first use of zoledronic acid hydrate injection in RA and non-RA. [Methods] 181 patients (15 males, 166 females, average age 77.6 years) who were using denosumab twice a year for osteoporosis were switched to zoledronic acid once a year, during the period from April 1 to September 30, 2018 at the Nagoya Medical Center. All patients were given acetaminophen 300 mg / day for 1 week to prevent acute phase reactions. Regarding the acute phase response in these cases, the presence or absence of onset and the number of days of continuation were examined at the outpatient examination, and further divided into rheumatoid arthritis (RA) and non-RA groups, and the use of other drugs was investigated. [Results] A total of 136 out of 181 cases could be investigated for the onset of acute phase reactions. The number of patients who developed an acute phase reaction was significantly higher in 9 patients in the RA group compared with 23 patients in the non-RA group (Mann Whitney U test, $p < 0.001$). [Conclusions] Cytokine expression is involved in the acute phase reaction when using a bisphosphonate preparation, but it was considered that the reaction might be suppressed in biologics users.

W73-5

Effects of Denosumab or Bisphosphonate on Glucocorticoid-Induced Osteoporosis

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Conflict of interest: None

[Objective] To clarify the effect of Denosumab (D) and bisphosphonates (B) in Glucocorticoid-Induced Osteoporosis (GIO). [Methods] A two year cohort study recruiting 89 patients with GIO were randomly assigned to the patients. The primary outcome was the changes in lumbar

BMD (l-BMD) at 2 years. Means of age, disease duration, and daily PSL dosages (dPSL) of the subjects were 66+/-12 (yo), 12+/-11 (y), and 6.2 (mg/day), respectively. vFx were defined from Xray films with the SQ method. Lumbar BMD were measured with Lunar 3030 (GE). [Results] 1) The BMD was showed no difference between treatment groups at the base line. 2) The change at 2 years in lBMD in group P (0.063+/-0.069 (mean+/-SD)) was significantly higher than that in group B (0.017+/-0.043) ($p< 0.001$). 3) The numbers (rates) of incident fracture at 2 year were 6 (15%) in group B and 0 (0%) in group P ($p< 0.01$). 4) Any serious adverse events due to the study drugs were not seen in the both groups. [Conclusions] These results suggest that denosmab is effective and safe for treatment of glucocorticoid-induced osteoporosis.

W73-6

Evaluation of Fall Risk Index in 3469 Japanese patients with rheumatoid arthritis: results from the IORRA cohort study

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Conflict of interest: None

Objective: The five items Fall Risk Index (FRI-5) has been used to detect elderly persons at high risk of falls. This study aimed to evaluate the FRI-5 in Japanese patients with RA. Methods: Patients with RA enrolled in the Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort completed five self-administered questionnaire about a history of falls during previous 12 months, a feel deterioration of walking speed, a daily use of cane, a feel getting hunchback, and a taking more than five kinds of medications regularly. Logistic regression analysis were used to evaluate associations with clinical variables for the high risk for falls. Results: Among 3024 female and 445 male patients with RA, 741 (21.4%) and 114 (32.9%) were at high risk for falls (FRI-5$\geqq$6), respectively. In multivative analyses, advanced age, high body mass index (BMI), high Japanese Health Assessment Questionnaire-Disability Index (JHAQ-DI), anti-osteoporosis medication use, NSAID use, and high daily prednisolone dose were significantly ($P<0.01$) associated with the FRI-5 $\geqq$ 6. Conclusion: Many patients with RA were at high risk for falls. Age, BMI, disability, NSAID use, anti- osteoporosis medication use, and prednisolone dose appeared to be associated with fall risk in Japanese patients with RA.

W74-1

The Study on Bone Geomery of RA patients using HR-pQCT

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Conflict of interest: None

[Objective] In this study, we investigated the bone geometry in RA patients using HR-pQCT. [Methods] The subjects were 80 female RA patients (RA group. 58 ± 12 years) with no RA lesions and synovitis of the wrist joint and 79 ACPA negative female without arthritis were used as control group (57 ± 10 years old). HR-pQCT measured cortical area (Ct. Ar), cortical thickness (Ct. Th), cortical periosteal perimeter (Ct. Pm), trabecular area (Tb. Ar), volumetric bone mineral density (vBMD) at the distal radius. [Results] Ct. Ar and Ct. Th were significantly lower in the RA group than in the control group, and there was no significant difference in Ct. Pm and Ct. Ar in both groups. In the control group, Tb. vBMD positively correlated with Ct. Ar and Ct. Th, and negatively correlated with Ct. Pm and Tb. Ar. In the RA group, Tb. vBMD was weakly correlated with Ct. Ar and Ct. Th, and not correlated with Ct. Pm and Ct. Ar. Ct. Pm positively correlated with age, Ct. Ar, negatively correlated with all vBMDs in the control group, However, there was no correlation between Ct. Pm and these values in the RA group. [Conclusions] In the control group, there was an increase in bone cross-sectional area associated with trabecular bone and endosteal bone resorption (adaptation of bone shaft geometry), but not in the RA group.

W74-2

The early effects of Romosozumab on bone geometry and bone microstructure in HR-pQCT study

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Conflict of interest: None

[Objective] In this study, we examined the early effects of Romosozumab (ROMO) on bone geometry and bone microstructure in patients with severe osteoporosis using by HR-pQCT. [Methods] ROMO was administered to 30 patients (73 ± 7 years old). Before, 3 and 6 months after administration, the distal radius was imaged by HR-pQCT and volumetric bone mineral density (vBMD: total vBMD, cortical vBMD, trabecular vBMD), geometry (cortical periosteal perimeter, cortical area, cortical thickness, trabecular area), bone microstructure (intra-cortical porosity, cortical pore diameter, trabecular bone volume fraction, trabecular number, trabecular thickness, trabecular separation) was measured. [Results] 3 months after, no significant change was observed in each measured value. 6 months after, total, cortical and trabecular vBMD were significantly decreased as compared to before administration. Cortical bone area and thickness showed a significant decrease. There was no significant change in bone microstructure. [Conclusion] There was no change in the cortical periosteal perimeter, and the cortical area and thickness decreased. Therefore, in the early stages of ROMO administration it was considered that the bone resorption was enhanced in the cortical bone in contact with the trabecular.

W74-3

Effects of denosumab versus teriparatide treatment on the BMD of glucocorticoid-induced osteoporosis patients with inadequate responses to bisphosphonates

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Conflict of interest: None

[Objective] We prospectively compared denosumab's and teriparatide's effects on the bone mineral density (BMD) of patients with glucocorticoid-induced osteoporosis (GIO) whose response to bisphosphonate treatment was inadequate. [Methods] After receiving oral bisphosphonates for $\geqq$2 years, GIO patients with low T-score BMD (< -2.5) were switched from bisphosphonates to denosumab (n=20) or daily teriparatide (n=21). We measured the BMD (lumbar spine, femoral neck, and total hip) in both groups every 6 months for 24 months. [Results] At 24 months of treatment, the lumbar spine BMD increased significantly from baseline in both the denosumab (5.3%) and teriparatide (7.9%) groups. A significant increase in femoral neck BMD occurred only in the teriparatide group (6.9%); denosumab (1.5%). No significant changes occurred in the total hip BMD in either group (-0.1% and 3.3%, respectively). [Conclusions] Teriparatide might have some advantages over denosumab and be a good alternative for treating GIO patients with an inadequate response to bisphosphonates.

W74-4

Higher d-ROMs levels are associated with vertebral fractures

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Conflict of interest: None

Objective: To examine the association between serum d-ROMs levels and vertebral fractures (VFs). **Methods:** The study included 118 patients who underwent TKA/UKA between January 2016 and May 2019 at our hospital. Patients included 23 men and 95 women, with a mean age of 73.3 years. They were classified into two groups with and without vertebral fractures by radiographs of the lumbar spine in lateral and anteroposterior projections. We investigated the associations between VFs and following factors: age, gender, BMI, and presence of DM, dyslipidemia, CKD, RA, glucocorticoids, bisphosphonates, low BMD, and higher d-ROMs levels. These factors were compared statistically between the VFs (-) and VFs (+) groups. **Results:** A univariate analysis demonstrated that there were significant differences in age and presence of RA, low BMD, and higher d-ROMs levels between the two groups. A multivariate logistic regression analysis demonstrated that there were significant differences in age and presence of RA and higher d-ROMs levels between the two groups. **Conclusions:** These results suggest that the presence of higher d-ROMs levels, in addition to age and the presence of RA, are associated with VFs.

W74-5

Zoledronic Acid Treatment in Patients with Osteoporosis Who Have Various Characteristics -Results in 12 months-

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Conflict of interest: Yes

[Objective] The aim of this study is to investigate efficacy of zoledronic acid (ZOL) in patients with osteoporosis (OP) in daily clinical practice. [Methods] 53 OP patients treated with ZOL were used. Time-course of BMD, time-course of bone turnover markers (BTM) and frequency of acute phase reaction (APR) were investigated. Comparison among RA patients taking no PSL (RA-N), RA patients taking PSL, (RA-S) postmenopausal OP patients (POP) and glucocorticoid-induced OP (GOP). Comparison among bisphosphonate pretreatment patients (BP) and no pretreatment besides vitamin D patients (DN) and denosumab pretreatment patients (DMB) were also performed. [Results] Mean age was 72 years. RA-N (n=23), RA-S (n=6), PMOP (n=19), GOP (n=5). BP (n=26), DN (n=19), DMB (n=7). %LSBMD at 12m was +4.9 in RA-N, +3.9 in RA-S, +2.8 in PMOP and +2.3 in GOP. %THBMD at 12m was +1.9 in RA-N, +1.4 in RA-S, +0.0 in POP and +0.4 in GOP. %LSBMD at 12m was +3.6 in BP, +5.1 in DN and +0.1 in DMB. %THBMD at 12m was +0.7 in BP, +2.8 in DN and -2.0 in DMB. APR occurred in 26%. [Conclusions] ZOL was comparatively effective in RA-N, POP, BP and DN with respect to LSBMD. ZOL was also comparatively effective in RA-N and DN with respect to THBMD. Decrease of BMD was observed in DMB. Most APR was mild but frequent.

W74-6

Serum vitamin D deficiency is a risk factor for fractures in Japanese patients with rheumatoid arthritis: results from the IORRA cohort study

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Conflict of interest: None

[Objective] Occurrence of new fractures in patients with rheumatoid arthritis (RA) significantly reduces their QOL and it is necessary to prevent it. Our previous study revealed the high prevalence of vitamin D deficiencies in Japanese patients with RA. The purpose of this study was to investigate whether vitamin D deficiency in Japanese RA patients could be a risk factor for new fractures. [Methods] We analyzed patients' data from the IORRA cohort from the spring of 2011 to 2017. Serum vitamin D deficiency was defined as less than 20 ng/ml following previous reports. Among only female patients over 50 age, we extracted cases of self-reported new fractures and validated them with image findings and medical record descriptions. We evaluated patients' parameters association with new fractures. [Results] New fractures occurred in 205 patients (vertebral fracuture: 73, non-vertebral fracture: 132) among the included 2600 cases. Cox proportional hazard model revealed that serum vitamin D deficiency, age, JHAQ, PSL dose, and bisphosphonate use were significantly associated with new fractures. [Conclusions] Since serum vitamin D deficiency can be a risk factor for new fractures in Japanese patients with RA, screening for serum vitamin D levels could be used to prevent fractures for the patients.

W75-1

Long term results and complication of FINE ELBOW total elbow arthroplasty for rheumatoid arthritis patients in twelve year follow-up

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Conflict of interest: None

[Objective] To investigate long term results and complication after FINE ELBOW total elbow arthroplasty (TEA) for rheumatoid arthritis patients in twelve year follow-up. [Methods] Retrospective analysis of consecutive semi linked type FINE ELBOW TEA performed in 2002-2010. [Results] The mean follow up periods was 147.4 month (54-228). Thirty one TEA was operated, all cases was for rheumatoid arthritis patients. At the end of follow up, the average of extension lag was 24.3. °, flexion 122.7°and complication rate was 16%. Kaplan-Meier survival rate was 89.7% in ten years. [Conclusions] Semi linked TEA, FINE ELBOW displayed promising clinical results. In the147.4 month follow up, there were five periprosthetic fractures and the overall complication rate was 16%.

W75-2

Patient trends from TKA for RA knee

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Conflict of interest: None

[Objective] To investigate the patient trend from TKA for RA knee. [Methods] The subjects were all TKA from November 2004 to August 2019. The number of cases was 220 knees, age at surgery 34-88 years (average 67.9 years), postoperative follow-up period 1 month to 15 years 4 months. [Results] Among the drugs used at the time of surgery, biologics were used on 21 knees. MTX was used in 75 knees, the average dose was 6.3 mg, and the dose rate and dose were on an upward trend. The preoperative CRP ranged from 0.02 to 4.78 mg / dl (average: 1.39 mg / dl), showing a slight downward trend. The preoperative standing FTA was 175.6 °, and there was no obvious trend over time. Complication were 7 knees, intraoperative fracture: 1 knee, reoperation due to skin necrosis: 3 knees, deep infection: 2 knees, patellar tendon ruptures: 2 knees. At the time of the final survey, all eleven knees that required bone graft to the tibia were engrafted, and the looseinig was 2 knees on the tibia side. The radiolucent line was 4 knees in the femur. [Conclusion] One knee needed revision surgery because of infection and loosening on X-rays were only 2 knees. TKA on RA knees was good in the last 15 years when disease control became possible. TKA will continue to be useful for achieving T2T in RA patients.

W75-3

Patient-specific prediction of joint line convergence angle after high tibial osteotomy using a whole-leg radiograph standing on lateral-wedge insole

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Conflict of interest: None

[Objective] To assess the usefulness of a whole-leg radiograph standing on lateral-wedge insole (LWI) for predicting the change in joint line convergence angle (JLCA) before vs. after high tibial osteotomy (HTO). [Methods] We analyzed 40 knees with medial osteoarthritis that underwent open-wedge HTO. Pre-operatively, all patients had whole-leg radiographs taken in three different conditions: supine, standing, and standing on LWI inclined at 20°. A standing whole-leg radiograph was also obtained post-operatively. Radiological measurements including JLCA and percentage of mechanical axis (%MA) were compared. [Results] In the pre-operative standing conditions, the mean JLCA of 3.8° was significantly decreased to 3.2° using LWI, which did not differ from post-operative JLCA of 3.1°. Mean %MA significantly shifted laterally from 20.6% to 24.8% using LWI, and was strongly correlated with the change in JLCA (coefficient, 0.83). The difference in calculated correction angle between standing with and without LWI was strongly correlated to the change in standing JLCA before vs. after HTO (coefficient, 0.73). [Conclusions] Whole-leg radiograph standing on LWI is a promising modality for correct pre-operative planning considering patient-specific changes in JLCA before vs. after HTO.

W75-5

Arthroscopic lavage with local anesthesia for acute inflammatory knees

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Conflict of interest: None

[Objective] Emergency surgery are necessary for septic arthritis, however it is sometimes difficult to distinguish between septic arthritis and others in real time. We report arthroscopic lavage with local anesthesia for acute inflammatory knees. [Methods] We treated 8 patients (5 men and 3 women, 50 ~93 years old). Because one patient had bilateral lesions, we treated 9 knees. We researched final diagnosis and clinical course. [Results] We diagnosed 5 knees as septic arthritis, 3 knees as pseudogout or gouty arthritis, one knee as rheumatoid arthritis. All patients showed good clinical course. [Conclusions] When we cannot exclude septic arthritis, arthroscopic lavage with local anesthesia can be an useful option. Septic arthritis with poor general condition may be a candidate.

W75-6

Examination of cases of PMR transfer to RA and merger who visited a specialized shoulder outpatient clinic

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Conflict of interest: None

[Objective] We occasionally see patients who come to the hospital because of difficulty in raising both shoulders. If it is different from trauma or OA, PMR and RA should be suspected and differentiated. [Methods] The subjects were 50 people with an average age of 73.7 (53-92) years and an average elevation angle of 85 (25-140) °. CRP, erythema, RA factor, and anti-CCP antibody were measured for these, and diagnosed as PMR to EULAR / ACR Rheumatoid Polymyalgia Diagnosis Criteria (2012). [Results] Of 21 cases diagnosed with PMR, 16 cases were improved by PSL administration, and 5 cases were positive for RA factor and judged to have been transferred to EORA. MTX administration and bDMARD were administered. In 5 cases, rotator cuff tear and joint destruction were seen, so shoulder arthroscopy and reverse shoulder arthroplasty were performed. Of these, 2 cases were transferred to RA, and 3 cases were a combination of PMR and RA based on intraoperative pathological findings. [Conclusions] There is an example of transition from PMR to RA, and steroids are diagnostic treatments, but regular observation and diagnosis review are necessary. In RA combined cases, there was a case where joint destruction progressed, it led to improvement in disease state and definitive diagnosis.

W76-1

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. The expression of cytokines, chemokine receptors, activation markers, and TCR Vb repertoire of Tph cells were examined by a flow cytometer. Autoreactivity of CD4 T cells was investigated in vitro by an autologous mixed lymphocyte reaction (AMLR) assay. Anti-PD-L1/L2 antibodies were added to examine the role of PD-1-signaling. [Results] Tph cells expressed high levels of activation markers and produced proinflammatory cytokines in addition to B cell-helping cytokines. Tph cells showed biased TCR Vb usages compared to other CD4 T cell subsets. Tph cells exhibited AMLR activity, which was pronounced by blocking PD-1-signaling and required recognition of self-MHC class II molecules. Blocking PD-1-signaling also enhanced cytokine production of Tph cells. [Conclusions] Tph cells might be the pathogenic autoreactive CD4 T cells in RA.

W76-2

Suppressive mechanism of RORgammat+Foxp3+ regulatory T cells in autoimmune arthritis

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Conflict of interest: None

[Objective] To clarify the role of RORγt^{+}Foxp3^{+} regulatory T (Tr17) cells in the development autoimmune arthritis. [Methods] 1) Lymph node (LN) cells were harvested from C57BL/6 mice on 10 days after CII immunization. Cytokine production from Tr17 cells was analyzed by flowcytometry (FCM). 2) Ankle joints infiltrating cells harvested from C57BL/6 mice after induction of CIA were analyzed by FCM. 3) LN cells were harvested from RORγt$^{fl/fl}$Foxp3^{cre} (cKO) mice on 10 days after first CII immunization. Expression of RORγt in Foxp3^{+} regulatory T (Treg) cells were analyzed by FCM. 4) Collagen induced arthritis (CIA) was induced in cKO mice and RORγt$^{fl/fl}$ (control) mice by CII immunization. Incidence and severity of CIA were evaluated. [Results] 1) IL-10 production was significantly increased in Tr17 cells compared with RORγt^{-}Treg cells ($p < 0.001$). 2) Frequency of RORγt^{+}Foxp3^{+}Tr17 cell was increased in ankle joints compared with LN and spleen. 3) Frequency of RORγt^{+}Foxp3^{+}Tr17 cell was decreased in cKO mice compared with control mice ($p = 0.001$). 4) CIA were exacerbated in cKO mice compared with control mice ($p = 0.042$). [Conclusions] Tr17 cells might infiltrate into inflamed joint and regulate the inflammatory response in CIA.

W76-3

Identification of pathogenic CD4+Th10 like 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 identify pathogenic $CD4^+$T cell in lupus model mice induced by Toll like receptor 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) Superficial antigens and transcription factors in splenic $CD4^+$ T cells of IMQ-treated mice were analyzed by flowcytometry (FCM). Cytokines production from $CD4^+$ T cells stimulated in vitro was also evaluated with FCM. 3) naïve B cells were co-cultured with splenic $CD4^+$ T cells of IMQ-treated mice or control mice, and then differentiation of B cell was assessed. [Results] 1) Anti-DNA IgG measured by ELISA was significantly increased, and immunofluorescent staining revealed marked deposition of C3 and IgG in kidneys in IMQ-treated mice. 2) CXCR3 and PD-1 were significantly up-regulated, and T-bet and Blimp-1 tended to be elevated in splenic $CD4^+$ T cells of IMQ-treated mice. IFNγ and IL-10 producing $CD4^+$ T cells also tended to be increased in IMQ-treated mice. 3) Differentiation of plasmablast was tended to be promoted by $CD4^+$ T cells of IMQ-treated mice. [Conclusions] $CXCR3^+PD\text{-}1^+CD4^+$ Th10 like cells might play a role in the generation of lupus phenotype induced by IMQ via B cell differentiation.

W76-4

Functional analysis of autoimmune disease-related gene NFAG1 in inflammation development

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Conflict of interest: None

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-like synoviocytes. Previous reports showed that an intergenic single nucleotide polymorphism (SNP) is genetically associated with autoimmune diseases and the risk allele correlates with elevated expression of an adjacent gene, NFκB-activating gene 1 (NFAG1). However, the biological function of NFAG1 in inflammation development remains unknown. Here, we show that NFAG1 is positively involved in the development of inflammatory diseases via the inflammation amplifier. Mechanistic analysis showed that NFAG1 knockdown in non-immune cells decreased the NFκB -target gene expression including IL-6 and chemokines after IL-6 and TNFα stimulation, while a forced expression of NFAG1 enhanced NFκB reporters in vitro. Detail analysis revealed NFAG1 enhanced RIP cleavage binding to Caspase-8 and RIP. Furthermore, NFAG1 knockdown suppressed a NFκB-dependent skin inflammation in vivo. These results suggest that NFAG1 is a new potential therapeutic target for autoimmune diseases via regulating NFκB activation in non-immune cells.

W76-5

CD30 target therapy for rheumatoid arthritis

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Conflict of interest: None

[Objective] CD30 is a member of the TNF-receptor family, commonly expressed on lymphocytes of Hodgkin lymphoma and anaplastic large cell lymphoma. The aim of this study was to investigate the potential of CD30 targeting therapy for RA. [Methods] (1) Immunohistochemical staining of CD30 was performed for fresh synovial tissues of osteoarthritis and RA. (2) Brentuximab vedotin (BV) is an anti-CD30 antibody conjugated with MMAE to induce apoptosis of CD30 expressing cells. We assessed the efficacy of BV for non-lymphoma cell line (RPMI8226) by cell counting and TUNEL assay. (3) We induced CAIA in DBA / 1 mice and administered BV to the treatment groups (30mg/kg and 70mg/kg n=6 each) and evaluated clinical score, histological findings and levels of SAA, IL-6, and TNFα in serum. [Results] (1) CD30 expression was significantly higher in RA synovial tissue. (2) RPMI8226 was CD30 positive and BV induced apoptosis of RPMI8226. (3) Treatment by BV significantly reduced the clinical score of CAIA. In the 70 mg/kg BV treatment group, histological findings of joint inflammation and bone destruction was ameliorated ($p<0.05$). [Conclusions] This study demonstrated that depletion of CD30 positive cells by BV suppressed arthritis and osteochondral destruction in CAIA mice.

W77-1

IL-6-PAD4 axis in the preclinical state of the synovium in gp130F759 -interaction between fibroblast-like synoviocytes and neutrophils-

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Conflict of interest: None

[Objective] A knock-in mouse gp130F759 is a rheumatoid arthritis (RA) model having gp130 with Y759F mutation and spontaneously develops arthritis at 8 months old (M.O.). Therefore, pathophysiological changes in gp130F759 at 5 M.O. were examined to dissect molecular mechanisms for pre-clinical phase of RA. [Methods] Severity of arthritis in gp130F759 was evaluated with a clinical score system and histological quantification. Serum cytokines and autoantibodies were measured. Changes in the synovium were analyzed by real-time PCR, flow cytometry, and immunohistochemistry. [Results] Around 5 M.O., IL-6 and anti-CCP IgM increased in the sera of gp130F759. Enhancement of neovascularization, synovial hyperplasia and fibrosis was observed. Also, increases in hematopoietic cells dominated by innate immune cells and gene expression of *Il6* and *Padi4* were detected in the joints. IL-6 was produced by non-hematopoietic synovial cells, whereas PAD4 protein was detected in the synovial neutrophils. *Padi4* is induced in neutrophils *in vitro* by IL-6. Increases of phospho-STAT3 and *Padi4* gene were detected in neutrophils. [Conclusions] In the preclinical state of arthritis in gp130F759, the IL-6-PAD4 axis, interaction between synovial fibroblasts and neutrophils, operates, implicating it in early RA.

W77-2

The molecular mechanism in citrullination of Inter alpha trypsin inhibitor heavy chain 4 (ITIH4) in inflamed joints

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Conflict of interest: None

Background/Purpose: Citrullinated ITIH4 (cit-ITIH4) was detected in blood, which is associated with disease activity in pGIA and RA. The aim of this study was to clarify the expression of native or cit-ITIH4 in pGIA mouse and its mechanism of citrullination. **Methods:** 1) ITIH4 and cit-ITIH4 were assessed by immunohistochemistry (IHC), IP-WB in pGIA joints. 2) Expression of padi 2 and 4 mRNA were measured by qPCR. 3) Expression of PAD4 was assessed by IHC and immunocytochemistry. 4) Expression of PAD4 in neutrophils was compared among peripheral blood, bone marrow, and joints. 5) Neutrophils were depleted by anti-Gr-1 antibody in pGIA. **Results:** 1) The increased amount of ITIH4 and its citrullination was observed in pGIA joints of day14. 2) In pGIA joints of day14, padi4 mRNA significantly increased in neutrophils. 3) PAD4 protein was positive in 90% of neutrophils, and IHC of serial section revealed ITIH4 protein existed around PAD4 positive neutrophils. 4) PAD4 expression was significantly increased in joints. 5) The level of citrullinated proteins in blood significantly decreased, accompanied with reduced intensity of arthritis. **Conclusion:** It was suggested that ITIH4 is increased, and its citrullination is specifically induced via PAD4 in neutrophils recruited in inflamed joints.

W77-3

Sustained activation of microglia in the area postrema of the mice with collagen-induced arthritis

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Conflict of interest: None

[Objective] Various psychosomatic symptoms, such as mood disorders, sleep disturbances, and hyperalgesias, lower the quality of life in rheumatoid arthritis (RA) patients. However, how RA affects brain functions remains unidentified. One possible pathway linking peripheral inflammation to the brain is the circumventricular organs (CVOs) that lack the blood-brain barrier. In particular, the area postrema (AP), a "sensory CVO", has the expression of cytokine receptors and the direct projections to brain regions underlying sleep, mood, and pain regulation. To clarify roles of the AP under RA pathology, we analyzed the AP of collagen-induced arthritis (CIA) model mouse. [Methods] The glial cells were observed by immunohistochemistry. The glial activities of CIA was compared to that of saline treated mouse from day 21 to day84. [Results] We observed an increase in the number of microglia, their morphological complexity and the portion of microglia expressing IL-1b. Surprisingly, microglia remained activated on day 84. Astrocytes did not show persistent changes. [Conclusions] These microglial changes are one of the longest in various disease model. These specific activation patterns of microglia might help understand the roles of CVOs in the RA-associated psychoneuronal comorbidities.

W77-4

The AP-1 transcription factor JunB plays an important role in development of regulatory T cells via promoting IL-2 signaling

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Conflict of interest: None

Objective: We recently reported that JunB is essential for development of Th17 cells, and thus *Junb*-deficient mice are resistant to T cell-mediated inflammatory disease models, such as experimental autoimmune encephalomyelitis. However, the role of JunB in $CD4^+$ T cells under other inflammatory disease conditions was not known. Methods: Dextran sulfate sodium (DSS) was administrated to $Junb^{fl/fl}$*Cd4-Cre* and littermate control ($Junb^{fl/fl}$) mice for induction of colitis, in which innate immune cells play a major pathogenic role. The severity of the colitis was assesed by body weight loss. The $CD4^+$ T cells in various tissues of $Junb^{fl/fl}$*Cd4-Cre* mice were analyzed by flow cytometry. Results: $Junb^{fl/fl}$*Cd4-Cre* mice were more susceptible to DSS-induced colitis, because of the reduction in Treg cells. Production of interleukin (IL)-2 and expression of CD25, a high affinity IL-2 receptor subunit, were decreased in *Junb*-deficient $CD4^+$ T cells *in vitro* and *in vivo.* Naive $CD4^+$ T cells from $Junb^{fl/fl}$*Cd4-Cre* mice were incapable of differentiating into Treg cells without addition of exogenous IL-2 in vitro. Conclusion: By up-regulation of IL-2 signaling, JunB promotes development of Treg cells and prevents from exacerbation of an innate immune-mediated colitis.

W77-5

The effect of Janus kinase inhibitors on the multi drug resistance factor MDR1 expression

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Conflict of interest: None

[Objective] Although Janus kinase inhibitor (JAKi) has been developed for the treatment of rheumatoid arthritis (RA), 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 MDR1 expression had any relations with JAKi. [Methods] Primary cultured RA synovial fibroblast-like cells and Human Umbilical Vein Endothelial Cells (HUVECs) were treated with rifampicin (RIF, known as MDR1 inducer), verapamil (VRP, known as MDR1), or JAK inhibitors (Tofacitinib, Baricitinib and Peficitinib). MDR1 expression was assessed by real time polymerase chain reaction. [Results] MDR1 expression in HUVEC was increased by RIF, decreased by VRP and by a single exposure to JAKi. In the synovium, the effects of RIF, VRP, and JAKi on MDR1 expression varied widely among individuals. JAKi suppressed MDR1 expression in HUVEC, suggesting that a single exposure to JAKi might suppress MDR1 expression. Furthur study is needed to investigate the effects of multiple exposures on MDR1 expression. [Conclusions] It was demonstrated that MDR1 expression in HUVEC was increased by RIF and decreased by VRP, and that a single exposure of JAKi decreased the MDR1 expression.

W77-6

The E3 ubiquitin protein ligase Wwp2 regulates Adamts5 through the degradation of Runx2 in articular cartilage

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Conflict of interest: None

[Objective] Our group previously reported that the induction of Wwp2, HECT-type E3 ubiquitin ligase, leads to the prevention of cartilage destruction in a mouse osteoarthritis (OA) model. We investigated the mechanism of Wwp2 replacement. [Methods] To detect pathological condition, we performed RNAseq for Wwp2 KO mice. Then, several methods, including luciferase assay, were used to clarify the functional coherence between an identified molecule and transcription factors. Finally, the target molecule (substrate) was determined using cell-based and cell-free assays. [Results] The expression of Adamts5 in the Wwp2 KO mouse articular cartilage was elevated. Runx2 is an essential transcription factor for Adamts5. Our results proved that Wwp2 can degrade Runx2 via poly-ubiquitination, and that intracellular Runx2 protein is subsequently decreased. The domain mapping of Wwp2 revealed that Adamts5 regulation is also induced by short Wwp2 variants such as N-terminal or C-terminal transcripts. [Conclusions] We propose that Wwp2 regulates Adamts5 via Runx2 poly-ubiquitination, which contributes to protecting against articular cartilage defects. Short Wwp2 variants potentially regulate Adamts5, as the same as full-length Wwp2. Thus, these variants might also prevent cartilage destruction.

W78-2

A case of intractable arthritis with chikungunya infection treated with prednisolone and salazosulfapyridine

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Conflict of interest: None

[Case] A 49-year-old Myanmar woman living in Japan. She had noticed fever and joint pain in her limbs since she came back to Myanmar two months ago. The joint pain persisted and she was referred to the hospital. [Symptoms] The left shoulder, left wrist joint, right knee joint, right foot joint were swollen and tender. WBC 6.2 × 10^3 / μl, CRP 0.68mg / dL, RF negative, anti-CCP antibody negative. [Course] Chikungunya infection was suspected and symptomatic treatment for pain was planned. The patient took oral prednisolone 10 mg for 5 days, but there was no improvement in pain. Chikungunya virus IgM antibody and IgG antibody were found positive, and the patient was diagnosed with refractory arthritis due to chikungunya infection. Oral administration of 15 mg of prednisolone and 1 g of salazosulfapyridine was started, and subjective symptoms were reduced from 1 week after the start of oral administration. Nine

weeks later, the tenderness of the joint disappeared. [Discussion] Chikungunya infection often causes chronic arthritis. There are no established treatments for refractory polyarthritis of Chikungunya infection, and we report a case where improvement was achieved by treatment according to rheumatoid arthritis.

W78-3

Intravascular Large B-cell Lymphoma (IVLBCL) with Dyspnea, Elevated PR3-ANCA and Proteinuria

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Conflict of interest: None

A 78-year-old man who had a past medical history of sinusitis was admitted to our hospital with dyspnea. A month before the current admission, the patient admitted to the respiratory medicine with 4-month history of shortness of breath that is not related to exertion. Radiography of the chest revealed ground glass opacity bilaterally and antibiotics was prescribed, which had no effect. He was discharged with home oxygen therapy. Later that day, dyspnea worsened and he was admitted again. The respiratory physician referred him to us because of elevated blood levels of PR3-ANCA and proteinuria on the suspicion of ANCA-associated vasculitis (AAV). A biopsy of the livedo reticularis on the thigh was performed and methylprednisolone therapy at the dose of 1g/day was initiated. Dyspnea was relieved and ground glass opacity vanished. The biopsy specimen showed IVLBCL. This is a case of ANCA-positive IVLBCL with lung, kidney and paranasal sinus lesions. The clinical course and laboratory findings were consistent with AAV alone, but pathologically, the presence of vasculitis could not be confirmed and that of IVL was proved. When the presence of vasculitis could not be proved pathologically even if ANCA was positive, we considered that IVL should be considered as a differential diagnosis.

W78-4

Three cases of hyponatremia caused by cyclophosphamide pulse therapy for past 10yeas in our department

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Conflict of interest: None

We report 3 cases diagnosed as hyponatremia associated with IVCY for past 10 years in our department. Case1: A 53yo woman with Sjögren's syndrome. Purulent limbs, numbness in both lower legs, chest CT showed glass shadows. We gave IVCY 500mg/2weeks. The day after 4th IVCY, nausea and disturbance of consciousness appeared, and the serum Na level was 125mEq/l. SIADH was diagnosed with serum osmotic pressure of 271mOsm/kg, urine osmotic pressure of 324mOsm/kg, urinary Na concentration of 66mEq/l, and antidiuretic hormone (ADH) of 3.1pg/ml. Case2: A 58yo woman with microscopic polyangiitis. We gave ICVY50mg/2weeks and the 3rd day after IVCY, there was no subjective symptom, the serum Na level dropped to 127mEq/l. SIADH was diagnosed with serum osmotic pressure 271mOsm/kg, urine osmotic pressure 349mOsm/kg, urinary Na concentration 124mEq/l, and ADH 0.6pg/ml. Case3: A 54yo woman with unclassifiable vasculitis. We gave IVCY 500mg/2weeks. Vomiting, seizures and disturbance of consciousness appeared the day after 3rd dose. SIADH was diagnosed with serum osmotic pressure of 236mOsm/kg, urine osmotic pressure of 434mOsm/kg, urinary Na concentration of 85mEq/l, and ADH of 3.1pg/ml. We need to pay attention to hyponatremia caused by drug-induced SIADH as a differential diagnosis after IVCY.

W78-5

A case of left atrial myxoma suspected of Behcet's disease due to fever and diffuse folliculitis

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Conflict of interest: None

The case is 45 years old woman with sporadic expression of folliculitis lasted for 10 years. From 30 days before admission, low back pain, arthritis of the lower extremities, and fever began to occur, and then diffuse folliculitis developed on the face and front chest 20 days before admission. Minocycline was prescribed at another hospital 3 days before hospitalization, but lip swelling also appeared on the following day. So she admitted to our hospital with suspicious of Behcet's disease. After admission, blood tests showed CRP 4.14mg / dl, ESR 75mm / 1h, WBC 12700 / μl, and cardiac ultrasound showed a 37 x 18mm mass attached to the left atrial septal base. The physical and laboratory findings improved with rest alone, but because of the risk of embolization due to collapse of the tumor, surgical resection was performed on the 26th day. The pathological finding of this tumor was myxoma. After tumor resection, folliculitis develops sporadic as before, but she never experienced systemic symptoms again. Cardiac myxomas are the most common cardiac tumors originated mainly from left atrium. Sometimes it induce constitutional symptoms suspicious of rheumatic diseases. But there is no description of folliculitis. We present this case with review of the literature.

International Concurrent Workshop

ICW1-1

High serum levels of anti-cyclic citrullinated peptide antibody and matrix metalloproteinase-3 at the time of diagnosis of rheumatoid arthritis are possible predictors of future initiation of biological agents

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Conflict of interest: Yes

[Objective] Damage to bones is accelerated during the first two years after developing rheumatoid arthritis (RA), thus the patients with poor response to csDMARDs need early intervention by biological agents (Bio). However, few markers have been established for the prediction of future use of Bio. Multi-Biomarker Disease Activity (MBDA) score is a blood-test based disease activity score using 12 biomarkers. This study aimed to clarify the predictors of future initiation of Bio at the time of RA diagnosis. [Methods] One hundred five consecutive new outpatients complaining arthralgia without a definite diagnosis of RA from 2012 to 2013 were included. The patients were followed by 2019 to discriminate Bio users from non-Bio users. The twelve biomarkers were measured. [Results] Among 105 patients, 48 were classified as having RA. Out of 48 patients, four patients were excluded from this study due to their ineligibility. The median disease duration was 40 months. During the observation period, 16 patients were initiated Bio. The clustering analysis using these 12 biomarkers revealed three robust subgroups of RA patients. The mean MBDA scores of groups A, B, and C were 23.3, 38.7, and 52.9 (p = 0.01). The patients in group C are older (median 76 years old) and had higher levels of CRP, IL-6, TNF-receptor 1, YKL-40, and resistin than those in other groups. The patients in group B had highest levels of ACPA and tended to have higher levels of MMP-3 than group A. In group A, B and C, 1 out of 21, 7 of 15, and 2 of 7 patients were initiated Bio in the first year from the diagnosis of RA, respectively. Multivariate analysis with Cox regression model showed that ACPA (HR for every 50 U/ml, 1.23, 95%C.I. 1.04-1.45 p = 0.01) and MMP-3 (HR for every 50 ng/ml, 1.14, 95%C.I. 1.01-1.29, p = 0.03) were statistically significant risk factors for future Bio users. [Conclusions] High serum levels of ACPA and MMP-3 at the time of diagnosis of RA are possible predictors of future Bio users.

ICW1-2

Clinical significance of myositis-specific autoantibody profiles in Japanese patients with polymyositis/dermatomyositis

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Conflict of interest: None

[Objective] Myositis-specific autoantibodies, such as anti-MDA5 and anti-ARS antibodies, are associated with interstitial lung diseases (ILD), which determine the prognosis of polymyositis/dermatomyositis (PM/DM) patients. However, there is a paucity of data on the clinical correlation between anti-SSA/Ro52 antibodies in PM/DM. We investigated the prevalence of myositis-associated autoantibodies including anti-SSA antibody and assessed the clinical significance of these antibodies in patients with PM/DM. [Methods] We retrospectively reviewed demographic data and clinical outcomes in patients with PM/DM. The study population comprised 24 patients with PM and 60 patients with DM. The presence of anti-myositis specific antibodies was determined by immunosorbent assay. [Results] Anti-MDA5 antibody was detected in 18 patients with DM patients. Anti-ARS/anti-SSA/Ro52 antibodies were detected in 31 and 39 patients of PM/DM patients. During the follow-up period, 9 patients died. We compared the baseline clinical features between survivors and non-survivors. The rate of anti-MDA5 Ab-seropositivity was significantly higher in non-survivors compared with survivors. PM/DM patients with double-positivity for both anti-MDA5 and anti-SSA/Ro52 Abs were significantly higher in non-survivors compared with survivors (44.4% vs 5.3%; $p < 0.001$). In Kaplan-Meier survival curves, DM patients with anti-MDA5 Abs had worse survival compared with anti-MDA5 Ab-negative DM patients. Anti-MDA5 Ab-positive DM patients with anti-SSA/Ro52 Abs showed worse survival than those without anti-SSA/Ro52 Ab, whereas there was no significant difference. In subgroup of anti-SSA/Ro52 Ab-positive patients, the seropositivity of anti-MDA5 Ab is associated with the significant worth survival compared with those without anti-MDA5 Ab. [Conclusions] Our results suggest that anti-SSA/Ro52 antibody positivity in DM patients with anti-MDA5 antibody reveals a subgroup of DM patients with poor prognosis.

ICW1-3

Establishment of a new murine model for anti-melanoma differentiation-associated gene 5 antibody-associated interstitial lung disease

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Conflict of interest: None

[Objective] Anti-melanoma differentiation-associated gene 5 (MDA5) autoantibody-associated dermatomyositis (DM) is a crucial disease with high mortality rate due to rapidly progressive interstitial lung disease (ILD), which etiology was still unclear. Here, we established a new murine model of ILD depending on autoimmunity for MDA5. [Methods] naïve C57BL6/J mice were subcutaneously injected with emulsion consisting of recombinant murine MDA5 whole protein produced by a baculovirus expression system and complete Freund's adjuvant (CFA) weekly for 4 times, accompanied by an intraperitonial injection of pertussis toxin at the first immunization. Subcutaneous injections of emulsion without MDA5 protein was used as a control. The sera, lung and femoral muscle samples were collected from the mice 2 weeks after the 4th immunization for analyses. An intranasal administration of bleomycin (BLM) was added some of the mice at the same time as the 4th immunization. A modified Ashcroft scoring system was used to evaluate the severities of their ILD. [Results] A western blotting assay indicated that antibodies against murine MDA5 protein were detected in the sera of the MDA5-immunized mice, but not in those of the control mice. Hematoxylin-eosin stained lung samples from MDA5-immunized mice presented more inflammatory foci in contiguity with the pleura than control mice. In the groups treated with BLM inhalation, MDA5-immunized mice definitely showed significant more severe lung fibrosis than control mice (median modified Ashcroft score [interquartile range] = 5.5 [5.0 - 6.0] vs. 4.5 [4.0 - 5.0], $p < 0.05$ by Mann-Whitney *U* test), and tended to have more inflammation. No muscle inflammation was observed. [Conclusions] The new murine model of ILD along with autoimmune reactions to the autoantigen MDA5 is conceivable to mimic ILD in patients of anti-MDA5 autoantibody-associated DM competently, and to be suitable to establish specific treatments for the fetal disease.

ICW1-4

The effect of antiphospholipid antibody on cognitive function and microglial activation in mice

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Conflict of interest: None

Backgrounds: Neuropsychiatric involvements include the most serious organ dysfunctions in systemic lupus erythematosus. Antiphospholipid antibody (aPL) is a significant risk factor for developing neuropsychiatric lupus. However, the pathogenic role of aPL in central nervous system have not been clarified. **Objective:** We aimed to investigate the effect of aPL on neuropsychiatric manifestations and central neuronal cells in a mouse model. **Methods:** We previously generated mouse monoclonal aPL against β2 glycoprotein I (β2GPI), named WBCAL-1, via hybridoma derived from NZW×BXSB F1 mice. We implanted 6- to 8-week-aged C57BL/6 mice with osmotic pumps to continuously infuse 200 μg of either WBCAL-1 or an IgG control antibody directly into the 3rd ventricle for 2 weeks. Behavior phenotyping and histopathological examination of the brain were performed after antibody infusion. We employed a novel object recognition test (NORT) to assess cognitive function, and the elevated plus maze test (EPM) to evaluate anxiety-like behavior. We identified the localization of β2GPI and IgG deposition by immunohistochemistry. We also analyzed microglial activation and neuronal cell phenotypes using Iba-1, CD68 and NeuN. **Results:** WBCAL-1 infused mice had a significantly lower discrimination index in NORT and shorter time in open arm in EPM than IgG control mice, indicating that WBCAL-1 contributed to cognitive dysfunction and anxiety. We detected β2GPI in the CA2 region of the hippocampus in wild type mice, and IgG deposition occurred in the same region of WBCAL-1 injected mice. Mice with WBCAL-1 injection demonstrated more $CD68^{+}Iba\text{-}1^{+}$ activated microglial cells in the hippocampus and lower NeuN expression of CA3 neurons than mice with an IgG control antibody. **Conclusion:** Mice with the intracerebroventricular infusion of aPL showed an altered microglial activation status as well as neuronal phenotypes in the hippocampus, which might lead to cognitive dysfunction and anxiety-like behavior.

ICW1-5

Antigen-driven autoantibody production in lung lesion of systemic autoimmune diseases

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Conflict of interest: None

[Objective] Lungs are affected in some systemic autoimmune diseases, but it is unclear what happens in these lesions and whether it differs from the other lesions. In this study, we investigated humoral immune response in lung lesions by examining antigen specificity of B cells in bronchoalveolar fluid (BALF) at single cell resolution. [Methods] We recruited patients with autoimmune disease with lung involvement, sorted the plasma cells of their BALF, read the sequence of antibody of each cell, and produced them as recombinant monoclonal antibodies *in vitro*. The reactivity of them were examined by ELISA and antigen-binding beads assay. We also examined the revertants of autoantibodies, which was reverted all somatic hypermutations (SHM) to the genomic sequence. [Results] We generated 123 antibodies from plasma cells in BALF of 4 organizing pneumonia of rheumatoid arthritis (RA), and identified 6 ACPAs and 5 RFs among them. Notably, one of them had the properties of both ACPA and RF. In addition, 146 antibodies were generated from 5 patients with Sjögren's syndrome (SjS) and mixed connective tissue disease (MCTD), and 7 anti-SSA antibodies, 15 anti-RNP antibodies, and one RF were identified. Some of them did not react in ELISA in which antigens were immobilized in solid phase, but reacted in beads assay in which antigens were immobilized in liquid phase, indicated that the proper conformation was important for antigen recognition. Revertants of autoantibodies significantly reduced their reactivity, and anti-RNP antibodies generated from one patient recognized various epitopes, indicating that autoantibodies were produced in lung lesion in an antigen-driven manner. [Conclusions] Autoantibodies were produced in an antigen-driven manner in lung lesion of RA, SjS, and MCTD, similar to reported main lesions such as synovium and salivary glands. Our results indicate that the same autoimmune reaction were occurred even at different sites of systemic autoimmune diseases.

ICW2-1

Comparison of the efficacy of Tumor Necrosis Factor Inhibitors and Interleukin-6 Inhibitors in patients with Elderly-onset Rheumatoid Arthritis by propensity score matching-the ANSWER cohort study

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Conflict of interest: None

[Objective] To compare the clinical outcomes at 1 year after the treatment with either Tumor Necrosis Factor inhibitors (TNFi) or Interleukin-6 Inhibitors (IL-6i) in patients with elderly-onset rheumatoid arthritis (EORA). [Methods] Patients with rheumatoid arthritis (RA) aged ≧18 years enrolled in a Japanese multicenter observational registry between 2009 and 2018 were included. EORA was defined as RA with onset at 60 or over. Considering selection bias to treatment with TNFi or IL-6i, a propensity score based on multiple baseline characteristics variables was used to compare the clinical effectiveness between TNFi and IL-6i. Primary outcome was Clinical Disease Activity Index (CDAI) score at 52 weeks. [Results] Among a total of 1292 biologic initiators with EORA, 136 of 434 patients treated with TNFi and 136 of 159 patients treated with IL-6i were statistically extracted. The baseline characteristics were comparable. At week 52, 62%/69% of patients (TNFi/IL-6i) were receiving treatment. The CDAI decreased from 16.1/16.5 at baseline to 6.9/7.0 at week 52 with TNFi/IL-6i, respectively. There was no significant difference in CDAI improvements at 52 weeks (-9.2 [-11.0--7.5] vs -9.5 [-11.5--7.7], p=0.92). At week 52, the CDAI remission rates for TNFi/IL-6i were 26%/38%, respectively (p=0.04). In the sub-analysis, using multiple regression, methotrexate use at baseline, baseline Disease Activity Score 28 using C-reactive protein, and disease duration were significantly associated with clinical remission at week 52 in patients treated with TNFi whereas only disease duration was associated with the clinical remission in patients with IL-6i. [Conclusions] In EORA patients initiating TNFi or IL-6i, improvements in clinical disease at 52 weeks were comparable between the two groups. Significantly higher clinical remission was seen in IL-6i group. There were some differences in the predictive factors for achieving clinical remission between the two groups.

ICW2-2

Safety of biologic disease-modifying antirheumatic drugs and remission induction strategy in elderly patients with rheumatoid arthritis from the FIRST registry

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Conflict of interest: None

[Objective] In Japan, the number of elderly RA patients who use bDMARDs is increasing. Here, we examined the effectiveness and safety for elderly RA patients. [Methods] Data from patients (n=3,138) who were treated with TNF inhibitors, abatacept, and tocilizumab between August 2003 and April 2019 were retrospectively extracted from our institute cohort, the FIRST registry. The patients were classified as <65 years-old (n=1,724), 65-74 years-old (n=912), and ≧75 years-old (n=502) at start of bDMARDs treatment. The incidence of adverse events (AEs) leading to withdrawal of bDMARDs was analyzed using Kaplan-Meier method and multivariate analysis was performed using cox hazard model and logistic

regression. [Results] Patients characteristics (all age/<65y/65-74y/≧75y) were as follows: median age 63/54/69/78 years-old, disease duration 5/4/6.7/6 years, DAS28-ESR 5.6/5.4/5.7/6.0, HAQ-DI 1.3/1/1.4/1.9, MTX use 77/84/72/64%, oral use of glucocorticoid (GC) 29/28/29/32%, and pre-existing lung disease 24/17/30/39%. The 5-year AEs incidence rates (all age/<65y/65-74y/≧75y) were 21/17/26/29%, and infection incidence rates (<65y/65-74y/≧75y) were 2.3/3.5/4.0%. Characteristics associated with AEs were oral use of GC (HR 1.43, p=0.049) in <65y group, MTX use (HR 0.38, p<0.001) and pre-existing lung disease (HR 1.77, p=0.007) in 65-74y group, and oral use of GC (HR 1.95, p=0.002) in ≧75y group. The 1-year DAS28-ESR remission rates (<65y/65-74y/≧75y) were 44/28/26%. In ≧75y group, characteristics associated with remission were female (OR 0.52, p=0.02), MTX use (OR 1.82, p=0.03), and HAQ-DI (OR 0.53, p<0.01, cutoff value 1.5). [Conclusions] As bDMARDs strategy in elderly RA patients aged ≧75y, it was suggested that use of oral GC should be avoid in terms of AE, and MTX should be tried to use together as far as possible in terms of remission induction.

ICW2-3

Clinical features of elderly-onset adult Still's disease

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Conflict of interest: None

OBJECTIVES: The peak age at the onset of adult Still's disease (ASD) has been between 20 and 35 years old. However, the proportion of elderly-onset ASD (EOASD) is increasing in Japan, a country of super-aged society. Therefore, we investigated the clinical features of EOASD in comparison with non-elderly-onset ASD. METHODS: A total of 20 patients with the diagnosis of ASD according to the classification criteria by Yamaguchi et al. between May 2013 and October 2018 in our department were enrolled in this study. Their medical records were intensively reviewed for demographics, clinical manifestations, laboratory data, treatments received and outcome. RESULTS: Six patients with the age of onset ≧65 years (median 71 years old, 5 women) and 14 patients < 65 years (median 38 years old, 12 women). There were no between-group differences in the frequency of fever, sore throat, arthralgia, leukocytosis, liver function abnormality, seronegativity and serum ferritin levels. However, typical rash (50% versus 92%) and lymphadenopathy (50% versus 92%) tended to be less frequently observed in EOASD as compared with non-elderly-onset ASD, and as a result, the number of fulfilled items of Yamaguchi criteria was significantly smaller in EOASD than non-elderly-onset ASD (the median value of 5.5 and 7.5, respectively, p=0.0036). Systemic feature score (SFS) was significantly smaller in EOASD than non-elderly-onset ASD (p=0.0129). With regard to the treatment, glucocorticoids were administered in 19 patients (initial daily dose of prednisolone 50 mg/day for both groups), and tocilizumab was added in 20% and 35% of EOASD and non-elderly-onset ASD patients respectively. The prognosis was fair except for one patient with non-elderly-onset ASD developing fatal sepsis. CONCLUSION: EOASD was not rare (30% of ASD) and showed comparable clinical features and outcomes with non-elderly-onset ASD.

ICW2-4

Pathomechanism of subtrochanteric and diaphyseal atypical femoral fractures in Super-aging area of North Japan

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Conflict of interest: None

[Objective] Pathomechanism of atypical femoral fracture (AFF) were still controversy. The developmental mechanism is reported to be significant differences between subtrochanteric and diaphyseal AFF. We analyzed retrospectively all cases of AFFs in all hospitals of our prefectural area. [Methods] Between 2009 and 2016, 119 AFFs were occurred in our prefectural area. Of those cases, we could survey bone healing and femoral neck angle, femoral shaft angle were 57 AFFs. We divided into subtrochanteric and diaphyseal AFF groups, and compared them about ages, femoral neck angle, femoral shaft angle, bisphosphonates (BPs) usage, glucocorticoids (GCs) usage, affecting collagen diseases, bone healing time. [Results] The subtrochanteric group were 11 AFFs and the diaphyseal group were 46 AFFs. The mean age was 58.2 (37-75) and 78.0 (60-89) year-old *($p < 0.05$), respectively*. Mean femoral neck angle was 130 (121-140) and 127 (113-141) degrees. Femoral shaft angle was 1.7 (-0.9-6) and 11.8 (0.8-24) degrees *($p < 0.05$)*. BPs usage was 73% (8/11) and 76% (35/46). GCs usage was 55% (6/11) and 4.3% (2/46) *($p < 0.05$)*. Affecting collagen diseases was 45% (5/11) and 4.3% (2/46) *($p < 0.05$)*. Bone healing time was 12.1 (6-20) and 8.1 (2-38) months *($p < 0.05$)*. [Conclusions] The subtrochanteric group were higher GCs usage, affecting collagen diseases, bone healing time. The diaphyseal group were higher ages, femoral shaft angle. A developmental mechanism is significant differences between subtrochanteric and diaphyseal AFF.

ICW2-5

Late-onset SLE is characterized by a low proportion of females and less frequency of skin rash at the onset

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Conflict of interest: None

[Objective] Late-onset systemic lupus erythematosus (LoSLE) has been considered to have the characteristics of atypical manifestations, which make diagnosis difficult. Although some papers have described the features of LoSLE, there is still little evidence in our country. Here we assessed the characteristic features of LoSLE using LUNA registry. [Methods] We collected the demographic, clinical and laboratory data from LUNA registry, which is the integrated SLE registry by 10 Japanese facilities. The registered patients, who met the 1997 American College of Rheumatology criteria for SLE, were included in the study. We compared the data from patients with LoSLE (≧50 years old at onset; LO group) with those from patients with early-onset SLE (<50 years old at onset; EO group). [Results] Among 894 enrolled patients, 100 and 794 belonged to LO (the mean age at onset 60.4 ± 7.42 years old) and EO (28.7 ± 10.5) groups, respectively. The male to female ratio was higher in LO group as compared to EO group (0.32 vs 0.11, $p = 4.9 \times 10^{-5}$). There was no significant difference in disease activity at onset between the two groups (SLEDAI 4.91 ± 8.20 vs 5.69 ± 8.69, p = 0.40). Myositis (11.9% vs 3.76%, $p = 3.1 \times 10^{-2}$) was observed more frequently whereas skin rash (33.3% vs 67.6%, $p = 9.4 \times 10^{-6}$), alopecia (7.32% vs 24.8%, $p = 1.0 \times 10^{-2}$) and lupus anticoagulant (LAC) positivity (10.6% vs 22.1%, $p = 1.1 \times 10^{-2}$) were less frequent at onset in LO group as compared to EO group. The usage rates of immunosuppressants were lower in LO group than in EO group (61.0% vs 75.6%, $p = 1.8 \times 10^{-3}$). By multivariate analyses, we identified female and new rash as negative factors for late onset (OR 0.41, $p = 4.8 \times 10^{-2}$ and OR 0.25, $p = 7.3 \times 10^{-4}$, respectively). The late onset was not identified as an independent factor for immunosuppressant use. [Conclusions] Late-on-

set SLE shows the lower proportion of females and less frequency of skin rash at the onset.

ICW2-6

Inter-rater reliability of radiographic posterior tibial slope and association between steep posterior tibial slope and complete disruption of anterior cruciate ligament in knee osteoarthritis

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Conflict of interest: None

[Objective] This study was designed to examine inter-rater reliability of posterior tibial slope (PTS) in knee osteoarthritis (OA) and also examine association between steep PTS and complete disruption of anterior cruciate ligament (ACL) in knee OA. [Methods] We reviewed 200 OA knees and three orthopaedic surgeons measured PTS using three measurement methods in lateral knee radiographs: angle between proximal tibia anterior cortex and tibial medial plateau line (slope A), angle between the line drawn from the centers of 2 circles on the shaft and tibial medial plateau line (slope B), and angle between fibular anatomical axis and tibial medial plateau line (slope C). Also, complete disruption of ACL was examined using magnetic resonance imaging. Intra-class correlation coefficient (ICC) was calculated for inter-rater reliability. Logistic regression analyses were performed to examine association between steep PTS and complete disruption of ACL. Furthermore, receiver operating characteristic (ROC) curves were depicted predicting complete disruption of ACL using these slopes. [Results] The inter-rater reliabilities of the measurements were ICC 0.848 (95% confidence interval (95%CI) 0.807-0.881) in slope A, 0.839 (95%CI 0.796-0.874) in slope B, and 0.862 (95%CI 0.826-0.892) in slope C. Steep PTS was significantly associated with complete disruption of ACL: odds ratio 1.193 (95%CI 1.100-1.295) in slope A, 1.267 (1.149-1.397) in slope B, and 1.220 (95%CI 1.113-1.336) in slope C. ROC curves showed that slope A more than 14 was significantly associated with complete disruption of ACL with area under the curve (AUC) 0.668 (95%CI 0.585-0.750), as well slope B > 11 with AUC 0.687 (95%CI 0.608-0.765), and slope C > 10 with AUC 0.670 (95%CI 0.592-0.748). [Conclusions] We identified that the inter-rater reliabilities of the three measurement methods of radiographic PTS were respectively favorable and steep PTS was significantly associated with complete disruption of ACL in knee OA.

ICW2-7

Mechanism of chondroprotective effects of 4MU and 2-deoxyglucose

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Conflict of interest: None

We reported that the inhibitor of hyaluronan (HA) biosynthesis, 4-methylumbelliferone (4-MU) has chondroprotective effects in human osteoarthritic (OA). This was a somewhat counterintuitive observation because we have also demonstrated that the overexpression of HAS2 (HAS2-OE) exerted the same chondroprotective effects. we hypothesized that the effect of HAS2-OE and 4-MU relate to changing metabolism and the possibility of inhibition of glycolysis induce chondroprotective effect. To determine that, we used the glycolysis inhibitor, 2-Deoxyglucose (2DG) as an alternative agent to change metabolism in chondrocytes. Methods: bovine and human chondrocyte were stimulated with IL-1β in the presence or absence of 4MU, 2DG. Bovine chondrocytes were tested using Seahorse Flux Analyzer (Agilent Tech) to determine rate changes in accumulation of +H protons and for O2 consumption. Accumulation of MMP13 and phosphor AMPK (pAMPK) protein was quantified with Western blotting. Cartilage explants were cultured with L-1β in the presence or absence of 2DG and stained with Safranin O. Results: Reduced mitochondrial potential and enhanced dependence on glycolysis was observed in IL-1β stimulated chondrocytes. In control chondrocytes, the use of glycolysis contributes to the majority of ATP produced approximately 1/5th from the TCA cycle. IL1β-activated chondrocytes display increase in glycolysis and decrease in mitochondrial contributions. These changes are reversed by co-treatment with 4MU and 2DG. 2DG reversed the IL1β-induced increases accumulation of MMP13 protein in human OA chondrocytes. Although IL-1β lost safranin O staining in human and bovine samples, co-incubation with 2DG blocked in the loss of proteoglycan. IL-1β treatment decreased accumulation of phosphor AMPK. Co-treatment with 4-MU and 2DG resulted in a rescue of the pAMPK status. Conclusion: 4-MU and 2DG have chondroprotective effect by changing metabolism and upregulate AMPK.

ICW3-1

Estimation of treatment and prognostic factors of pneumocystis pneumonia (PCP) in patients with connective tissue diseases (CTD-PCP): an analysis of a national administrative database in Japan

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Conflict of interest: None

Objectives; Pneumocystis pneumonia (PCP) in patients with connective tissue diseases (CTD-PCP) is life-threatening. CTD-PCP patients are treated with a combination of antibiotics for PCP (such as sulfamethoxazole/trimethoprim (ST), pentamidine (PTM) and atovaquone (ATO)) and glucocorticoids (GC). However, no large clinical studies have examined the prognosis or efficacy of its treatments. The purpose was to clarify the current status of CTD-PCP and to search for prognostic factors. **Methods;** We enrolled CTD-PCP patients who received PCP-specific therapies (definition: CTD-patients who were treated with 4 or more tablets per day of ST, or PTM, or ATO for 7 days or more.) between Apr. 2013 and Mar. 2015. Records were extracted from a Japanese nationwide inpatient database. **Results;** Total number of patients with CTD-PCP was 333 (male n=123). Median age 71.0 [62.0-77.0]. Types of CTD; vasculitis (n=116), myositis (n=60), systemic lupus erythematosus (n=49) and like. 214 cases treated with ST alone. PTM and ATO were used in 95 and 44 cases. GC was used 322 cases. 30- and 60-days survival rate after starting of PCP therapies were 66.0% and 53.7%. Survivors were significantly younger ($p<0.01$), more frequently treated single (ST alone, $p<0.01$) or combination (ST and ATO, $p=0.03$). A multivariate Cox hazard ratio analysis demonstrated that age (HR 1.05, 95% CI 1.03-1.07, $p<0.01$), male (HR 1.61, 95% CI 1.12-2.34, $p=0.01$) and complication of rheumatic lung diseases (HR 4.71, 95% CI 1.14-19.45, $p=0.03$) were associated with poor prognosis. Completion of treatment with ST alone or ATO (including changes from ST) had significantly higher survival rates than PTM (including changes from ST). Use of ventilator (HR 2.95, 95% CI 1.82-4.78, $p<0.01$) was significantly associated with a poor prognosis. **Conclusion;** CTD-PCP was still life-threatening. The prognosis of CTD-PCP patients who were able to complete the treatment with ST alone or switching from ST to ATO might be relatively better.

ICW3-3

The Effect of Janus Kinase Inhibitors on Patients with Anti-Melanoma Differentiation-associated Protein 5 antibody-positive clinically amyopathic dermatomyositis complicating rapid progressive interstitial lung disease

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Conflict of interest: Yes

[Purpose] The aim of this study is to investigate effects of Janus kinase inhibitors (Jakinibs) on clinically amyopathic dermatomyositis (CADM) patient positive for anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5) complicated with rapid progressive interstitial lung

disease (RP-ILD). [Patients and Methods] In patients with CADM positive for anti-MDA5 initiated with Jakinibs for refractory RP-ILD, the changes of serological markers, images, complications and prognosis were investigated. [Results] 3 female patients had received Jakinibs at the age of 66, 71 and 76 years old, respectively. The initial value of anti-MDA5 was 3100, 1450 and 5350 index, and that of ferritin was 176, 561 and 1070 ng/mL. Tofacitinib (TOF) was initiated to these patients with RP-ILD inspite of remission induction therapy by high dose corticosteroid following steroid pulse combined with calcineurin inhibitor and intravenous cyclophosphamide. The time for initiating TOF was 66, 134 and 56 days after admission. Two alive patients (66- and 71-year-old cases) were surviving for 215 and 152 days. The value of anti-MDA5 decreased from 2700 to 46 index in 21 weeks (66 year-old case), did from 300 to 92 in 3 weeks (71 year-old case) after TOF, that of ferritin did from 5620 to 666 and from 4282 to 1266ng/mL, but that of KL-6 did not from 1029 to 4984 and did from 1775 to 1966, respectively. Whereas, the dead patient (71-year-old case) survived for 111 days. The anti-MDA5 value decreased from 2500 (before TOF) to 94 index, ferritin did from 2018 (peak after TOF) to 1076ng/mL, and KL-6 did from 4768 to 1601U/mL in 8 weeks. However, she died from candidemia. In all cases, the pulmonary lesions of CT were not exacerbated after TOF. Cytomegalovirus antigenemia was recurrent despite of antivirals. [Conclusions] Jakinibs could be effective for patients with CADM positive for anti-MDA5 complicating RP-ILD, but total systemic management should be required especially for controlling infection.

ICW3-4

Therapeutic Strategies And Long-term Outcome In Patients With Interstitial Pneumonia With Autoimmune Features: A Single Center Large-scale Observational Cohort Study

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Conflict of interest: None

[Objective] Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue diseases (CTDs). The term interstitial pneumonia with autoimmune features (IPAF) has been recently proposed for such patients. To date, only few studies have comprehensively described outcomes over a long-term period and choices of treatment. The aim of this study was to investigate the therapeutic strategies in patients with IPAF, and compare long-term outcomes among patients with IPAF, IIP, and CTD-ILD. [Methods] Of 672 patients who had visited our department between April 2009 and March 2019, 68 patients who diagnosed as IPAF were enrolled. Of 68 patients, 30 patients were treated with glucocorticoid or/and immunosuppressants. The treatment group was divided into two groups, which started treatment at diagnosis and at exacerbation. Clinical, laboratory and imaging data were collected from medical records and statistically analyzed. [Results] In start at diagnosis group, exacerbation rate in monotherapy group or combination group was 42.9% and 16.7%, while in start at exacerbation group, those was 60% and 37.5%. No significant difference, regardless of monotherapy or combination therapy in each group (P=0.30 and 0.43). An immunosuppressant was prescribed in 17 patients (namely tacrolimus in 5, ciclosporin in 11, and azathioprine in 1, respectively). Then, we compared exacerbation rate among these immunosuppressants in both groups. There was no significant difference in each group (P=0.093 and 0.51). When we compared long-term outcomes among patients with IPAF, IIP, and CTD-ILD, 5-year non-exacerbation rate in IPAF patients with treatment, those without treatment, CTD-ILD patients, and IIP patients was 36.5%, 83.3%, 59.5%, and 28.3%, respectively. [Conclusions] Our large-scale cross-sectional cohort study showed no significant difference in therapeutic strategies and identified long-term outcome in patients with IPAF.

ICW3-5

Protective roles of TGF-β3 in interstitial pneumonia with autoimmune features

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Conflict of interest: Yes

[Objective] We have reported that $CD4^+CD25^-LAG3^+$ regulatory T cells regulate humoral immune responses in a TGF-β3-dependent manner. Recent GWAS reveals that *TGFB3* is a systemic sclerosis (SSc) susceptibility gene in African Americans. In this study, we assessed the roles of TGF-β3 in systemic fibrotic responses. [Methods] Conditional knockout mice with TGF-β3 deficiency in $CD4^+$ T cells ($Tgfb3^{fl/fl}CD4^{Cre}$) were generated. Histopathology and expression of fibrosis-related genes in lungs from $Tgfb3^{fl/fl}CD4^{Cre}$ mice were compared with $Tgfb3^{fl/fl}$ mice. Also, the effects of a continuous bleomycin infusion delivered by osmotic minipumps as a disease model of SSc in lung pathologies and genes from $Tgfb3^{fl/fl}CD4^{Cre}$ mice were evaluated. Either pCAGGS-Mock or pCAGGS-Tgfb3 plasmid vectors were intravenously administered to lupus prone MRL/*lpr* mice and the effects of these vectors on the spontaneous interstitial pneumonia were histologically assessed by semi-quantitative Ashcroft score. Further, we evaluated the effects of TGF-β3 on the proliferation of normal human lung fibroblasts (NHLFs) by a MTS-based colorimetric method. [Results] $Tgfb3^{fl/fl}CD4^{Cre}$ mice spontaneous developed interstitial pneumonia with autoantibody production. The bleomycin-induced lung fibrosis were exacerbated with elevated Ashcroft score, and fibrosis-related genes such as *Col1a2*, *Serpine1*, and *Spp1* were significantly up-regulated in lung tissues from $Tgfb3^{fl/fl}CD4^{Cre}$ mice. Also, pCAGGS-Tgfb3, but not pCAGGS-Mock, ameliorated interstitial pneumonia in MRL/*lpr* mice. Further, TGF-β3 inhibited the proliferation of NHLFs in a dose-dependent manner. [Conclusions] Our findings indicate that TGF-β3 has anti-fibrotic effects and contributes to regulate systemic fibrotic responses. Inhibitory cytokine TGF-β3 with anti-fibrotic potential might provide novel therapeutic approaches for SSc and interstitial pneumonia with autoimmune features.

ICW4-1

Significance of nailfold videocapillaroscopy (NVC) in patients with mixed connective tissue disease (MCTD) differs from systemic sclerosis (SSc)

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Conflict of interest: None

[Objective] MCTD is characterized by overlapping clinical features with SSc, SLE and IIM. In addition to immunological dysregulation, vasculopathy in causing Raynaud's phenomenon (RP) and pulmonary arterial hypertension (PAH) plays a prominent role in the pathogenesis of MCTD. The aim of this study is to investigate how the microvasculopathy contributes to the pathogenesis of MCTD. [Methods] This prospective study enrolled 35 untreated MCTD patients, and 60 age- and sex- matched SSc patients as the controls. The microvasculolathy was evaluated using NVC. The clinical features were assessed at baseline and after 52wks. [Results] The patients were 94% female at 49 year-old mean age. All MCTD patients had RP, among which 86% with skin thickening of the fingers, 51% with interstitial lung disease (ILD), and 26% with PAH. NVC abnormalities were observed in 43% of MCTD patients, though the prevalence was lower compared with SSc patients (83%). When we compared between the patients with and without NVC abnormalities, the prevalence of skin thickening and ILD were comparable. However, the prevalence of PAH and muscle weakness were significantly increased in patients with NVC abnormalities ($p<0.001$, 0.03, respectively). Notably, NVC changes were detected in all of the patients with PAH, in comparing to only 23% in patients without PAH. NVC abnormalities were improved in 86% of MCTD patients after 1-year intensive immunosuppressive therapy including glucocorticoids. In contrast, the improvement of the abnormalities was not

seen in patients with SSc (The improvement rate was 8%). [Conclusions] The proportion of MCTD patients with NVC abnormalities is significantly lower than SSc patients. However, the NVC abnormalities strongly correlate with PAH, highlighting to be the clinical marker in predicting the presence of PAH. In addition, immunosuppressive therapy improves the abnormalities. This study clarifies the significance of the NVC abnormalities in MCTD differing from that in SSc.

ICW4-2

Involvement of Th22 cells in the pulmonary fibrosis and microvascular damage in patients with systemic sclerosis

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Conflict of interest: None

[Objective] Although $CD4^+$ T cells play a pivotal role in autoimmune diseases, little is known about its role in the pathogenesis of systemic sclerosis (SSc). We have reported the proportions of activated Th17 cells was higher in SSc compared to healthy control (HC). $CCR10^+$ Th22 cells have recently been identified to be another distinct subset from Th17 cells; however, the relevance of Th22 cells to SSc pathology remains unknown. We examined the frequencies of Th22 cells in peripheral blood and lung tissue in a correlation with clinical findings in patients with SSc. [Methods] The characteristics and proportion of circulating T helper (Th) subset including Th22 cells in 71 patients with SSc and 14 HCs were analyzed by multi-color flow cytometry. IL-22 producing $CD4^+$ T cells in lung tissues in patients with SSc (n=5) and heart disease were evaluated by immunohistochemistry. [Results] The proportion of Th17 cells (SSc/HC=12.5/8.4, p=0.02) and Th22 cells (2.6/1.9, p=0.04) was increased in SSc, compared to HC. In contrast, other helper subsets such as Th1, Treg or Tfh cells did not differ between SSc and HC. The proportion of activated Th22 cells was increased in SSc patient with active nailfold videocapillaroscopy (NVC) pattern (p=0.04). The immunophenotype of the patients with SSc-associated interstitial lung disease (SSc-ILD) showed a higher proportion of Th17 cells (ILD/non-ILD 13.6/10.6, p=0.03) and Th22 cells (2.8/2.2, p=0.04) compared to non-ILD-SSc patients. IL-22 and IL-17 producing $CD4^+$ T cells were markedly infiltrated in fibrotic lung tissue in patients with SSc, but not in patients with heart disease. [Conclusions] The proportion of Th22 cells increased in patients with NVC abnormalities and ILD, and Th22 cells infiltrated fibrotic lung tissue in SSc. These data suggest that Th22 cells may migrate and accumulate into lung tissues in SSc patients, thus highlighting the relevance of Th22 cells in the pathogenesis of vascular abnormalities and fibrosis in SSc.

ICW4-3

Monocytes/macrophages may contribute to the fibrotic process of systemic sclerosis via downregulation of interferon regulatory factor 8

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Conflict of interest: None

[Objective] Recent observations have suggested that monocytes/macrophages play important roles in the pathogenesis of systemic sclerosis (SSc). Interferon regulatory factor (IRF) 8 is a transcriptional regulator which plays essential roles in the differentiation and function of monocytes/macrophages. We hypothesized that IRF8 may be involved in the fibrotic process of SSc by regulating phenotypes of monocytes/macrophages. [Methods] We first determined IRF8 levels in monocytes from 26 SSc patients (diffuse cutaneous SSc (dcSSc), n=11; limited cutaneous SSc (lcSSc), n=15) and 14 healthy controls by quantitative real time PCR (qRT-PCR). IRF8 was next silenced in monocytes by RNA interference, and these monocytes were differentiated into macrophages (siIRF8-MDMs). Cell surface markers, cytokine/chemokine profiles, and expression levels of extracellular matrix (ECM) were assessed. Also, these macrophages were co-cultured with fibroblasts, and expressions of pro-fibrotic factors in fibroblasts were analyzed. Finally, bleomycin-induced skin fibrosis was assessed in myeloid cell-specific IRF8 conditional knockout mice (IRF8cKO mice). [Results] Significantly suppressed IRF8 levels were observed in monocytes from dsSSc patients, and its levels were negatively correlated with modified Rodnan total skin thickness score. siIRF8-MDMs exhibited M2 phenotype, and their mRNA and protein levels of pro-fibrotic factors and ECMs were significantly upregulated. Co-culture analysis revealed that siIRF8-MDMs activated fibroblasts. Finally, in bleomycin-induced skin fibrosis model, dermal thickness, skin infiltrating macrophages, hydroxyproline contents, and levels of pro-fibrotic factors were aggravated in IRF8cKO mice. [Conclusions] IRF8 was significantly downregulated in circulating monocytes from dcSSc patients, and pro-fibrotic phenotype was induced *in vitro* and *in vivo*. Altered regulation of IRF8 in monocytes/macrophages may be involved in the pathogenic process of SSc.

ICW4-4

Pneumonia in patients with rheumatoid arthritis: impact of microbial airway colonisation

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Conflict of interest: None

[Objectives] Clinical evidence on the relation between the microorganisms colonising the lower respiratory tract (LRT) and the subsequent incidence of pneumonia in patients with rheumatoid arthritis (RA) is limited, although RA frequently complicates airway diseases and is associated with high rates of pneumonia incidence and mortality. Therefore, we aimed to evaluate whether a specific microorganism colonising the LRT of patients with RA could be a risk factor for the subsequent incidence of pneumonia. [Methods] We retrospectively included the electronic medical records of 88 patients (median age, 67 years; women, 73.9%) with RA who underwent bronchoscopy at two hospitals from January 2008 to December 2017 and extracted the data (detected microorganisms, patient characteristics, and subsequent incidence of pneumonia). Patients with active infections were excluded from the study. 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] The most frequently isolated microbes from LRT, in descending order, were *Pseudomonas aeruginosa* (15.9%), *Staphylococcus aureus* (14.7%), and *Haemophilus influenzae* (6.8%). The *P. aeruginosa* group showed higher frequency of macrolide use than did the control group (n=55). We found that the rate of subsequent incidence of pneumonia was higher in the *P. aeruginosa* group (100 vs 30 per 1,000 patients, $P = 0.025$) and that the isolation of *P. aeruginosa* was an independent risk factor for pneumonia (hazard ratio, 9.797; 95% confidence interval, 2.165-51.090). [Conclusions] Our study demonstrated that colonisation of the LRT by *P. aeruginosa* in patients with RA is associated with the subsequent incidence of pneumonia. [Acknowledgments] We thank Dr. Shuhei Ideguchi[1] and Dr. Masahiro Tahara, University of Occupational and Environmental Health, for data collection and analysis.

ICW4-6

High prevalence of infection-related comorbidities among Japanese Rheumatoid Arthritis patients treated with csDMARDs or bDMARDs: A claims database analysis

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Conflict of interest: Yes

[Objectives] Rheumatoid Arthritis (RA) patients may discontinue their treatment due to infections. This study aimed to describe infection-related comorbidities among Japanese RA patients who were treated with conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) or biological DMARDs (bDMARDs). [Methods] This study included adult patients (aged ≧18 years) with RA in the Medical Data Vision (MDV) hospital claims database. Patients who switched/cycled to another DMARD after discontinuing csDMARD or bDMARD were classified as csDMARD- and bDMARD-groups respectively. Patients with RA were identified via International Classification of Diseases 10th Revision (ICD-10) codes and DMARDs were discontinued between 4/2009-4/2018, with the index date (ID) defined as the date of initiation with a new DMARD treatment. Prevalence of comorbidities during the 1-year pre-ID period was assessed via ICD-10 code grouping, and Charlson Comorbidity Index (CCI) was used to measure overall pre-index comorbid disease burden. [Results] Of the 8,361 patients in bDMARD-group (median age 65 years, 79.8% female), and 23,294 patients in csDMARD-group (median age 67 years, 75.8% female), the mean CCI scores were 0.56 and 0.51 respectively. Infection-related comorbidities such as intestinal (12.5% vs 10.0%), respiratory (10.8% vs 7.0%), viral (9.2% vs 5.4%), and fungal (8.6% vs 5.4%) were prevalent in bDMARD and csDMARD-groups respectively. The prevalence of hepatitis increased over time from 3.3% (4/2008-4/2011) to 8.3% (5/2015-4/2018) in the bDMARD and 1.2% (4/2008-4/2011) to 4.1% (5/2015-4/2018) in the csDMARD-group. An increased prevalence of tuberculosis from 1.3% (4/2008-4/2011) to 2.0% (5/2015-4/2018) was observed in the bDMARD-group. [Conclusions] Patients who switched/cycled to another DMARD after discontinuing csDMARD or bDMARD treatment had a prevalence of infection-related comorbidities. Comorbidities, including infections, should be carefully considered in this population.

ICW4-7

15-year risk manegement for molecular target therapy in RA - FIRST registry-

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Conflict of interest: None

[Objective] To verify the safety of b/tsDMARDs in RA over a 15-year period in clinical practice. [Methods] The analysis method was a prospective cohort study. Data on clinical characteristics, demographics and medical history among all patients with RA who initiated b/tsDMARDs during 2003-2019 were identified by linking the FIRST registry. [Results] The study population comprised 3501 patients with RA, of which 2752 who had been observed for more than 1 year were analyzed. The retention rate at month 12 was 82.7%. The proportion of patients who achieved remission and low disease activity was 65.4%. Over a 15-year observation period, the proportion of discontinuation due to inefficacy was 19.6% and discontinuation due to adverse event was 12.2%. The incidence of discontinuation due to adverse event, including infection, malignancy and infusion reaction, was 4.48 (100patient-year). In the Cox proportional hazards regression model, the risk factors of inadequate response were SDAI [HR 1.02 95%CI 1.01-1.04] and history of b/tsDMARDs [HR 1.31 95%CI 1.06-1.65]. The risk factors of adverse event were age [HR 1.01 95%CI 1.00-1.02], SDAI [HR 1.02 95%CI 1.00-1.04] and lung disease [HR 1.56 95%CI 1.16-2.08]. In logistic regression analysis, the factors that associated with lung disease were age (over 60 years) [OR 2.83 CI95% 2.31-3.47], ACPA positive [OR 1.66 CI95% 1.29-2.12] and RF titer (over 100 IU/ml) [OR 2.11 95%CI 1.76-2.53]. [Conclusions] For the long-term safety of b/tsDMARDs, it is necessary to assess lung disease. In particular, we have to pay attention for over 60 years old, ACPA positive and over 100 IU/ml RF titer.

ICW4-8

The risk of developing herpes zoster differs among biologics in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] To investigate the factors for developing herpes zoster (HZ) in patients with rheumatoid arthritis (RA) receiving adalimumab (ADA), tocilizumab (TCZ), and abatacept (ABT). [Method] RA patients who had started to receive ADA, TCZ or ABT in our hospital since 2008 to 2019 were enrolled and the risks for HZ development was retrospectively analyzed. [Results] Patients were treated with ADA (n=81), TCZ (n=128) and ABT (n=101) group. Age was 55 (19-82) (median, range), 59.5 (19-81) and 66 (23-86) years old, daily dose (rate) of prednisolone (PSL) use was 2 mg (0-21) (54.3%), 3 mg (0-20) (57.8%) and 3 mg (0-16) (62.4%), weekly dose of methotrexate (MTX) was 10 mg (0-16) (86.4%), 6.5 mg (0-16) (58.6%) and 8 mg (0-16) (66.3%), respectively. ABT group was significantly older, compared to ADA ($p<0.001$) or TCZ ($p=0.001$). There was no difference in PSL use among these groups. The dose and rate of MTX use were both significantly higher in ADA, compared to TCZ ($p<0.001$ and <0.001) or ABT ($p<0.001$ and $=0.008$) group. HZ was complicated in 5, 6 and 5 patients in ADA, TCZ or ABT group respectively. Overall, initial age, disease duration, MTX dose, PSL dose, CRP level and being the first molecular-targeting therapy were all not significant risks for HZ development. Whereas, in comparison between each group, higher dose of MTX in ADA (odds ratio (OR) 1.30, 95% confidence interval (CI) 0.994-1.969, $p=0.056$) and the higher age in ABT (OR 1.11, 95%CI 1.006-1.265, $p=0.035$) increased the risk for HZ development. Time to HZ development was 1100 (385-2706) days in TCZ, 239 (28-1081) in ADA and 380 (2-854) in ABT group. Cox proportional hazard model demonstrated significantly lower risk for HZ development in one year after initiation of TCZ, compared to ADA (risk ratio <0.001, 95% CI 0.000-0.548, $p=0.016$). [Conclusion] The risk factor for HZ development is different among biologics in the treatment of patients with RA.

ICW5-1

Comprehensive gene expression analysis of peripheral blood immune cells of primary Sjogren's syndrome

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Conflict of interest: Yes

[Objective] Sjogren's syndrome (SS) is an autoimmune disease, and various types of immune responses are involved in the pathophysiology. To elucidate the functions of each immune cell subset in SS, we performed comprehensive gene expression analysis of peripheral blood immune cell subsets in SS patients. [Methods] Cell sorting of 19 PBMC subsets were performed in primary SS patients (n=18) and healthy controls (HC; n=28), and RNA sequence was performed for each cell subset. The relationship between gene expression and clinical parameter was analyzed. [Results] The network analysis for the gene expression showed the module, a majority of which were interferon-related genes, had strong correlation to SS in every subset. Gene modules that correlated to ESSDAI or ESSPRI scores were found in naïve B cells, myeloid dendritic cells, $CD16^+$ monocytes, Th2 cells, memory $CD8^+$ T cells, and they contained relatively less IFN-related genes. Serum IgG level in SS was correlated to modules in switched memory B cells and double-negative B cells. [Conclusions] The result indicated that IFN-related genes were upregulated in a broad range of immune cell subsets in SS, while clinical parameters for disease activity might be related to the gene expression profile less relevant to IFN-related genes.

ICW5-2

Immunoglobulin G4-Related Disease (IgG4-RD): Clinical and Laboratory Characteristics in One Hundred Five Patients

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Conflict of interest: None

[Objective] IgG4-RD is a systemic fibro-inflammatory condition with incompletely understood that is capable of affecting multiple organs. This study was undertaken to report detailed clinical and laboratory findings in a Japanese patients with IgG4-RD. [Methods] Date on clinical characteristics, laboratory features, and treatment response from patients with igG4-RD in our hospital were reviewed retrospectively. [Results] Of the 105 patients, 48% were female and 88% were biopsy-proven. The median age of the patients was 66 years, their medina duration of follow-up was 45 months. 48% of the patients had allergic history (including sinusitis, asthma, hay fever). Salivary and lacrimal grand involvement (60%) and dacryoadenitis and ocular and orbital inflammatory disease (56%), autoimmune pancratitis type 1 pancreatitis (18%) predominantly occurred. 84% of the patients had serum IgG4 higher than 135mg/dL, and high IgG4 concentration was associated with lower complements levels. Mean serum IgG was 1860mg/dL, and IgG4 was 449mg/dL. Male patients show older age at diagnosis and higher serum IgG and IgG4 concentrations at baseline. Younger patients tend to need treatment, 60 of them used steroid, and the mean dose of predninesone they used was 30mg. Most of them responded well and tapering steroid. Maintenance therapy with Immunosuppressants was required in 23%. [Conclusions] Our study revealed that IgG4-RD occurred in middle age patients with allergic disease. The pattern of head and neck was predominance. For the most part of the patient serum IgG and IgG4 concentrations was high. Younger patients tend to treat with steroid and they responded well.

ICW5-3

Eotaxin-3 is a novel biomarker for IgG4-related disease with lymphadenopathy, a phenotype associated with disease activity, eosinophilia and poor prognosis

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Conflict of interest: None

[Objective] To clarify the clinical characteristics and associated factors for IgG4-related disease (IgG4-RD) with lymphadenopathy. [Methods] We retrospectively reviewed all consecutive patients with newly diagnosed IgG4-RD in our department between January 2000 and June 2018. We divided patients into two groups according to the presence or absence of lymphadenopathy (lymph group and non-lymph group) and compared baseline characteristics and prognosis. We performed proteomics analysis and measured serum concentrations of 1129 proteins among patients with lymph and non-lymph group of IgG4-RD and normal healthy control. [Results] A total of 85 patients with IgG4-RD were included. Of them, 47 (55.3%) was lymph group. Baseline serum IgG, IgG4, IgG4/IgG ratio, IgG4-RD responder index, soluble interleukin-2 receptor, absolute eosinophil count were significantly higher, and serum IgM was lower in lymph group ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p=0.002$, and $p=0.04$, respectively). Lymph group was significantly associated with higher rate of future relapse ($p=0.02$). Serum eotaxin-3 was higher in lymph group and significantly correlated with serum IgG4, IgG4-RD responder index, soluble interleukin-2 receptor and eosinophil count, and decreased after induction therapy. [Conclusions] IgG4-RD with lymphadenopathy is characterized by high disease activity, eosinophilia and poor prognosis, and eotaxin-3 can be a novel surrogate marker.

ICW5-4

Detection and clinical significance of circulating M3 muscarinic acetylcholine receptor (M3R) reactive Th17 cells in patients with primary Sjögren's syndrome

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Conflict of interest: None

[Objective] We previously detected anti-M3R antibodies (Abs) and M3R reactive $CD4^+IFN\gamma^+$helper T (Th1) cells in patients with Sjögren's syndrome (SS). The purpose of this study was to identify circulating M3R reactive $CD4^+IL\text{-}17^+$helper T (Th17) cells, and the relationship of clinical features in patients with primary SS (pSS). [Methods] 1) 10 pSS patients, 10 healthy controls (HCs), and 5 IgG4-related disease (IgG4-RD) patients were recruited. According to their HLA-DRB1 typing, M3R peptides predicted to be the epitope for each HLA typing were selected using website database. PBMCs were stimulated with these M3R peptides mixture, and IL-17 producing ($IL\text{-}17^+$) cells were detected by ELISPOT. 2) PBMCs from 5 pSS patients positive for M3R reactive $IL\text{-}17^+$cells were stimulated with 12-20 mers M3R peptides separately to identify the dominant peptides. 3) $CD4^+$T cells co-cultured with monocyte derived dendritic cells (DCs) were stimulated with dominant M3R peptides, and $IL\text{-}17^+$cells (Th17 cells) were detected by ELISPOT. 4) Clinical features were compared between M3R reactive $IL\text{-}17^+$cells positive and negative pSS patients. 5) Anti-M3R Abs against extracellular domains of M3R were examined by ELISA. [Results] 1) 50% (5/10) of pSS patients were positive for M3R reactive $IL\text{-}17^+$cells, while none of HCs and IgG4-RD patients were positive. 2) M3R AA76-95 was the dominant M3R peptide responsible for IL-17 secretion among all 5 M3R reactive $IL\text{-}17^+$cells positive pSS patients. 3) M3R reactive Th17 cells were confirmed in pSS patients. 4) M3R reactive $IL\text{-}17^+$cells positive pSS patients had significantly higher ESSDAI score (8.0±4.3) than negative patients (2.8±1.7). 5) Titers of anti-M3R Abs against 2nd and 3rd extracellular loops of M3R were significantly higher in M3R reactive Th17 cells positive pSS than negative pSS patients. [Conclusions] We detected circulating M3R reactive Th17 cells in pSS patients using ELISPOT, which positivity might associate with higher disease activity and anti-M3R Abs.

ICW5-5

Fractalkine receptor (CX3CR1) positive helper T cells characterize IgG4-related disease (IgG4-RD)

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Conflict of interest: None

[Objective] Fractalkine is a chemokine which is expressed in peripheral tissues and mediates adhesion and migration via $CX3CR1^+$cells. Since the pathological changes of IgG4-RD include lymphocyte infiltration and fibrotic changes in the lesions, we investigated the significance of CX3CR1 in patients with IgG4-RD. [Methods] Human $CX3CR1^+CD4^+$Tcells were induced from naïve $CD4^+$Tcells under various stimulations in vitro, and the characteristics of $CX3CR1^+$cells were investigated. The proportion of $CX3CR1^+$cells in peripheral blood from healthy controls (HCs, n=6) and IgG4-RD patients (n=15) was analyzed by flow cytometry. The localization of $CX3CR1^+CD4^+$Tcells was demonstrated by immunohistochemistry staining on salivary glands from patients with either IgG4-RD or Sicca syndrome. [Results] Following TCR and IL-12 simulation for 5days, 20% of $CD4^+$Tcells expressed CX3CR1. $CX3CR1^+$Tcells also highly expressed both CXCR5 and CXCR3. Moreover, they coexpressed Bcl-6 and T-bet. After stimulation with PMA and ionomycin, $CX3CR1^+$Tcells produced both IFN-γ and IL-21. In the PBMCs of both IgG4-RD patients and HCs, CX3CR1 was highly expressed on $CD14^+$monocytes but not on Bcells. However, the proportion of $CX3CR1^+CD4^+$Tcells was higher in IgG4-RD patients (13.8%) compare to HCs (5.0%, $p=0.01$). Next, we isolated $CX3CR1^+$or $CX3CR1^-CD4^+$Tcells from peripheral blood and cocultured them with naïve Bcells for 7days. In comparison to their CX-

3CR1$^-$cells, CX3CR1$^+$cells induced plasmablast differentiation more efficiently (15.0 vs 5.0%, p=0.01) and increased the production of IgG and IgG4. In addition, CX3CR1$^+$CD4$^+$Tcells localized in salivary glands of IgG4-RD patients but not Sicca syndrome patients. [Conclusions] Our findings suggest that CX3CR1$^+$CD4$^+$Tcells have both Th1-like cytotoxic function and Tfh-like Bcell helper function. Furthermore, the proportion these cells is increased in the peripheral blood and tissues in patients with IgG4-RD. Thus, the anti-CX3CL1 antibody could be a new targeted therapy for IgG4-RD.

ICW6-1

Risk factors for vasculitis-derived manifestations in patients with dermatomyositis

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Conflict of interest: None

Objective: Clinical profile of dermatomyositis (DM) includes a complement-mediated vasculopathy affecting small vessels in muscular and other tissues. DM patients with the manifestations derived from vasculitis are often difficult to treat for remission induction and maintenance. In this study, we assessed the risk factors for vasculitis-derived manifestations in patients with DM. **Methods**: This retrospective study comprised 80 patients with DM treated in our hospital. The vasculitis-derived manifestations were defined as skin ulcer, rapidly progressive interstitial lung disease, diffuse alveolar haemorrhage, serositis, pulmonary hypertension, neuropathy, mediastinal emphysema, intestinal emphysema. Other vascular lesions identified by CT scan or MRI such as vascular stenosis, aneurysms and bleeding were also included. **Results**: Among 80 patients, 28 were clinically amyopathic DM and 30 patients had vasculitis-derived manifestations. Five-year survival rate was significantly lower in patients with vasculitis-derived manifestations than in those without (75.9% vs 91.3%, p=0.017). Vasculitis DM patients had higher prevalence of anti-melanoma differentiation-associated gene 5 (MDA5) antibody (60% vs 12%, p<0.001), higher CRP levels (median: 1.13 vs 0.23, p<0.001) and higher aldolase/creatine kinase (CK) ratio (median: 0.051 vs 0.016; p<0.001) compared with non-vasculitis patients. In multiple logistic regression analysis, positive anti-MDA5 antibody test (odds ratio = 37.9, 95% CI: 5.88-245.35, p<0.001), high CRP (odds ratio = 2.29, 95% CI: 1.24-4.22, p=0.008) and high aldolase/CK ratio (odds ratio = 1.14, 95% CI: 1.01, -1.30, p=0.031) were identified as independent risk factors for having vasculitis-derived manifestations. **Conclusion**: Anti-MDA5 antibody, high CRP and high aldolase/CK ratio might be useful for prediction of vasculitis in DM, ultimately leading to poor prognosis.

ICW6-2

RNA-Seq of immune cell subsets in PBMC identified the importance of specific monocyte gene signatures for idiopathic inflammatory myopathy pathogenesis

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Conflict of interest: None

Objective: Although type I interferon (IFN) signature is shown to be highly expressed in muscle, skin and blood from active idiopathic inflammatory myopathy (IIM) patients, the etiology of IIM is still unknown partly because of its heterogeneity. In this study, we investigated specific gene signatures which have potential for bringing deep insights into IIM pathogenesis. Methods: 37 IIM patients and 37 age- and sex-matched healthy controls (HCs) were recruited. We performed RNA-seq of 21 immune cell subsets in peripheral blood. Among 37 IIM patients, 14 were before treatment (active IIM) and 10/7/4 had anti-ARS/MDA5/Mi-2 Ab. Prednisolone dosage was 5.3 mg/day on average. Results: Type I IFN signature score was especially high in active IIM with anti-MDA5 Ab all through the subsets. By using weighted gene co-expression network analysis (WGCNA) and random forest, a machine learning method, we identified two gene sets (modules) from CD16-positive monocyte which were suggested to be important for discrimination IIM from HC. None of the IFN-related modules were ranked high. One of the modules, called X, was strongly correlated with type I IFN signature score, while the other module Y expression was not. Interestingly, module scores of X and Y showed higher correlation, indicating any common molecular mechanism other than type I IFN signal underlying these gene sets expression. Pathway analysis revealed that LXR/RXR activation pathway was enriched in module X, which was consistent with the result of our differentially expressed genes (DEGs) analysis; LXR/RXR activation pathway was also enriched in CD16-positive monocytes DEGs between HC and IIM. LXR/RXR activation in CD16-positive monocytes might reflect an aberrant activation through pattern recognition receptors. Conclusions: Monocytes, especially CD16-positive monocyte, could play a key role in IIM pathogenesis. In addition, we would like to discuss the clinical characteristics of IIM patients with monocyte signature high.

ICW6-3

Immunosuppressive treatment promptly improves abnormalities in nailfold capillaries in patients with dermatomyositis

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Conflict of interest: None

[Objective] To clarify whether morphological abnormalities in nailfold capillary (NFC) in patients with dermatomyositis (DM) could be quickly improved by immunosuppressive treatment along with disease activity. [Methods] Among 24 patients with DM classified according to Bohan & Peter's criteria and performed Nailfold video-capillaroscopy (NVC), 14 patients including 6 who had already received immunosuppressive intervention prior to the first visit, 6 without any abnormalities at the initial evaluation, 2 who were unable to visit our clinic regularly, and 1 without any immunosuppressive intervention, were excluded. Therefore, 10 patients were chronologically evaluated for changes in NFC abnormalities with clinical features including myositis specific autoantibodies (MSA), interstitial lung diseases (ILDs) and malignancies. The NVC tests were re-examined within at least 3 weeks and repeated up to every months in case of patients who had abnormalities in NVC testing prior to treatment. [Results] The mean age was 60.1. Females were 6 (60**%**). Positive test for MSAs were; anti-ARS in 4, anti-MDA-5 in 1, anti-TIF-1γ in 3, and anti-Mi-2 in 2. ILDs were identified in 5 patients and malignancies were detected in one. All patients received steroid therapy, with concomitant use of immunosuppressants in 7 patients. All patients except one with anti-TIF-1γ with only skin lesions were clinically improved. In the former 9 patients NFC abnormalities almost normalized within 1 to 3 months, whereas the latter one showed no improvement. In addition, anti-TIF-1γ DM patients with lung cancer showed improved NVC findings with initial treatment, but relapsed with relapse of lung cancer. Second line anticancer drug treatment improved the lung cancer and NVC findings again. [Conclusions] NFC abnormalities in patients with DM improved promptly along with disease activity.

ICW6-4

Targeting necroptosis in muscle cells ameliorates inflammatory myopathies

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Conflict of interest: None

[Objective] Muscle cell death in polymyositis (PM) is assumingly induced by $CD8^+$ cytotoxic T lymphocytes (CTLs). We presumed that injured muscle cells release inflammatory mediators, which would accelerate further CTL-mediated muscle injury. The aims of this study are to clarify the mechanisms of CTL-mediated muscle cell death of PM and the effects of inhibition of muscle cell death on *in vitro* and *in vivo* models of PM. [Methods] Muscle tissue of PM patients were examined with terminal deoxynucleotidyl transferase nick-end labeling assay, and immunolohistological staining for the necroptosis associated proteins. 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 to clarify the mechanisms of CTL-mediated muscle death *in vitro.* C protein induced-myositis (CIM) was used as an *in vivo* model of PM. The levels of high mobility group box-1 protein (HMGB1), IL-1, and IL-6 of CIM were measured by ELISA. [Results] Muscle cells of PM patients were non-apoptotic and expressed Fas and necroptosis associated proteins such as receptor-interacting serine-threonine kinase (RIPK3). OT-I CTLs lacking perforin 1 or granzyme B were as cytotoxic to the myotubes as wild type OT-I CTLs. Inhibition of Fas ligand with Fas-Fc chimeric protein reduced cytotoxicity against the myotubes. The CTL-mediated cell death of myotubes was inhibited by necrostatin-1s (nec1s), a necroptosis inhibitor, or *Ripk3* silencing with siRNA, but not by an apoptosis inhibitor. The treatment with nec1s on CIM reduced the areas of dying muscle cells and the inflammatory infiltrates in the muscles, and improved the grip strength. The levels of HMGB1 in the serum and IL-1 and IL-6 in the muscle were lower in nec1s-treated mice compared to those in untreated mice. [Conclusions] Necroptosis is involved in muscle cell death in PM. Necroptosis can be a novel therapeutic target in PM.

ICW6-5

Differences of coinhibitory molecule expression on lung T cells from patients with rheumatoid arthritis- and idiopathic inflammatory myopathies-associated interstitial lung disease

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Conflict of interest: None

Objective: To identify immunologic factors in the lungs of patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD) and idiopathic inflammatory myopathies-associated interstitial lung disease (IIM-ILD), and to examine their pathological mechanisms. Methods: A total of 11 patients with RA-ILD, 16 with IIM-ILD, and 6 with drug-induced interstitial lung disease and 8 healthy controls were enrolled. The peripheral blood and bronchoalveolar lavage fluid (BALF) were immunophenotyped by flow cytometry. Alveolar macrophages (AMs) and naïve CD4+ T cells from the peripheral blood of healthy individuals were cocultured. Results: Several coinhibitory molecules were coexpressed on BALF T cells in the order of CTLA-4, PD-1, Tim-3, and LAG-3 from most to least, whereas only PD-1 was expressed on peripheral T cells among them. The coexpression of CTLA-4 and PD-1 on both CD4+ and CD8+ T cells is a characteristic of BALF T cells of RA-ILD patients. In contrast, CTLA-4+PD-1+CD4+ T cells and CTLA-4+PD-1+Tim-3+CD8+ T cells are a characteristic of BALF T cells of IIM-ILD patients. PD-1+CD4+ T cells in the BALF rarely expressed CXCR5, and the proportion of them were correlated with the proportion of plasmablasts and plasma cells, indicating most of them are considered to be Tph cells. In the coculture experiments, AMs from RA-ILD and IIM-ILD patients induced more PD-1 and Tim-3 on naïve CD4+ T cells, indicating that the expression of coinhibitory molecules on BALF T cells may be partly due to AMs. Conclusions: We reveal the differences in coinhibitory molecule expression between RA-ILD and IIM-ILD patients. PD-1 on T cells in the RA-ILD patients and Tim-3 on CD8+ T cells in the IIM-ILD patients might be key factors in the disease process. Moreover, the evaluation of the coinhibitory molecules expressed on BALF T cells could be useful for differential diagnosis.

ICW7-2

Soluble Triggering Receptor Expressed on Myeloid Cells 2 is related with Prognosis of Diffuse Psychiatric/neuropsychiatric Syndromes in Systemic Lupus Erythematous

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Conflict of interest: None

[Objective] Soluble form of triggering receptor expressed on myeloid cells 2 (sTREM2) can promote survival and activation of microglia, which level in serum is predicting Alzheimer's disease development. The aim of this study is to clarify the association of serum sTREM2 and neuropsychiatric syndromes in SLE (NPSLE). [Methods] sTREM2 was measured in sera from 38 patients with NPSLE and those from 40 SLE patients without NPSLE (non-NPSLE) by ELISA. Association of NPSLE based on 1999 ACR nomenclature and the serum sTREM2 were analyzed. Clinical data were reviewed based on their medical charts. [Results] The serum level of sTREM2 was significantly higher in NPSLE (median: 253.9 pg/ml) compared to non-NPSLE (39.8 pg/ml) ($p=0.04$). There was no significant difference between patients with focal/neurologic (fNPSLE; 489.4 pg/ml, n=11) and those with diffuse psychiatric/neuropsychiatric syndromes in NPSLE (dNPSLE; 217.5 pg/ml, n=27). Highest median sTREM (489.4 pg/ml) was observed in 4 patients with fNPSLE developing demyelinating syndrome. Among the dNPSLE, significant decrease of sTREM2 was observed in those with improvement of psychiatric manifestations who had certain serum followed-up after treatment (n=14, $p=0.02$) and on the other hand initial increase (>1000 pg/ml) or an increase following treatment of sTREM2 was observed in 4 of 5 fatal patients. Of note, dNPSLE patients with a flared psychiatric manifestation due to steroid psychosis had sustained high sTREM2 level throughout the clinical course (n=2). [Conclusions] Serum sTREM2 predicts prognosis of patients with dNPSLE, which might be one of the pathogenesis through neural remodeling by microglial activation. Also, sTREM could be reflecting microglial activation occurring demyelination in the fNPSLE.

ICW7-3

Identification and functional analysis of SLE rare variants using patients-derived iPS cells

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Conflict of interest: None

[Objective] Familial systemic lupus erythematosus (SLE) is sometimes associated with rare variants. Rare variants with strong genetic contribution, such as BANK1 and IFIH1, were reported, and they are associate with Type I interferon (IFN) pathway. We aimed to identify and functionally investigate familial SLE-associated rare variants using patients-derived iPS cells and genome editing. [Methods] iPS cells were established from healthy donors (HD) and SLE sisters. Whole exome analysis was performed in SLE sisters and identified candidate rare variants. For screening, Type I IFN secretion was examined from 293T cells with forced expression of wild type (WT) and variant genes. Genome editing was performed to established iPS cells with knocked in of IFIH1 gain-of-function variant and WT gene X. Type I IFN-producing DC (iPS-DC) was differentiated from iPS cells and Type I IFN secretion was measured by secreted alkaline phosphatase (SEAP) assay and enzyme-linked immuno sorbent assay (ELISA). [Results] SLE-iPS-DCs showed significantly increased production of Type I IFN with dsRNA stimulation compared to HD-iPS-DCs. Knock in IFIH1 gain-of-function variant induced higher IFN secre-

tion in SLE-iPS-DCs than HD-iPS-DCs. Whole exome analysis revealed 316 non synonymous exonic rare variants. Among them, 8 variants on interferon signature gene (ISG) were thought to be candidates. By screening of 293T cells, a functional rare variant on gene X was identified. Indeed, SLE-iPS-DCs lost their IFN secreting potential by editing rare variant to WT sequence on gene X. [Conclusions] We identified new rare variant on gene X. Integration of genomic analysis and iPS cell assays provided strong evidences of the function of rare variants, which could have a causality of SLE, and will be therapeutic targets for SLE.

ICW7-4

SH3BP2 deficiency ameliorates clinical manifestations of Fas-lpr lupus mice

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Conflict of interest: Yes

[Objective] An adaptor protein, Src homology 3 domain-binding protein 2 (SH3BP2), is widely expressed in immune cells and controls intracellular signaling pathways such as Syk and Src. We have previously reported that, SH3BP2 deficiency suppresses antibody production against type II collagen and markedly prevents the development of arthritis in a collagen-induced arthritis model (Mukai T, et al. Arthritis Rheumatol 2015). To further investigate the role of SH3BP2 in autoimmune diseases, we explored the effect of SH3BP2 deficiency in a murine systemic lupus erythematosus model. [Methods] Fas-lpr mice (C57BL/6 background), with impaired Fas signaling were used to generate the lupus model. Clinical and immunological phenotypes were compared between Fas-lpr and SH3BP2-deficient Fas-lpr mice. Splenomegaly and renal involvement were assessed in 35-week-old animals. Serum levels of anti-dsDNA antibody and rheumatoid factor were determined by ELISA. Lymphocyte subsets in spleen and lymph nodes were analyzed by flow cytometry. We also analyzed B cell-specific SH3BP2-deficient lupus mice. [Results] The Fas-lpr mice exhibited splenomegaly, renal involvement, elevated serum dsDNA antibody and rheumatoid factor, and increased splenic B220+CD4-CD8- T cells. SH3BP2-deficiency significantly reduced the lupus-like phenotypes. In addition, SH3BP2 deficiency decreased the proportion of activated (CD25+CD69+) CD4+ T-cell subset in the spleen of test mice compared to that of Fas-lpr mice. Notably, we found that SH3BP2-deficiency in B cells did not rescue the lupus-like phenotypes, suggesting the pathological role of SH3BP2 expression in other cells (e.g., T and antigen-presenting cells) in the lupus mice. [Conclusion] SH3BP2 deficiency ameliorated the clinical manifestations in the lupus mouse by suppressing the production of autoantibodies and decreasing the accumulation of B220+CD4-CD8- T cells in the spleen. Therefore, SH3BP2 could potentially serve as a therapeutic target for lupus.

ICW7-5

IL-2 restores the balance of circulating Tfh and Tfr cells in systemic lupus erythematosus

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Conflict of interest: None

[Objective] T follicular helper (Tfh) cells are critical for the B cell help and autoimmunity, whereas T follicular regulatory (Tfr) cells suppress Tfh-mediated antibody responses. In this study, we aimed to identify the molecular mechanisms underlying the plasticity between Tfh cells and Tfr cells in the pathogenesis of systemic lupus erythematosus (SLE). [Methods] Peripheral blood mononuclear cells from SLE patients (n=21) and healthy donors (HD; n=15) were analyzed by flow cytometry. Naive $CD4^+$ T cells and memory $CD4^+$ T cells were cultured with TCR and various cytokines in vitro. Expression of characteristic markers of T helper subsets were analyzed by flow cytometry and qPCR. [Results] The proportion of $CXCR5^+FoxP3^+$ Tfr cells in $CD4^+$ T cells was increased (2.5% vs 1.1%, $p<0.01$); however, that of $CD4^+CD45RA^-FoxP3^{hi}$ activated Tfr cells in Tfr cells was decreased (5.1% vs 8.9%, $p<0.01$) while $CD4^+CD45RA^-FoxP3^{low}$ non-suppressive Tfr cells was increased (47.6% vs 38.8%, $p=0.03$) in SLE compared to HD. The percentage of PD-1^{hi} activated Tfh cells was significantly higher in SLE compared to HD (12.1% vs 6.1%, $p<0.01$). Furthermore, active patients had higher ratio of activated Tfh/Tfr cells compared to inactive patients. In vitro study showed that, IL-2, but not other cytokines such as TGF-β1, IL-12, IL-27 and IL-35, induces the conversion of memory Tfh cells to functional Tfr cells characterized by $CXCR5^+Bcl\text{-}6^+Foxp3^{hi}pSTAT3^+pSTAT5^+$cells. The relative level of IL-2 mRNA in $CD4^+$ T cells was significantly lower in SLE compared to HD (0.7 vs 1.2, $p=0.04$). Finally, stimulation with IL-2 increased activated Tfr cells in $CD4^+$T cells isolated from SLE patients. [Conclusions] Our findings indicated that the regulatory function of Tfr cells is impaired due to low ability of IL-2 production by $CD4^+$ T cells and that IL-2 restores the function of Tfr cells in SLE. Thus, the reinstatement of the balance between Tfh and Tfr cells will provide important therapeutic approaches for SLE.

ICW7-6

Comprehensive transcriptome approach of immune cells reveals pathways for systemic lupus erythematosus patient stratification with insights into the mechanisms underlying its pathogenesis

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Conflict of interest: Yes

[Objective] Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with complex phenotype and its etiology remains unclear. We performed a comprehensive transcriptome analysis to identify the immune cell subset-specific gene expression patterns characteristic of some clinical manifestations. [Methods] 88 SLE patients and 53 age- and sex-matched healthy controls (HCs) were included in the study. 23 immune cell subsets from peripheral blood were sorted by flow cytometry and RNA-Seq was performed. Differentially expressed genes (DEGs) were identified by edge R and weighted gene co-expression network analysis (WGCNA) detected modules of correlated genes. [Results] From pathway analysis of WGCNA modules, type I interferon (IFN) signatures showed a strong correlation with disease activity (SLEDAI-2K), active lupus nephritis (LN), rash and autoantibodies profiles all through the subsets. Random forest, a machine learning method, suggested that some modules without IFN signature gene enrichment in plasmablasts and classical monocytes could also characterize lupus disease activity. Network analysis using the correlation coefficients between each module revealed the importance of neutrophils and unswitched memory B cells for LN development. Our analyses have revealed the significance of oxidative phosphorylation in B cells for SLE pathogenesis. We picked up an anti-oxidant enzyme *PRDX6* as a key driver for lupus pathogenesis by integration of *cis*-expression quantitative trait locus (eQTL) analysis of SLE GWAS SNPs and DEGs analysis especially in B cell subsets. The results of antigen immunization or imiquimod-induced lupus model of *Prdx6*-KO mice supported our hypothesis that *PRDX6* could play a protective role in SLE. [Conclusions] Our analysis revealed some immune cell-specific gene sets with potential for patient stratification as well as a key gene for lupus pathogenesis. Further studies are needed to clarify the molecular mechanisms in SLE.

ICW8-1

Risk factors for developing systemic lupus erythematosus in patients with primary antiphospholipid syndrome

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) is the most frequent

underlying disease in patients with antiphospholipid syndrome (APS). However, few studies have analyzed the characteristics of primary APS (PAPS) patients associated with the development of SLE. The objective of this study is to investigate the risk factors for developing SLE in PAPS. [Methods] Patients with PAPS that attended to Hokkaido University Hospital between April 1990 and October 2019 were included. Those patients with less than 2 years follow-up were excluded. Medical records were retrospectively reviewed. The risk factors for developing SLE were assessed by Cox proportional hazards model. [Results] A total 79 PAPS patients were recruited (69 females, median age at APS onset was 44.95 years [range 31 - 60 years], followed-up for a median of 9.2 years [range 4 - 14 years]). The main manifestations were venous and arterial thrombosis in 22 (27.8%) and 49 (62 %) patients respectively, obstetric complications in 26 out of 69 females (37.1%), hypocomplementemia in 32 out of 69 (47.8%), thrombocytopenia in 13 (18.8%), anti-DNA antibody (aDNA) in 13 (18.8%), proteinuria in 6 (8.7%), neuropathy in 14 (20.3%), direct Coomb`s test in 8 out of 26 (30.8%). The prevalence of aPL is as follows. Lupus anticoagulant (LA) was detected in 64 patients (81.0%), anticardiolipin antibodies (aCL) IgG/IgM in 44 and 12 (55.7%, 15.2%), anti-β2-glycoprotein-I antibodies (aβ2GPI) IgG/IgM in 31 and 15 (41.9%, 20.3%) and phosphatidylserine-dependent antiprothrombin antibodies (aPS/PT) IgG/IgM in 35 and 19 (44.3%, 24.1%). During the observation, 9 out of 79 PAPS patients were newly diagnosed with SLE (11.4%, incidence rate 1.23 per 100 patient-years). In multivariate analysis, IgG aPS/PT (p=0.0436) and aDNA (p=0.0031) were found as risk factors for developing SLE in PAPS. [Conclusion] IgG aPS/PT and aDNA might be risk factors of new-onset of SLE in PAPS.

ICW8-2

Examination about the prevention effect of hydroxychloroquine toward severe infectious disease in patients with systemic lupus erythematosus: date from the LUNA registry

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Conflict of interest: None

[Objective] Infections are leading causes of mortality despite the improvement of clinical course in systemic lupus erythematosus (SLE). Morbidity of severe infections is reported by up to 40% in the previous report of SLE. Although previous reports suggested hydroxychloroquine (HCQ) has the infection protective effect, it has not been examined with Japanese patients. We performed a retrospective cohort study to reveal them in the LUNA registry. [Methods] The cross-sectional study was included 604 patients registered in the multicenter SLE registry "LUNA" . The endpoint of this study was the development of the severe infection requiring hospitalization during 1year after observation. The patients were divided into two groups: HCQ and non-HCQ groups. Morbidity of severe infections, patients' background and medications were compared between the groups. [Results] One hundred fifty-six patients had received HCQ (18% of the cohort). Forty-three patients suffered at least one severe infection during one year after observation in the registry. There was no significant difference in the development of the severe infection during one year after observation compared between HCQ group and non-HCQ group (4.6 % vs 5.3 %, $p = 0.84$). However, the HCQ group had the tendency to become more susceptible to infections at the observational points than non-HCQ group such as the past episode of infection (1.6 ± 1.6 times vs 0.9 ± 1.1 times, $p < 0.01$), the usage of any immunosuppressants (70.5 % vs 60.6 %, $p = 0.02$), and the dose of prednisolone (7.0 mg/day vs 5.7 mg/day, $p = 0.01$). [Conclusions] Although there was no significant difference in the severe infection compared between the HCQ and non-HCQ groups, this study shows that HCQ has the possibility of the suppressive effect of severe infections in SLE patients using immunosuppressants or/and having past infections. Further examination using propensity score matching for adjustment of patient background would be required.

ICW8-3

Withdrawal of glucocorticoids maintaining patients in clinical remission with HCQ and immunosuppressants is an achievable goal in recently diagnosed SLE patients

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Conflict of interest: None

[Objective] Long-term maintenance therapy with glucocorticoids (GC) could be a cause of severe side effects such osteoporosis, atherosclerosis, and especially adrenal insufficiency. In the present study, we aimed to validate whether it is possible to completely withdraw GC in SLE patients in a few years of the initiation of it. [Methods] Patients diagnosed with SLE according to the 1997 revised ACR classification criteria between Apr. 2016 and Mar. 2019 in our hospital and treated with GC were included. We retrospectively reviewed the electric medical records and collected data about the treatment and activity of the patients. Whether the patients were in clinical remission was also analyzed according to the definitions of remission in SLE (DORIS) clinical remission on therapy (ClinROnT). [Results] Eighteen patients were included. Median age was 30 (IQR 21-47) and 15/18 (83%) cases were females. The starting dose of PSL was 50 (33-60) mg, and baseline SLEDAI was 12 (8-21). Involved organs were as follows: Kidney 4, nervous system 1, PAH 2, enteritis 1, AIHA 2, and others. HCQ was used in all patients and immunosuppressants (IS) were used in 14/18 cases (IVCY 3, MMF 2, TAC 8, and MTX 1). The patients were followed up for 508 (374-961) days. The dose of PSL was successfully tapered to 2mg in 14/18 cases and stopped in 7/18 cases maintaining the patients in ClinROnT 387 (310-445) and 813 (509-951) days after the initiation of GC, respectively. There were no significant differences in baseline GC dose or SLEDAI between patients who achieved GC withdrawal and those who did not. Three relapses (2 arthritis and 1 serositis) occurred and were managed with the addition of IS to GC and HCQ without escalation of GC dose. [Conclusions] Early tapering of the dose of PSL to 2mg in about one year and GC withdrawal in a few years of the initiation of GC are both achievable goal in SLE patients concomitantly treated with HCQ.

ICW8-4

The Additional Effects of Belimumab on Patients with Systemic Lupus Erythematosus Remaining Low Disease Activity under Hydroxychloroquine Treatment

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Conflict of interest: None

[Objective] The aim of this study is to investigate the effects of belimumab (BEL) on patients with systemic lupus erythematosus (SLE) who remained low disease activity despite of using hydroxychloroquine (HCQ). [Methods] We collected SLE patients who had treated In Kitasato University Hospital until September 30, 2019. SLE patients who had been treated by BEL additive to HCQ for more than three months (BEL group) was retrospectively compared with those who had been treated with HCQ alone, arbitrarily picked-up to have characteristics similar to patients in BEL group (controls). [Results] Of 526 SLE patients in our hospital, 31 patients (5.9%) had received BEL. 6 of 31 patients who had received BEL

was treated by HCQ as well. Patients of BEL group were all female with the mean age of 40.7 years old and their mean disease duration was 189.5 months. Controls (n=5) were also all female with the mean age of 41.8 years old observed for 68.4 months. SLEDAI decreased from 5 (median) to 4 (p =0.250) in BEL group, but it was not improved in controls (4 to 4, p=0.999) three months after BEL initiation. Items of SLEDAI scored by skin lesion, arthritis and immunological data contributed to improvement of SLEDAI in BEL group. Daily PSL dose decreased in BEL group (10 to 9 mg/day, p=0.125), and also did in controls (13 to 10mg/day, p=0.250) in three months. Whereas, anti-DNA antibody decreased from 7.9 to 5.8 U/ml (p=0.250) in BEL group, but not in controls (31.5 to 26.5 U/ml, p=0.625). The complement 3 level was improved (59.5 to 67 mg/dl, p=0.188) in BEL group, but it was rather decreased in controls (63 to 61 mg/dl, p=0.750). [Conclusions] BEL could be reducing PSL dose and serological activity, sustaining low disease activity even in SLE patients with inadequate response to HCQ. However further investigation is still required to reveal it adequately.

ICW8-5

Relationship between LLDAS attainment and anti-SS-A antibody: The prospective observational study from the LUNA registry

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Conflict of interest: None

[Background/Purpose] Recently, treat-to-target has recently been proposed as a management strategy for systemic lupus erythematosus (SLE), and the lupus low disease activity state (LLDAS) has been validated as a treat-to-target endpoint. Because patients in LLDAS have few organ damages and better health-related quality of life, LLDAS is considered as a good endpoint to be achieved. We have previously performed a cross-sectional analysis using a multicenter SLE registry and reported that patients who did not achieve LLDAS showed a significantly higher frequency of anti-SS-A antibody (Ab) seropositivity as compared to LLDAS-achieved patients. Here we investigated the relationship between LLDAS attainment and anti-SS-A Ab by the longitudinal analysis to gain stronger evidence. [Methods] The patients who were registered in the multicenter SLE registry "LUNA" and assessed both annual LLDAS and anti-SS-A Ab were included in the study. They were divided into two groups based on the anti-SS-A Ab seropositivity, and the baseline parameters including LLDAS and LLDAS at one year were compared between anti-SS-A positive and negative groups. [Results] A total of 23 patients (anti-SS-A positive group; 14, anti-SS-A negative group; 9) were enrolled. There were no significant differences in female ratio and age between the anti-SS-A Ab positive and negative groups (100% (14/14) vs 100% (9/9), $p = 1.00$, and 51.4 ± 12.8 vs 46.3 ± 14.0 years, $p = 0.34$, respectively). Although the anti-SS-A Ab positive group tended to show a lower LLDAS-maintaining rate during the one-year observation period than the negative group, there was no significant difference between the two groups (35.7% (5/14) vs 55.6% (5/9), $p = 0.35$). [Conclusion] We could not find the significant relationship between maintaining LLDAS and anti-SS-A Ab seropositivity. Future studies with a larger population and more extended observation periods should be needed.

ICW8-6

Impact of belimumab on immunophenotypic features in patients with Systemic Lupus Erythematosus ~ LOOPS registry ~

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Conflict of interest: None

[Objective] Belimumab (BLM), a human monoclonal antibody neutralizing BAFF, could suppress B cell proliferation and plasma cell differentiation; however, immunophenotypic features and pathological immune cell subsets targeted by BLM in systemic lupus erythematosus (SLE) are unclear. We investigated the clinical efficacy and immunophenotypic changes by the treatment with BLM in patients with SLE. [Methods] 20 of inactive SLE patients treated with BLM in order to reduce glucocorticoid (GC) dose were enrolled. Primary outcome was dose of GC (PSL equivalents) at 12 months (12M) after treatment with BLM. Peripheral immunophenotypes were evaluated by multicolor flow cytometry. [Results] At baseline, mean age was 42.7 y.o., SLEDAI was 3.6, and dose of PSL was 5.2 mg. After 12 M, SLE activity (SLEDAI 1.9) and dose of GC (PSL 2.4 mg) were significantly reduced and 45 % of SLE patients have achieved GC free. At baseline, 6M and 12M, both proportion (%) and actual peripheral number (/μL) of naïve B cell (57.2 (22.1)→24.2 (5.5)→22.5 (2.8)) was notably decreased. However, actual peripheral number of class switched memory B cell was increased at 6M and then turned to be decreased at 12M (20.6 (3.9)→43.7 (8.0)→50.7 (5.0)). Moreover, actual peripheral number of Plasmablast was also decreased (2.5→0.7→0.4 /μL). In $CD3^+CD4^+$ T helper (Th) cells, the proportion of both $CXCR3^+CCR6^-CD38^+HLA\text{-}DR^+$ activated Th1 cell (2.74→1.78%) and that of $CXCR3^-CCR6^+CD38^+HLA\text{-}DR^+$ activated Th17 cell (1.02→0.47%) was significantly decreased at 12M, whereas these changes were not observed at 6M. [Conclusion] BLM could further reduce dose of GC without flare. It is reported that BAFF-receptor is expressed not only B cells but Th cells and BAFF promotes the proliferation of activated Th cell in mice *in vitro*. Our results suggest that BLM seems to inhibit the differentiation of B cells, as well as the activation of pathological Th cells, thus targeting the interaction between B cells and T cells in the pathogenesis of SLE.

ICW9-2

The role of semaphorins in the regulation of granulocytic inflammation

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Conflict of interest: None

[Objective] Although semaphorins are originally identified as neuronal guidance factors, it is becoming clear that they play key roles in immune regulation and inflammatory diseases (Nishide and Kumanogoh, ***Nat Rev Rheumatol.*** 2018). We previously found an inhibitory function of semaphorin 4D (SEMA4D) in neutrophil activation (Nishide et al. ***Ann Rheum Dis.*** 2017). Based on these findings, we further investigated how Semaphorin-mediated signaling is involved in the regulation of granulocytic inflammation. [Methods] We focused two diseases, ANCA-associated vasculitis (AAV) and Eosinophilic chronic rhinosinusitis (ECRS). Serum soluble SEMA4D levels in patients were measured by ELISA. The expression of SEMA4D in granulocytes was assessed by flow cytometry. In *in vivo* study, a passive transfer model of acute AAV or *Aspergillus* protease-induced allergic chronic rhinosinusitis was used. The efficacy of treatment with anti-SEMA4D antibody was evaluated by histologically and nasal lavage fluid analysis. [Results] Serum soluble SEMA4D levels

were elevated in patients with AAV and ECRS and positively correlated with disease severity. Cell surface expression of SEMA4D on granulocytes from patients was reduced, which was due to metalloproteinase-mediated cleavage of membrane SEMA4D. Soluble SEMA4D enabled eosinophil trans-endothelial migration, and treatment with anti-SEMA4D antibody ameliorated eosinophilic infiltration in sinus tissues in the ECRS animal model. [Conclusions] According with granulocytes inflammation, cell surface SEMA4D on granulocytes are cleaved and elevated levels of serum SEMA4D reflect disease severity of AAV and ECRS. Moreover, anti-SEMA4D antibody has therapeutic potential as a treatment for ECRS (Manuscript in revision).

ICW9-5

Resolvin D5 modulates Th17/Treg cell differentiation and suppresses osteoclastogenesis

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Conflict of interest: None

[Objective] Resolvins, parts of specialized proresolving mediators (SPMs) derived from n-3 PUFA, contribute actively to the resolution of inflammation. However, little have been known about how resolvins are involved in chronic inflammation, such as rheumatoid arthritis (RA). Our aim is to investigate whether lipid mediators (LM) are involved in the pathogenesis of RA. [Methods] We investigated lipid mediator profiling in the paws of SKG arthritis mice by using LC/MS/MS-based LM metabololipidomics. $CD4^+$ T cells from spleens of SKG mice were cultured on anti-CD3/ CD28Abs precoated plate with IL-6/TGF-β, anti-IFNγ/IL-4 and analyzed by flow cytometry. $CD4^+$ T cells were labeled with CFSE, and cell proliferation was analyzed by flow cytometry. Mouse bone marrow cells were cultured with M-CSF and RANKL, and TRAP-positive multinucleated cells were defined as osteoclasts. Osteoclast differentiation markers were analyzed by qRT-PCR. RvD5 or normal saline was administered daily into the peritoneal cavity of arthritic SKG mice. [Results] We found that RvE3, RvD1, RvD3, RvD5 and Maresin2 were significantly elevated on the paws of arthritic SKG mice. Among the elevated SPMs, only RvD5 levels on arthritic paws were significantly correlated with arthritis disease activity. We demonstrated that RvD5 suppressed Th17 cell differentiation, and facilitated Treg cell differentiation *in vitro*. In addition, RvD5 inhibited $CD4^+$ T cell proliferation. Furthermore, RvD5 attenuated osteoclast differentiation and interfered osteoclastogenesis at the molecular level. In the *in vivo* experiment, incidence of arthritis tended to be lower in RvD5-treated mice than that in control group, although there was no significant difference. [Conclusions] We demonstrated that RvD5 was increased in the paws of arthritic mice, and that RvD5 suppressed Th17 cell differentiation and $CD4^+$ T cell proliferation, facilitated Treg cell differentiation, and suppressed osteoclastogenesis.

ICW9-6

Inhibition of calcium/calmodulin-dependent protein kinase IV in rheumatoid arthritis: Dual effect on Th17 cell activation and osteoclastogenesis

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Conflict of interest: None

[Objective] We investigated the role of calcium/calmodulin-dependent protein kinase IV (CaMK4) in the expression of joint injury in rheumatoid arthritis (RA). [Methods] We induced collagen-induced arthritis (CIA) in *Camk4*-sufficient or -deficient mice and compared the clinical score, histology, Th17-related chemokine expression and numbers of IL-17-producing cells in the spleen. We also evaluated the efficacy of the CaMK4 antagonist KN-93 in mice subjected to CIA by micro-computed tomography (μ-CT) and histology. The effect of CaMK4 inhibition on inflammatory cytokines and humoral immune response was also examined. *CAMK4* gene expression was measured in $CD4^+$ T cells from healthy controls and patients with active RA. $CD4^+$ cells were isolated from RA patients to determine the effect of KN-93 on T cell differentiation. We also isolated $CD14^+$ cells from RA patients to investigate osteoclast differentiation. [Results] Camk4-deficient mice displayed less joint injury after the induction of CIA. Treatment of CIA mice with KN-93 reduced significantly the arthritis clinical score and joint destruction as evaluated by μ-CT and histology. Further analysis revealed that CaMK4 inhibition in CIA mice suppressed the production of inflammatory cytokines including IL-6, IL-17, G-CSF, and MCP-1. The expression of CAMK4 was significantly higher in $CD4^+$ T cells from patients with RA compared with cells from healthy controls. CaMK4 inhibition mitigated IL-17 production by $CD4^+$ cells from patients with RA. The number of in vitro differentiated osteoclasts from CD14+ cells from RA patients was significantly decreased in the presence of the CaMK4 inhibitor. [Conclusions] Our results demonstrate that CaMK4, besides its role in promoting an inflammatory response, is important in osteoclast differentiation which is directly responsible for joint destruction. We propose that CaMK4 inhibition represents a new approach to control the development of arthritis.

ICW10-1

The risk factors of recurrence in relapsing polychondritis; a study of 46 cases

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Conflict of interest: None

[Objectives] Relapsing polychondritis (RP) is a rare disease characterized by recurrent multiple cartilaginous inflammation and systemic manifestation. Despite its high recurrent rate, there has been few data about the risk of recurrence. We aimed to evaluate the risk factors of recurrence. [Methods] We analyzed patients who were diagnosed as RP by Damiani's or Michet's criteria and treated in Kyoto University Hospital from 2001 to 2019. [Results] Forty-six patients (Male: Female 19:27, age 49.2 ± 18.2 yrs, disease duration 7.8 ± 7.3 yrs.) were included. The patients presented with auricular (78%), articular (57%), airway (50%), eye (37%), nasal (33%), and vestibulocochlear (26%) lesions. Twenty-nine patients (63%, M: F 13:16) experienced 66 relapses (average 2.3 times, max 8 times). Intervals from initial treatment to relapse was 532 ± 825 days. Prednisolone (PSL) dose at the 1st. relapse was 11.3 ± 8.9 mg/day. Univariate analysis revealed airway lesion (p=0.032), auricular lesion (p=0.046, negatively associated), CRP levels (p=0.027), ESR levels (p=0.031), and IgG levels (p=0.047) as risk factors of recurrence. The relapsed patients were treated with methotrexate (69%), tocilizumab (35%), calcineurin inhibitors (28%), cyclophosphamide (28%), azathioprine (24%) and infliximab (24%). Initial relapse-free period was longer in PSL plus early immunosuppressants (IS) group (366 ± 282 days) than in PSL-alone group (109 ± 95 days) (p=0.011). [Conclusions] It is suggested that airway involvement, high CRP, ESR and IgG levels can be risk factors of recurrence, whereas patients with auricular involvement are at low risk. Early use of IS might extend the relapse-free period.

ICW10-2

Tocilizumab discontinuation in patients with Adult Still's Disease who are in remission treated with tocilizumab: 6 months outcome

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Conflict of interest: None

[Background] The clinical course of adult Still's disease (ASD) are relapsing. Tocilizumab, an interleukin (IL)-6 inhibitor, is effective in patients with ASD, however, whether tocilizumab can be discontinued after remission achievement is unclear. [Objective] To investigate clinical courses in patients with ASD who discontinued tocilizumab after remission achievement and find clues to optimal tocilizumab use in patients with ASD. [Methods] Patients with ASD who were in remission with tocilizumab were included in the analysis for their clinical courses. [Results] We identified 11 patients with ASD who were in remission with tocilizumab. The mean age was 50.1 years old, and female was 81.8%. Tocilizumab was administered for 155.7 weeks, and the mean interval of administration was 4.2 weeks. Six of the patients discontinued tocilizumab or prolonged its interval to more than 8 weeks whereas the other five continued tocilizumab with the same intervals or one week extension. No significant difference was found between the patients who continued tocilizumab and the others in tocilizumab duration (149.0 vs 161.3 weeks), dose of prednisolone (PSL) (1.3 vs 2.0 mg/day), the interval of tocilizumab (3.8 vs 4.5 weeks) and serum ferritin levels (53.0 vs 60.8 ng/ml). One patient who discontinued tocilizumab relapsed 19.0 weeks after discontinuation. The other five patients were still in remission, however, the levels of CRP tended to increase (from 0.01 to 0.34 mg/dL). [Conclusions] Tocilizumab discontinuation in patients with ASD may be related to recurrence.

ICW10-3

Searching for a new perspective on the classification of Eosinophilia with Systemic Involvement

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Conflict of interest: None

[Objective] Systemic eosinophilic disorders are clinically heterogenous, and differential diagnosis among them is often difficult without disease-specific antibodies and pathological findings. We searched a novel viewpoint on classification of eosinophilia with systemic involvement. [Methods] In this single center study, we enrolled 58 consecutive patients with eosinophilia (>500 /mm^3) and signs of organ involvement having required hospitalization from February 2001 to September 2019. Hierarchical clustering analysis with Ward's method was performed based on 20 clinical parameters including age, sex, eosinophil counts, organ involvement, comorbidity, and laboratory findings. Further, a set of key covariates were compared between the phenotype clusters and statistically analyzed by Fisher test or χ square test. [Results] Two groups with distinct manifestations were identified based on the hierarchical clustering: group A (n=30) and group B (n=28). Comparing clinical features, peripheral neuropathy ($p<0.0001$), purpura ($p=0.0016$) and lung involvement ($p=0.0029$) were more frequent in group A. In addition, group A had a significantly higher rate of RF positivity ($p<0.0001$), MPO-ANCA positivity, IgE elevation, and extravascular eosinophils in biopsy specimen ($p= 0.0107$, 0.0088, 0.0195, respectively). The proportion of patients fulfilling ACR criteria for the classification of EGPA was higher in group A (56.7% vs 3.6%). [Conclusions] This study suggests two phenotypes in eosinophilia with systemic involvement. Each group was distinctively characterized by organ involvements and immunological findings. Considering the presence of pathological findings and the fill-rate of ACR criteria, one group may virtually be close to EGPA. These findings could contribute to perceive the unclear boundary of systemic eosinophilic diseases.

ICW10-4

Mediterranean Fever (MEFV) gene exon 2 or exon 3 polymorphisms in Japan have additional effects on manifestations of familial Mediterranean fever having heterogenous MEFV exon 10 mutations

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Conflict of interest: None

[Objective] The genetic characteristics of patients with FMF in Japan include a higher percentage of *MEFV* exon 2 or exon 3 polymorphisms with low penetrance compared with patients with FMF in Western countries. However, in Japan, a relatively high proportion of healthy individuals have *MEFV* exon 2 or exon 3 polymorphisms. Therefore, the pathogenesis and modification of *MEFV* exon 2 or exon 3 polymorphisms to FMF have been unclear. Using data from a nationwide multicenter prospective study in Japan, we sought to compare the clinical and laboratory characteristics between the presence and absence of *MEFV* exon 2 or exon 3 polymorphisms among patients with FMF having a heterogenous *MEFV* exon 10 mutation and aimed to reveal the pathogenesis and modification of such polymorphisms to FMF. [Methods] In order to observe the pure pathogenesis and modification of *MEFV* exon 2 or exon 3 polymorphisms, we excluded patients with FMF having two *MEFV* exon 10 mutations in one or more alleles and/or having *MEFV* mutations in exons other than in exon 2, 3, or 10. Finally, we reviewed 131 Japanese patients with FMF having a heterogenous *MEFV* exon 10 mutation, and they were divided into *MEFV* exon 2 or exon 3 polymorphism non-coexisting and coexisting group of 34 and 97, respectively. [Results] In the univariate analysis, our data showed that the polymorphism coexisting group significantly had an earlier onset, a higher frequency of attack, a higher percentage of thoracic pain at febrile attacks, and a higher IL-18 level at remission compared with the polymorphism non-coexisting group (all, $p < 0.05$). Importantly, multivariate analyses showed that coexistence of *MEFV* exon 2 or exon 3 polymorphisms was significantly and independently associated with earlier onset of FMF and thoracic pain (both, $p < 0.05$). [Conclusions] Our results suggested that sharing *MEFV* exon 2 or exon 3 polymorphisms have additional effects on manifestations of FMF having *MEFV* exon 10 mutations.

ICW11-1

Long-term persistence of IgM antiphospholipid antibodies and thrombotic risk

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Conflict of interest: None

[Objective] Antiphospholipid antibodies (aPL) are risk factors for thrombosis in antiphospholipid syndrome (APS). The relevance of testing IgM aPL is still discussed. In most studies, IgM aPL are examined only at a certain point, however, IgM aPL titres fluctuate and frequently turn negative. We conducted a retrospective follow-up of patients with IgM aPL and evaluated whether IgM aPL long-term persistence associated with thrombosis. [Methods] Samples remitted to our laboratory for aPL screening during a 15-year period were investigated. aPL testing comprised of IgG /IgM anticardiolipin antibodies (aCL), antib2Glycoprotein I antibodies (ab2GPI), and phosphatidylserine-dependent antiprothrombin antibodies (aPS/PT) analyzed by enzyme linked immunosorbent assays, and lupus anticoagulant by clotting assays. Persistent IgM aPL was defined as either aCL, ab2GPI or aPS/PT IgM positive in $\geqq$ 2 occasions >12 weeks apart. Transient IgM aPL was defined as aCL, ab2GPI or aPS/PT IgM positive only once. Clinical records were retrospectively reviewed. [Results] 1146 samples in 143 patients were analyzed. Fifty-three patients with thrombotic APS at the beginning of the observation were extracted and analyzed; 40 had persistent and 13 transient IgM aPL. There were no thrombotic events in APS patients with transient IgM aPL whereas 11 (28%) patients with persistent aPL had thrombosis recurrence. Thrombotic APS patients (n=40) were divided into 2 groups: long-term persistent IgM aPL group (either IgM aPL positive $\geqq$ 3 occasions >6 months apart over 2 years) and short-term IgM aPL persistent group (either IgM aPL positive $\leqq$ 2 occasions over 2 years). Patients with long-term persistent IgM aPL showed lower rates of thrombosis-free survival (log-rank test, $p=0.0841$). [Conclu-

sions] Persistent IgM aPL could represent a risk factor for thrombosis. Determination of IgM aPL contributes to an accurate assessment of the thrombotic risk.

ICW11-2

Efficacy of rituximab and treatment outcome in Japanese patients with ANCA-associated vasculitis: a single center study

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Conflict of interest: None

[Objective] Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) usually occurs in relatively late phase of life. Recently, efficacy of rituximab (RTX) has been reported in large randomized studies, however, the efficacy of RTX in Japanese AAV patients in daily clinical practice is not well known. The aim of this study is to clarify the clinical efficacy and outcome of Japanese AAV patients who received RTX treatment. [Methods] Fifty-two AAV patients who newly diagnosed and treated in our hospital from April 2004 to March 2019 were included in this study. Clinical records and laboratory data were retrospectively reviewed. Clinical efficacy and outcome (one-year survival) were compared between RTX treatment group (15 cases) and conventional therapy group (immunosuppressive therapy other than RTX, 37 cases). Outcome of immunosuppressive therapy including RTX in the elderly-onset AAV (75 years or older) were also evaluated. [Results] After 6 months of RTX treatment or therapy with other immunosuppressive agents, Birmingham vasculitis activity scores were successfully decreased in both groups. Prednisolone doses were significantly lower in RTX group than conventional therapy group (16 mg vs 11mg, respectively, P<0.01). RTX treatment group showed similar one-year survival compared to conventional therapy group (100% vs 84.6%, respectively, P=0.13). Whereas elderly-onset AAV patients showed significantly better one-year survival in patients with immunosuppressive treatment including RTX than those who received glucocorticoids only (100% vs 40%, P<0.05). Infection-free survival is similar between the RTX and conventional therapy group (84% vs 76.3%, P=0.59). [Conclusions] RTX treatment seems to be effective in Japanese AAV patients, even if elderly-onset AAV. Infection risk was similar between RTX group and conventional therapy group.

ICW11-3

Therapeutic Efficacy of Mycophenolate Mofetil as Remission Induction Therapy in ANCA-Associated Vasculitis: A Meta-Analysis

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Conflict of interest: None

[Objective] In the treatment of antineutrophil cytoplasmic associated vasculitis (AAV), there are a few researches that report the therapeutic efficacy of mycophenolate mofetil (MMF). However, the efficacy of MMF in patients with AAV compared with cyclophosphamide (CYC) has not been established so far. The objective of this study is to investigate the efficacy of MMF as remission induction therapy in patients with AAV. [Methods] We searched randomized control trials (RCTs) compared the efficacy of MMF with that of CYC in patients with AAV by using three websites; PubMed, Cochrane Library and Google Scholar. We compared the difference in the odds ratio (OR) of each outcome by Mantel-Haenszel random-effects model. [Results] A total of four RCTs with 300 patients were included in the study. Remission rate at 6 months, ANCA negativity at 6 months and relapse rate at several years were not different between the two groups (OR 1.49, 95% CI 0.59-3.78, P=0.40; OR 1.56, 95% CI 0.86-2.82, P=0.14; OR 1.69, 95% CI 0.85-3.36, P=0.14, respectively). Rate of death, infection, and leukopenia were not different between the two groups (OR 1.05, 95% CI 0.38-2.93, P=0.93; OR 1.36, 95% CI 0.76-2.46, P=0.30; OR 0.42, 95% CI 0.13-1.35, P=0.14, respectively). [Conclusions] There was no difference between the therapeutic efficacy of MMF and that of CYC in patients with AAV. MMF might be an alternative drug as remission induction therapy in patients with AAV.

ICW11-4

Effects of tocilizumab on immunophenotypic features in patients with large vessel vasculitis: 6-month results of FLOW study

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Conflict of interest: None

[Objective] The pathogenesis of large vessel vasculitis (LVV) consists of the excessive immune responses including not only innate immunity but also acquired immunity mediated by cytokines such as IL-6. However, immunophenotypic features and pathological immune cell subsets targeted by immunosuppressants and/or molecular target therapy in LVV patients are unknown. Here, we analyzed the immunophenotype and responsiveness to the treatment such as tocilizumab (TCZ) in patients with LVV. [Methods] The patients with new onset LVV (GCA n=19, TKA n=13) and age- and sex-matched healthy controls (HC: n=48) were enrolled. Based on the standard human immune cell subset classification protocol by NIH/FOCIS, peripheral immune cell phenotypes at baseline and at 24 wks after induction therapy by high dose glucocorticoid with TCZ (n=9) or without TCZ (n=5) were analyzed. [Results] The immunophenotype of LVV patients with high disease activity showed a higher proportion of activated Th17 cells (p<0.01) and a lower proportion of activated Treg cells (p=0.05) than HC. LVV patients had a higher proportion of double negative (DN; IgD^-CD27^-) B cells than HC (p<0.01). After 24-week treatment, disease activity improved in all LVV patients, and reduction rate of glucocorticoid dose was higher in the TCZ group than in the non-TCZ group (p=0.03). The percentage of activated Th17 cells was significantly reduced in the TCZ group (1.3±0.7% at baseline to 0.6±0.4% at 24 wks, p<0.01) and that of DN B cells showed similar tendency (9.3±5.2% at baseline to 6.8±4.8% at 24 wks, p=0.19), whereas that of activated Treg cells was tended to be increased (0.9±0.6% at baseline to 1.3±0.4% at 24 wks, p=0.10). However, no changes were observed in the non-TCZ group. [Coclusions] Immunophenotypic features in LVV patients were characterized by increase of activated Th17 cells and DN B cells and decrease of activated Treg cells. TCZ may correct the impaired balance of Th17 and Treg and B cell differentiation in patients with LVV.

ICW11-5

Pathogenic potential of novel autoantibodies in Takayasu arteritis

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Conflict of interest: Yes

[Objective] Takayasu arteritis (TAK) is one of large-vessel vasculitis. Anti-endothelial cell antibodies (AECA) have been detected in TAK, but target antigens of AECA as membrane protein remain unclear. By a serological identification system for autoantigens using a retroviral vector and flow cytometry, we identified two novel autoantigens: endothelial protein C receptor (EPCR) and scavenger receptor class B type 1 (SR-BI). The aim of this study was to clarify the pathogenic roles of autoantibodies in TAK. [Methods] Activity of autoantibodies against EPCR or SR-BI, which was overexpressed on a rat myeloma cell line, was measured by flow cytometry. Association between autoantibodies activity and clinical course was analyzed. The influence of autoantibodies on activation of endothelial cells (ECs), and functional significance of anti-EPCR IgG in human T cells under Th17 differentiation condition were evaluated by qRT-PCR and flow cytometry. [Results] Anti-EPCR or anti-SR-BI IgG was found in 67.3% of TAK patients. Autoantibodies activity was correlated with disease activity. Activated protein C (APC), a ligand for EPCR, and HDL, a ligand for SR-BI, suppressed TNF-induced upregulation of adhesion mol-

ecules on ECs, indicating APC and HDL were negative regulators for activation of ECs. This effect was blocked by anti-EPCR or anti-SR-BI IgG in dose dependent manner. Recombinant EPCR or SR-BI proteins reversed the blocking effect of autoantibodies. In mechanism study, anti-SR-BI IgG inhibited HDL uptake and nitric oxide synthase activity. Additionally, expression of EPCR was induced on Th17 cells. APC suppressed IL-17A production and downregulated RORgT and Th17-related cytokines expression; however these effects were blocked by anti-EPCR IgG. [Conclusions] Autoantibodies against EPCR or SR-BI disturbed negative regulation of their targets, resulting in chronic vascular inflammation in TAK. These findings provide new insight into pathogenesis of TAK.

ICW11-6

Metabolic Profiling in CD4+ T cells Identifies Succinate Dehydrogenase as a Novel Therapeutic Target in Giant Cell Arteritis

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Conflict of interest: None

Background: Giant cell arteritis (GCA) is categorized as vasculitides and causes granulomatous inflammation in medium and large arteries. CD4+ T cells play a key role in vascular remodeling such as intimal hyperplasia and adventitial neoangiogenesis. We have previously shown that CD28 blockade effectively suppressed metabolic activity of CD4+ T cells and inhibited vascular remodeling. However, metabolic profile in CD4+ T cells from patients with GCA has not been studied yet, and it remains unclear whether these metabolic profiles contribute to vascular inflammation. **Methods:** Blood samples were obtained from patients with GCA. Demographically matched healthy individuals were recruited from the Stanford Blood Bank Research Program. naïve CD4+ T cells were activated with CD3/CD28 for six days. Intermediate metabolites including pyruvate, lactate, and succinate as well as mitochondrial enzymes involved in tricarboxylic acid (TCA) cycle were analyzed. A humanized vasculitis model was generated by grafting human medium-sized arteries into immunocompromised NSG mice followed by adoptive transfer of peripheral blood mononuclear cells from patients with GCA. Using this mouse model, in vivo function of intermediate metabolites was tested. **Results:** Production of pyruvate and lactate was significantly increased in GCA CD4+ T cells ($P<0.05$, $P<0.0001$, respectively). In TCA cycle, mitochondrial enzymes leading to succinate production were all upregulated in GCA CD4+ T cells, whereas succinate dehydrogenase (SDH), which catalyzes the oxidation of succinate to fumarate, was downregulated ($P<0.01$), resulting in accumulation of intracellular and extracellular succinate ($P<0.01$, $P<0.01$, respectively). Succinate supplementation worsened vascular inflammation and remodeling in vivo. **Conclusions:** These data indicate that GCA CD4+ T cells have altered metabolic profile and SDH could be a potential therapeutic target in GCA.

ICW12-1

Can the Combination of MRI and Ultrasound at Baseline Identify Definite Inflammatory Arthritis Patterns in Undifferentiated Arthritis?

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Conflict of interest: None

[Objective] When diagnosing inflammatory arthritis (IA) early, a single imaging method may not accurately reflect the overall inflammatory status. Combining MRI and US may identify patterns associated with definite IA. The aim was to describe the combination of MRI and US findings in early IA for identifying the patients with persistent arthritis. [Methods] Patients were recruited with early inflammatory joint symptoms and/or signs of IA. Baseline clinical data included symptom duration, CRP, CCP and tender/swollen joint counts (TJC/SJC). 3D VIBE Dixon images from 3T MRI with contrast were acquired. MRI images were consensus scored as positive if synovitis or erosion was detected at the wrist, MCP, PIP, knee, ankle, MTP and SI joints. US was performed except SI joints by an experienced sonographer or rheumatologist. US findings were scored as positive if synovial thickening (grade≧2), power doppler signal (grade≧1) or bone erosion was detected. Subjects were clinically classified without MRI and US at baseline and 1 year. [Results] 42 patients were recruited. At baseline, 13 were classified as RA with median symptom duration 14 months, TJC 2, SJC 3, CRP 1.0mg/dl. 25 were classified as undifferentiated arthritis (UA), including 12 persistent UA (pUA), 12 resolved UA (rUA) and PsA at 1 year. All of the UA patients were CCP negative. The remaining 4 patients were 2 AS, 1 SpA and 1 ReA. At baseline, the pUA group had a median symptom duration of 26 months, TJC 0, SJC 2, CRP 1.1mg/dl. The rUA group had a median symptom duration of 17 months, TJC 1, SJC 1, CRP 1.0mg/dl. The MRI and US findings matched in 46% of pUA, 0% of rUA, and 100% of the RA. MRI of the SI joints was positive in 38% of pUA, 0% of rUA, 0% of CCP positive RA and 80% of CCP negative RA. [Conclusions] A combined MRI and US assessment in early IA at baseline is able to predict persistent IA at 1 year. Combining MRI and US findings and MRI for SI joints appears to be most discriminatory.

ICW12-2

Automatic finger joint detection and bone erosion scoring in x-rays by deep learning

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Conflict of interest: None

[Background/Object] Previously we have developed an annotation tool for evaluation of joint destruction[1] and have developed deep learning-based models to automatically detect hand joint region[2]. Using the annotation tool, we aimed to develop learning-based models to automatically evaluate hand joint erosion score of van der Heijde-modified total Sharp scores in radiographic images. [Methods] A total of 130 radiographic image sets of both hands were randomly obtained from rheumatoid arthritis patients who had visited our division at Keio University Hospital in 2015. Well-trained rheumatologists determined the erosion scores of each hand joint in radiographs according to the van der Heijde-modified total Sharp score. These evaluations of hand joints were performed using our developed annotation software tool. In learning phase, joint images were randomly divided into five sets for 5-fold cross validation. As deep learning models, we utilized convolutional neural network for classification of the scores. The models were designed in consideration of the difference in erosion scores of each patient between the 2 time points of x-rays. [Results] Our models showed 94.6% detection rate of erosion score 5 (complete collapse) in each MP and PIP/IP joint region. As a performance of predicting the difference in erosion score between the 2 time point of each patient's x-ray, our models presented mean difference of 0.412. [Conclusions] Deep learning-based models to predict hand joint erosion scores in radiographic images were developed with relatively small samples, which suggests that the predictive performance may increase by collecting more training dataset. [Reference] (1) Izumi K, Hashimoto M, Suzuki K, et al. *Arthritis Rheumatol* 2018;70 (suppl 10). (2) Izumi K, Suzuki K, Hashimoto M, et al. *Ann Rheum Dis* 2019;78:1364. *Izumi and Suzuki contributed equally.

ICW12-3

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

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Conflict of interest: Yes

[Objective] In patients with rheumatoid arthritis (RA), systemic bone loss has been observed from the onset, and high rates of the vertebral and non-vertebral fracture have been reported. Denosumab, an anti-RANKL monoclonal antibody, was approved in Japan for the osteoporosis and the inhibition of bone erosions in RA. While the increase in bone mineral density by denosumab has been reported in patients with RA, few reports are available about the bone fracture reduction. In this study, we investigated the effect of denosumab on clinical fracture reduction in patients with RA. [Methods] Using ANSWER (Kansai consortium for well-being of rheumatic disease patients) cohort data, patients with RA who used denosumab between 2013 and 2019 were included. Since this is a multicenter cohort study and there is no control group, the half year after first administration was set as the control period. [Results] Denosumab was used in 873 patients. Baseline data are as follows; male/ female: 12/88%, mean age at the start of treatment: 68%, disease duration: 14.5 years, ACPA positivity: 75%, RF positivity: 72.7%, usage of bDMARDs or tsDMARDs: 32%. Clinical fractures occurred in 3 cases within 6 months, and 6 cases after 6 months. The clinical fracture rates per 100 person-years were 0.69 and 0.35. Clinical vertebral fracture (CVF), non-vertebral fracture (NVF) and clinical fracture (all fracture) rates decreased 51, 51, and 51%, respectively, for > 6 months versus 0 to 6 months. When limited to patients aged 60 and older, the CVF, NVF and clinical fracture rates decreased 45, 53, and 40%, respectively. The percentage of glucocorticoid users was 58.6% (mean prednisolone-equivalent dose: 5.2 mg/day). When limited to glucocorticoid users, the reduction rates were 50, 50 50%, respectively. [Conclusions] Reductions in the rates of CVF, NVF and clinical fracture were observed after 6 months of administration of denosumab in the patients with RA.

ICW12-4

Mid-term patient-reported outcomes after joint-preserving surgery for rheumatoid forefoot deformities

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Conflict of interest: None

[Objective] Foot and ankle joint disorders are major issues for patients with rheumatoid arthritis (RA). Many recent studies have reported good clinical and radiographic outcomes of joint-preserving surgery for rheumatoid forefoot deformities. However, only a few studies have investigated the mid-term and long-term outcomes. This study aimed to evaluate the mid-term patient-reported outcomes after joint-preserving surgery for rheumatoid forefoot deformities. [Methods] From January 2012 to September 2014, 94 feet of 79 RA patients with rheumatoid forefoot deformities were treated with joint-preserving surgery. The mean follow-up duration was 6.0 ± 0.8 years, and all feet were followed up for a minimum of 5 years. A self-administered foot-evaluation questionnaire (SAFE-Q), as a patient-reported outcome, was evaluated preoperatively and at the latest follow-up. The hallux valgus angle (HVA) and the intermetatarsal angle (IMA) were measured on preoperative and the latest postoperative radiographs. The differences in the measured variables were analyzed with paired t-test. [Results] The mean age of the patients at surgery was 59.7 ± 9.3 years, and the mean duration of RA affliction was 18.8 ± 9.0 years. The mean DAS28 at surgery was 3.4 ± 1.2. All the five subscales of SAFE-Q ("Pain and Pain-Related," "Physical Functioning and Daily Living," "Social Functioning," "Shoe-Related," and "General Health and Well-Being") had improved significantly at the last follow-up. The mean HVA and IMA decreased significantly from 45.0 ± 11.5 preoperatively to 16.8 ± 13.9 postoperatively and from 16.0 ± 3.8 preoperatively to 8.1 ± 4.5 postoperatively (P<0.01, respectively). [Conclusions] To our knowledge, this is the first study to evaluate patient-reported outcomes before and after joint-preserving surgery in patients with rheumatoid forefoot deformities. The mid-term patient-reported outcomes and radiographic outcomes after forefoot joint-preserving surgery in patients with RA were satisfactory.

ICW12-5

Shoulder joint Gadolinium-Enhanced Magnetic Resonance Imaging Contributes Diagnosis and Predicting Prognosis with Polymyalgia Rheumatica Patients

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Conflict of interest: None

Objective: Polymyalgia rheumatica (PMR) is diagnosed based on the clinical symptoms. However, its diagnosis is sometimes difficult because PMR symptoms can be found in many other rheumatologic diseases. Recently, magnetic resonance imaging (MRI) has been reported as useful tool for diagnosis of rheumatic diseases, but the effectiveness to PMR diagnosis has not been established. Thus, we evaluated the effectiveness of gadolinium (Gd) -enhanced MRI findings in PMR patients. We also analyzed associations between characteristics of MRI findings and clinical prognosis. **Methods**: This study included patients who visited our hospital with complaint of bilateral shoulder pain and fulfilled the Bird classification criteria for PMR during June 2012 to June 2018. All patients underwent both US and gadolinium-enhanced MRI in shoulders. Twenty mg/day of prednisolone was administered as initial treatment to all PMR patients and its dose was tapered after remission. They were observed until June 2019 on recurrences. **Results**: US and Gd-enhanced MRI were conducted to 137 of 175 patients and 58 patients were diagnosed as PMR. Enhancement of joint capsule, rotator cuff, biceps tendon and glenohumeral joint, synovial hypertrophy, joint effusion, focal or diffuse bone edema in caput humeri were found. Enhancement of joint capsule or rotator cuff tendon and focal edema in caput humeri were significantly frequent in PMR patients. Using these findings on MRI in combination to diagnose PMR, the sensitivity and specificity were higher (76% and 85%) than using only US findings (50% and 72%). During observation, 24 patients (44%) recurred PMR. Characteristics of these patients were young, less enhancement of rotator cuff tendon and more synovial hypertrophy findings on MRI. **Conclusion**: We found relatively specific MRI findings for PMR and the association between several MRI findings and prognosis. Our study suggested that Gd-enhanced MRI could contribute to diagnosis and predicting recurrence of PMR.

ICW12-6

Development of intravital imaging system for the synovial tissue and pannus

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Conflict of interest: None

[Objective] There have been many attempts to visualize the inflamed ankle joints using multiphoton microscopy. However, due to the hypervascular and multilayered structure of the inflamed synovium, intravital imaging of the deep synovial tissue has been difficult. [Methods] We established original protocols to visualize living synovial tissue and pathological osteoclasts at the pannus-bone interface using multiphoton microscopy. Biological agents were labeled with AF647, which is optimized for in vivo imaging by controlling the ratio of dye to protein, and the temporal distribution was tracked in vivo. Biological agents were injected into TRAP-td-Tomato transgenic and CX3CR1-EGFP knock-in mice in the DBA/1J

background after the onset of collagen-induced arthritis. Biological agents-binding cells were analyzed in vivo by multiphoton microscopy and flow cytometry. [Results] Fluorescence-labeled biological agents were successfully visualized in vivo and bound to two kinds of immune cells in the inflamed synovium. Bone-resorbing osteoclasts formed at the pannus-bone interface was directly visualized in situ with pH-sensing chemical probe, although biological agents did not bind to these cells. [Conclusions] We developed intravital imaging protocols to visualize the synovial tissue and osteoclasts at the pannus-bone interface under arthritic conditions, which revealed the intravital target population of the specific biological agents. This intravital synovial imaging system can serve as a platform for exploring the dynamics of immune cells, osteoclasts, and biological agents within the synovial microenvironment.

ICW13-2

HLA serotypes in Japanese spondyloarthritis population

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Conflict of interest: None

[Objective] HLA-B27 is known as the major genetic risk factor for spondyloarthritis (SpA). However, it is still unclear whether HLA-B27 is also useful for SpA in Japanese population, because the frequency of HLA-B27 in general population in Japan is quite different from those in the Western countries (0.3% vs. 10-40%). This study aimed to investigate HLA serotypes of SpA in Japanese. [Methods] Consecutive patients diagnosed with axial or peripheral SpA based on modified NY criteria or ASAS criteria at Keio University Hospital between January 2016 and September 2019 were included in this study. We investigated the HLA-A, -B, -DR serotypes in these patients and compared with the frequency of the serotypes in Japanese general population. Statistical analysis was performed by Fisher's exact test with Bonferroni correction. [Results] We included 30 SpA (16 axial SpA, 14 peripheral SpA; 9 with psoriasis, 7 with inflammatory bowel disease) patients in this study. Reference of 18604 samples previously published (Tissue Antigens. 2015;85:252) was used as the control of HLA serotypes in Japanese general population. The frequency of HLA-B27 was higher in the SpA patients compared to the general populations (3.3% vs. 0.3%), although not significant. Alternatively, HLA-B46 was significantly higher in the SpA patients (30.0% vs 9.3%, $p<0.05$, relative risk: 4.2). Since an association with HLA-B46 and psoriasis in Japanese has been previously reported, we further compared 21 SpA patients without psoriasis and general population, and found the similar tendency in these groups as well (23.8% vs 9.3%, $p<0.05$, relative risk: 3.0). [Conclusions] HLA-B46 can be a unique HLA serotype of SpA in Japanese population.

ICW13-3

The risk assessment of developing deep vein thrombosis in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The aim of this study was to clarify the clinical features and risk factors of deep vein thrombosis (DVT) in patients with rheumatoid arthritis (RA). [Method] We retrospectively reviewed the incidence of DVT in RA patients who visited Hokkaido University Hospital with more than 2 years follow-up from 2010 to 2017. DVT was confirmed by the venous ultrasound and/or contrast-enhanced CT regardless of symptoms. To evaluate the risk factors for the development of DVT, we randomly selected 144 patients without DVT (non-DVT) and identified the risk factors by multivariate logistic regression analysis. [Result] This study comprised 813 cases and follow up duration was 5 years (IQR 3-7). The incidence of DVT was 0.34 % (28 of 813 cases) and the median age at the time of diagnosis of DVT was 74 years (IQR 65.5-79). Based on univariate analysis, the presence of smoking history, hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, cancer, and treatment with JAK inhibitor or NSAIDs were comparable between DVT and non-DVT cases. Body mass index (BMI), the presence of interstitial lung diseases and glucocorticoid usage were identified as risk factors of DVT ($p=0.001$). Furthermore, the rates of moderate and high disease activity in RA (DAS-28CRP > 2.7) were higher in DVT cases ($p=0.01$). In multivariate logistic regression analysis, only moderate and high RA disease activity was significantly associated with the development of DVT ($p= 0.02$, OR 5.88, 95%CI 1.32-26.17). [Conclusion] High disease activity in RA was found as a risk factor of DVT, suggesting that clinical remission would be beneficial for preventing DVT as well as bone destruction.

ICW13-4

Utility of right atrium area size to predict prognosis of pulmonary artery hypertension with connective tissue diseases

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Conflict of interest: None

[Objective] Recently studies demonstrated the utility of right atrium area size (RAas) to predict prognosis in pulmonary artery hypertension (PAH). This study aimed to clarify the utility of RAas for PAH with connective tissue diseases (CTD-PAH). [Methods] CTD-PAH (N=134) diagnosed by right heart catheterization treated in our institute from 2001 until 2019 were included. Ultrasound-cardiography reports (N=579) were analyzed. We utilized individual fluctuation due to repeat measurement as a factor of fluctuation and survival as a fixed factor and compared RAas and left atria area size (LAas) in survive group and non-survive group by the mix model. [Results] The CTD-PAH (N=134) were Age 50.8±13.7 (mean±SD) years old and estimated systolic PAP 60.3±21.2mmHg at first ultrasound-cardiography. 45 patients were diagnosed systemic sclerosis. Among CTD-PAH treated by PAH specific Drugs (N=126), 78 patients received treatment by PD5 inhibitor and 63 patients received treatment by Endothelin receptor antagonist. RAas in survive group was significantly smaller compared to non-survive group (18.1 cm^2 vs. 26.5 cm^2). The analysis of only SSc-PAH showed the same tendency (18.3 cm^2 vs 27.4 cm^2). There was no difference in LAas between two groups (19.4 cm^2 vs 18.8 cm^2). [Conclusions] Our results demonstrated that RAas might relate with survival in patients of CTD-PAH. We indicate that the evaluation of RAas is useful for treatment of CTD-PAH.

ICW13-5

The assessment of left heart disease phenotype in patients with systemic sclerosis associated pulmonary arterial hypertension

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Conflict of interest: None

[Objective] Systemic sclerosis associated pulmonary arterial hypertension (SSc-PAH) patients frequently develop left heart disease (LHD) due to fibrotic myocardial damages. Since LHD also causes pulmonary hypertension (Group 2 PH), the pathogenesis of SSc-PAH is complicated. Although group 2 PH is defined by pulmonary arterial wedge pressure (PAWP)>15mmHg, the 6th World Symposium on PH (WSPH) proposed an algorithm to assess the probability of LHD phenotype in PAH patients with PAWP13>mmHg. We herein aimed to assess the probability of LHD phenotype in SSc-PAH patients. [Methods] This study included 76 SSc patients, underwent right heart catheterization. According to the proposal by the 6th WSPH, patients were classified into high, intermediate and low probability of LHD phenotype groups using following variables: age, metabolic and cardiovascular complications, electrocardiogram, echocardiography, and cardiac magnetic resonance imaging (MRI). PAWP and enhanced MRI-detected myocardial abnormalities (delayed enhancement) were compared among those groups. [Results] The median [range] values of mean pulmonary arterial pressure (mPAP) and PAWP were 24 [9-65] and 8 [2-26] mmHg, respectively. 56, 20, and 0 patients were classified

into high, intermediate and low probability groups, respectively. PAWP was not significantly different between high and intermediate probability groups (p=0.21). Conversely, myocardial delayed enhancement was frequently observed in high probability group (p=0.006). In patients with mPAP >20 mmHg (n=43), multivariate logistic regression analysis revealed a significant correlation between myocardial delayed enhancement and the necessity of two or more diuretics (p=0.02). [Conclusions] Our results suggest that most of SSc and SSc-PAH patients, even those with normal PAWP, have LHD phenotype. Delayed enhanced cardiac MRI may reflect LHD phenotype in SSc-PAH patients since it correlates with a non-invasive probability of LHD and the necessity of diuretics.

ICW13-6

Establishment and transcriptome analysis of systemic sclerosis associated pulmonary arterial hypertension-specific endothelial cells

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Conflict of interest: Yes

[Objective] Patient with systemic sclerosis associated pulmonary arterial hypertension (SSc-PAH) has poorer prognosis compared to other PAH patients despite the recent progress in pulmonary vasodilator therapies. We aimed to clarify the pathogenesis of SSc-PAH using disease-specific induced pluripotent stem cells (iPSc). [Methods] The iPSc were established from pheripheral blood mononuclear cells of a 76-year-old female with SSc-PAH and pulmonary veno-occlusive disease, and a 29-year-old female healthy donor by transfecting Oct3/4, Sox2, Klf4 and L-Myc using Sendai virus vectors. The quality of iPSc was validated by the expression of alkaline phosphatase, that of undifferentiated markers, and the triploblastic differentiation potential. Endothelial cells (EC) were differentiated from iPSc in the culture system containing BMP-4, Activin, bFGF, CHIR99021, Y-27632, VEGF and SB431542. The proliferative and vasculogenic capacity of EC was evaluated by BrdU assays and tube formation, respectively. RNA-sequencing was performed to analyze the difference in the transcriptome between SSc-PAH and healthy EC. [Results] SSc-PAH and healthy EC were morphologically similar. The proliferation of SSc-PAH EC was increased compared to that of healthy EC (0.49±0.05 (abs) vs 0.295±0.01 (abs), $p<0.05$, n=3). The vasculogenesis of SSc-PAH EC was impaired with 33.5% reduced tube formation compared to that of healthy EC (31.2±2.0 (mm) vs 47.0±1.3 (mm), $p<0.01$, n=3). RNA-sequencing detected some significantly enriched Gene Ontology terms in SSc-PAH EC compared to healthy EC, including blood vessel development, VEGF-activated receptor activity, regulation of cell proliferation and cell adhesion. [Conclusions] SSc-PAH-specific EC were successfully established with facilitated proliferation and impaired vasculogenesis. Enriched Gene Ontology terms were found out for the first time in SSc-PAH EC, characteristic in the pathogenesis of SSc-PAH.

ICW14-1

Prediction of myocardial fibrosis in rheumatoid arthritis, assessed in cardiac magnetic resonance imaging, by using artificial neural networks models

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Conflict of interest: None

[Objective] Cardiac involvements cause of morbidity and mortality globally in rheumatoid arthritis (RA). Global longitudinal strain (GLS) using feature tracking cardiac magnetic resonance (FT-CMR) and Late gadolinium enhancement (LGE) has been reported to be significantly associated with the extent of myocardial fibrosis. In the last years, artificial neural networks (ANNs) could be a useful prediction tool in medical scenarios. We aimed prediction of myocardial fibrosis in RA assessed by GLS and LGE, by using ANNs models. [Methods] RA patients and controls without cardiovascular disease were enrolled. A three-layered feedforward neural network model was structured to detect a myocardial abnormality from LGE and GLS. Inputs for the network were totally 22 variables including attributes (e.g. Age, Sex) and observed values (e.g. DAS28, ACPA). 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] We evaluated 88 patients with RA and 30 healthy controls. All 118 subjects underwent FT-CMR and 51 patients underwent LEG. Abnormal GLS value and LGE were seen in 67/88 subjects and 19/51 subjects, respectively. The accuracy, sensitivity, specificity, positive predictive value and negative predictive value for prediction of LGE and abnormal GLS value were 80.7%, 88.1%, 57.1%, 86.8%, 60.0%, and 74.5%, 73.7%, 70.6%, 58.3%, 82.8%, respectively. [Conclusions] We applied ANNs to identify a prediction model for myocardial fibrosis in RA assessed by CMR. The use of laboratory and clinical items, and treatment, resulted able to construct a mathematical model, potentially identifying asymptomatic RA patients with myocardial fibrosis. This prediction tool could be used potentially in a clinical practice setting to stratify RA patients according to myocardial fibrosis.

ICW14-2

Increased serum adiponectin levels are associated with the disease activity of underweight refractory rheumatoid arthritis (RA): a cross-sectional study of Japanese RA patients

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Conflict of interest: None

[Objective] To clarify the relationships among serum adiponectin, body composition, disease activity and therapeutics of rheumatoid arthritis (RA). [Methods] A total of 351 subjects from the Kyoto University RA Management Alliance cohort (KURAMA) were enrolled in our cross-sectional study. We used cut-off points of body mass index (BMI) (18.5 kg/m^2 for underweight and 25.0 kg/m^2 for obesity) and visceral fat area (VFA) (100 cm^2 for visceral adiposity), and classified the participants into five body composition groups (overweight with or without visceral adiposity, normal with or without visceral adiposity, and underweight). A one-way analysis of variance (ANOVA) and Steel-Dwass post-hoc tests were performed to compare serum adiponectin levels and DAS28-ESR among the groups. We also assessed effects of serum adiponectin on DAS28-ESR by a multiple regression analysis, accounting for covariates including BMI, serology and the use of therapeutic agents. [Results] The classification of body composition revealed that serum adiponectin levels (20.9±12.5 vs. 14.7±8.4 μg/ml, $p < 0.001$) and DAS28-ESR (3.0±1.0 vs. 2.6±0.9, $p = 0.017$) in underweight group were significantly higher than those in the others. In a multiple regression analysis, serum adiponectin levels were positively associated with DAS28-ESR ($p = 0.026$). In a subanalysis, the use of biological disease-modifying antirheumatic drugs (bDMARDs) or JAK inhibitor did not have obvious influence on circulating adiponectin levels. [Conclusions] We detected a positive correlation between serum adiponectin and DAS28-ESR in Japanese RA patients regardless of current medications. The classification of body composition also revealed that serum adiponectin was a possible marker to identify underweight refractory RA with high disease activity.

ICW14-4

Immune cell profiling of rheumatoid arthritis identified plasmablast pathways as key correlates with treatment resistance

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Conflict of interest: None

[Objective] We performed transcriptome analyses of cell subsets of peripheral blood taken from rheumatoid arthritis (RA) patients and tried to identify cell subsets and its pathways closely associated with treatment resistance. [Methods] Peripheral blood mononuclear cells were obtained from 20 healthy donors and 33 RA patients, who were just before the induction of treatments. 17 patients were starting abatacept. We isolated 16 cell subsets and performed RNA sequencing. 21 out of 33 RA patients were reanalyzed 6 months later. A network analysis WGCNA and BCR repertoire analysis were performed for each subset. Patients were classified with treatment response in accordance with EULAR response criteria, and differential expression analysis was performed for each. Ingenuity pathway analysis predicted upstream regulator of these differentially expressed genes (DEG). [Results] WGCNA and BCR repertoire analysis of the pre-treated patients revealed that the treatment resistance was correlated most to a gene network module in plasmablast (PB) subset ($r = -0.53$, $p = 0.01$), and also to PB BCR repertoire diversity ($r = 0.64$, $p = 0.005$). Differential expression analysis between before and after treatment revealed that subset with the most DEG was naïve $CD4^+$ T cells in the abatacept-resistant group ($n = 5$). In the abatacept-responsive group ($n = 9$), subset with the most DEG was PB. Pathway analysis identified Blimp1 as the candidate upstream regulator of PB DEGs in abatacept-responsive group. [Conclusions] Polyclonal activation of PB was associated with treatment resistance in RA. Suppression of PB Blimp1 activity, a master regulator of the development and function of antibody-producing B cells, was associated with abatacept response. Therefore, control of polyclonal activation of PB could be a therapeutic target for RA in the next generation.

ICW14-5

Reciprocal repression of STAT3 and SMAD3/SMAD4 in Th17 predicts therapeutic response to biologic disease-modifying antirheumatic drugs

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Conflict of interest: None

[Objective] Interleukin (IL)-6 and transforming growth factor (TGF)-β cooperatively induce differentiation of IL-17-producing $CD4^+$ T helper cells (Th17), which play crucial roles in the pathogenesis of RA. Targeting IL-6 and JAK-STAT signaling is effective in the treatment of RA, whereas roles of canonical TGF-β signaling via SMAD in RA are still controversial. We sought to investigate whether and how canonical SMAD-mediated TGF-β signaling affects STAT3-mediated signaling in arthritogenic Th17 and RA. [Methods] We investigated the interaction between STAT3 and SMAD-mediated TGF-β signaling pathways in Th17 cell polarization culture and murine collagen-induced arthritis (CIA) model. Peripheral blood mononuclear cells (PBMCs) from RA patients before and after treatment with biologic disease-modifying antirheumatic drugs such as anti-TNF-α agents, tocilizmab (TCZ) or abatacept (ABT) for six months were used for quantitative PCR. [Results] T cell-specific SMAD4 deletion and SMAD3 deficiency significantly exacerbated CIA with increased STAT3-induced Th17. C-terminally phosphorylated SMAD3 and SMAD4 repressed the transcription of STAT3, whereas phosphorylated STAT3 (Y705 and S727) repressed the transcription of SMAD3 and SMAD4, reciprocally. Patients with low SMAD3/STAT3 and SMAD4/STAT3 ratios in PBMCs were refractory to anti-TNF-α agents, whereas they were sensitive to TCZ. [Conclusions] These results suggest that canonical TGF-β signaling rather suppresses STAT3-induced arthritogenic Th17 differentiation by reciprocal repression and the ratios of SMAD3 and SMAD4 to STAT3 in PBMCs in RA patients could be predictive biomarkers of therapeutic responses.

ICW15-1

Role of amino acid cystine in cytotoxic effects of CD8+ cells and the relevance to pathological processes of rheumatoid arthritis

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Conflict of interest: None

[Objective] $CD4^+$/$CD8^+$ cells play a crucial role in rheumatoid arthritis (RA). Recently, "immunometabolism" attract much attention. mTORC1 is well known as a key player of anabolic process in immunocompetent cells. It is proposed that mTORC1 promote terminal differentiation of effector T cells by inducing the transcriptional factor T-bet. However, it remained elusive by which mTORC1 and T-bet in T cells are involved in the pathogenesis of RA. [Methods] PBMCs were obtained from 27 healthy controls (HCs) and 86 patients with RA who were refractory to MTX-treatment and bio-naïve. The expression of p-mTORC1 and T-bet in T cells were analyzed by FACS. In addition, we examined the role of mTORC1 in T cells *in vitro*. [Results] (1) The level of p-mTORC1 in $CD4^+$ cell was higher, while the level of both p-mTORC1 and T-bet in $CD8^+$ T cell were higher in RA. (2) Unlike $CD4^+$ cells, the level of p-mTORC1 in $CD8^+$ cells was correlated with disease activity scores such as DAS28-CRP and CDAI but not auto-antibodies such as RF and ACPA. (3) The expression of p-mTORC1 and T-bet in $CD8^+$ cells were decreased in TNF inhibitors treatment group ($n=23$), but not in abatacept treatment group ($n=10$) at 1 year. (4) *In vitro*, TCR stimulation induced the expression of T-bet and p-mTORC1 in $CD8^+$ T cells, producing IFN-γ, TNF-α and Granzyme B, to a lesser extent GNLY, but not Granzyme K. (5) It has been reported that mTORC1 activation is regulated by the amino acid level. IFN-γ, TNF-α and Granzyme B was abrogated by mTORC1 inhibitor, rapamycin and in the absence of cystine, and to a lesser extent methionine and glutamine, but not leucine. (6) IFN-γ and Granzyme B were abrogated by TNF inhibitors such as certolizumab and adalimumab but not abatacept. [Conclusions] Taken together, amino acid cystine plays an important role in cytotoxic effects such as IFN-γ, TNF-α and Granzyme B production through mTORC1-T-bet axis in $CD8^+$ cells. TNF inhibitors eliminate this pathway as a new mode of action.

ICW15-3

HGF/c-MET signaling inhibition abrogates joint destruction by suppressing migration of monocyte to the synovium in rheumatoid arthritis

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Conflict of interest: None

[Objective] Hepatocyte growth factor (HGF) / c-MET signaling promises therapeutic targets in the treatment of cancer. We examined the expression of HGF in rheumatoid arthritis (RA) biological fluids and the role it plays in monocyte migration. Then the therapeutic effect of c-MET inhibitor was examined in arthritis model mice. [Methods] The expression of HGF / c-MET in the serum, synovial fluid (SFs), synovial tissues (STs) of RA patients and controls (NL) and RA fibroblast-like synoviocytes (FLSs) was evaluated by ELISA and immunostaining. To determine the function for HGF in RA SFs, we preincubated RA SFs with neutralizing anti-HGF antibody and measured the ability of these synovial fluids to induce THP-1 (human acute monocyte leukemia cell line) chemotaxis. Finally, Arthritis model mice, SKG mice induced by mannan were treated

with specific c-MET inhibitor (savolitinib 2.5 mg/kg/day) intravenously. Ankle bone destruction and histopathologic features were assessed using μCT and tartarate-resistant acid phosphatase (TRAP) staining after 6 weeks of treatment with savolitinib. [Results] HGF in RA serum was significantly higher than that in NL and was decreased by drug treatment for 6 months. HGF in RA synovial fluids was also higher than that in OA synovial fluids. HGF and c-MET were expressed on RA STs. Stimulation of RA-FLS with TNF increased HGF / c-MET expression in a concentration-dependent manner, and c-MET signal inhibition suppressed the production of fractalkine, CXCL16, and MIP1a. Furthermore, the migration of THP-1 by RA SFs was suppressed when HGF was removed by immunoprecipitation. Savolitinib significantly suppressed ankle bone damage on μCT, with marked reduction in the number of TRAP-positive osteoclasts in SKG mice. [Conclusions] HGF is produced by inflammation in the RA synovium and activates monocyte migration to the synovium and promotes bone destruction through its own chemotactic effect and enhanced chemokine production in the synovium.

ICW15-5

A novel role of epigenetic dysregulation of ubash3a in the pathogenesis of rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] We identified the *ubash3a* gene, encoding a suppressor of T cell receptor (TCR) signaling, by integrated multiple meta-analysis using GWAS, dbSUPER (a database of super enhancer (SE) that forms clustered enhancers related to powerful transcription) and BioGPS (a database of gene expression profiling) as a novel susceptible gene for RA. In this study, we aimed to assess a novel molecular basis for expression and function of UBASH3A in the pathogenesis of RA. [Methods] 1) $CD4^+$ T and $CD4^-$ cells were isolated from RA patients (n=37) and healthy donors (HD; n=11), and then subjected to qPCR to compare expression level of UBASH3A. 2) Effect of alleles at rs1893592 on the expression level was further studied. 3) IHC was performed to compare the level of UBASH3A protein in lymph nodes (LNs) between RA and dermatomyositis (DM). 4) Epigenetic modification in the *ubash3a* promoter in $CD4^+$ T cells was studied by ChIP. 5) Cytometric beads array was performed to compare the level of pro-inflammatory cytokines in RA-derived $CD4^+$ T cells transfected with *ubash3a* plasmid or mock. [Results] 1) The mRNA and protein expression of UBASH3A significantly decreased in $CD4^+$ T cells of RA compared to those of HD. 2) RA patients with AC and CC at rs1893592, but not AA, showed low level of *ubash3a* in $CD4^+$ T cells. 3) Clear staining for UBASH3A was detectable in $CD4^+$ T cells of LNs from patients with DM, but not with RA. 4) Suppressed recruitment of transcriptional coactivators (MED1 and BRD4) to *ubash3a* SE in $CD4^+$ T cells of RA patients, but not those of HD, was detectable. 5) CD3/CD28-stimulated RA $CD4^+$ T cells transfected with *ubash3a* compared to mock showed lower level of phosphorylated NF-kB and suppressed expression of IL-6, but not IL-1b. [Conclusions] Allele C at rs1893592 decreased *ubash3a* in $CD4^+$ T cells. UBASH3A is down-regulated through disrupted chromatin looping via epigenetic mechanism, that leads to up-regulation of IL-6, possibly contributing to the pathogenesis of RA.

ICW16-1

Antigen specific suppression can be mediated through Antigen presenting cells in the absence of Treg cells

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Conflict of interest: None

[Background/Purpose] Foxp3+ T regulatory cells (Tregs) suppress immune responses such as autoimmune or allergic diseases. However, how they mediate their suppressive function remains unresolved. To further understand the cellular mechanism, it is needed to investigate the antigen specificity of suppressor function in more detail. [Methods] (1): Two antigen-specific naive effector (Teff) cells from TCR transgenic RAG2-/- mice (OTII Tg mice and LCMV Tg mice) were transferred to syngenic recipient mice together with dendritic cells (DCs) pulsed with two antigens and antigen-specific Tregs. Two antigen peptides were pulsed either on separate DCs or on the same DCs. Splenocytes from the recipient mice were analyzed to determine the Treg suppression on each Teff. (2): DCs pulsed with both peptides were co-cultured with antigen-specific Tregs, and Tregs were depleted out at 18 hours by cell sorting and suppressive function on two TCR Tg Teffs by the sorted DCs was analyzed. [Results] (1): In the co-transfer with distinct DCs, Tregs suppressed the cognate antigen specific Teffs, but not the non-cognate antigen specific Teffs. Treg suppressed only the cognate antigen-specific Teffs even when both antigen peptides were pulsed on the same DCs. (2): In the absence of Tregs, only the Teff specific to the cognate antigen was suppressed by the sorted DCs that had been cocultured with antigen-specific Tregs. Antigen-specificity of the suppression was also maintained by the suppressed DCs. [Conclusions] Under the suppression of Tregs, both the suppressed Teffs and the non-suppressed proliferating Teffs were able to co-exist in the same environment, indicating that DCs are capable of stimulating the non-cognate Teffs even though they suppress the cognate Teffs. These results suggest that antigen-specific Treg can mediate antigen specific suppression through a modification of antigen presenting cells (APCs), but not through global suppression of APC's stimulatory function.

ICW16-3

The relevance of mTORC1-phosphorylated CXCR3+ memory B cells to the pathogenesis of rheumatoid arthritis

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Conflict of interest: None

[Objective] B cells play a crucial role in RA. Recently "Immunometabolism" attract attention. mTORC1 is well known as a key player for anabolic change and contributes to B cell activation. However, it remained elusive by which mTORC1 in B cells involved in the pathogenesis of RA. [Methods] PBMCs were obtained from 32 healthy controls and 86 patients with RA who were refractory to MTX-treatment and bio-naïve. mTORC1 phosphorylation in B cells was analyzed by FACS. In addition, we examined the role of mTORC1 in B cells *in vitro*. [Results] (1) The level of p-mTORC1 in $CD19^+$ cells was increased in RA. In addition, the ratio of $CD27^+CD19^+$ cells were decreased in periphery in RA. We hypothesized that these cells migrated to synovium. Therefore, we next examined chemokine receptors on $CD19^+$ cells. (2) Unlike CXCR5 and CCR6, the ratio of $CXCR3^+CD27^+CD19^+$ cells among $CD19^+$ cells was decreased in RA. The level of p-mTORC1 in $CXCR3^+CD27^+CD19^+$ cells was higher than that in $CXCR3^-CD27^+CD19^+$ cells. (3) The level of p-mTORC1 in $CXCR3^+CD27^+CD19^+$ cells was correlated with disease activity scores, but not auto-antibodies. (4) The ratio of $CXCR3^+CD27^+CD19^+$ cells was recovered in TNF inhibitors (TNFi) treatment group (n=19), but not in ABT treatment group (n=15) at 1 year. (5) *In vitro*, stimulation of BCR, CD40L and IFN-γ induced differentiation to $CXCR3^+$ B cells, which was abrogated by mTORC1 inhibitor, rapamycin. (6) It has been reported that mTORC1 activation is regulated by amino acid level. The level of CXCR3 and p-mTORC1 in B cells were decreased in the absence of methionine and glutamine, but not cystine and leucine. (7) CXCL10, which is a ligand of CXCR3, was produced by RA patient-derived FLS by stimulation with TNF-α, which was abrogated by TNFi such as etanercept, adalimumab and certolizumab. [Conclusions] Taken together, activation of mTORC1 is involved in the accumulation of CXCR3-expressing B cells in RA synovium and TNF inhibitors possibly target at this in patients with RA.

ICW16-4

Deficiency of transcription factor T-bet accelerates the development of collagen-induced arthritis by promoting the differentiation of T helper type 17

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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) emulsified in CFA, and the incidence and severity of CIA were assessed. 2) Anti-CII antibodies in the sera at day 60 post the first immunization were measured. 3) At day 10 post first immunization, CD4+ T cells and CD11c+ dendritic cells isolated from the draining lymph nodes (LNs) were cultured with CII, and the levels of IL-17A and IFNγ were measured by enzyme-linked immunosorbent assay (ELISA). 4) The expression levels of *rorc*, *il17a*, and *ifng* in naïve CD4+ T cells were measured by quantitative real-time polymerase chain reaction (qRT-PCR). 5) The expression levels of Th17 related-genes in CD4+ T cells at day 10 post first immunization were measured by qRT-PCR. [Results] 1) The arthritis score and the incidence were significantly more severe in T-bet KO mice compared with WT mice. 2) The level of total IgG antibodies against CII was significantly higher in T-bet KO mice. 3) CII-reactive IL-17 production was significantly higher but that of IFNγ was significantly lower in T-bet-deficient CD4+ T cells compared with CD4+ T cells from WT mice. The CII-reactive production of these cytokines from CD4+ T cells was comparable when cultured with DCs from WT or T-bet KO mice. 4) The expression levels of *rorc*, *il17a*, and *ifng* in naïve CD4+ T cells were comparable in the two strains. 5) In CD4+ T cells at day 10 post first immunization, the expression levels of *rorc* and its downstream genes including *il17a*, *il17f*, *il22*, *il23r*, *ccr6*, and *ccl20* were significantly higher in T-bet-deficient CD4+ T cells. [Conclusions] Our results suggested that T-bet in CD4+ T cells protected against the development of CIA. T-bet might directly regulate *rorc* gene expression, resulting in the inhibition of IL-17A production from CD4+ T cells.

ICW16-5

Splicing factor SRSF1 is indispensable for regulatory T cell survival and function

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Conflict of interest: None

[Objective] The molecular mechanisms underlying regulatory T cell (Treg) survival and function are not fully understood. We previously found that Serine/arginine-rich splicing factor 1 (SRSF1) expression levels are decreased in T cells from SLE patients, and deletion of Srsf1 in T cells leads to systemic autoimmunity. We performed this study to elucidate the role of SRSF1 in Tregs. [Methods] We generated Treg specific *Srsf1* conditional knockout (Treg *Srsf1*-KO) mice. Peripheral lymphoid organs were analyzed for immune cell phenotype and function by flow cytometry. Serum autoantibodies were measured by ELISA. Treg function was assessed in vitro by co-culture assays with conventional T cells, and in vivo by the adoptive transfer of Tregs in colitis models. [Results] Treg *Srsf1*-KO mice develop early fatal systemic autoimmune disease. Mice develop systemic autoantibodies, abnormal production of proinflammatory cytokines, and inflammatory infiltration in lungs and liver. Tregs are severely reduced in the peripheral lymphoid tissues and display increased levels of apoptosis. *Srsf1*-deficient Tregs exhibit defects in suppressive function assessed by both in vitro and in vivo suppression assays. In addition, these Tregs produce proinflammatory cytokines including IFN-γ, IL-17 and IL-4. RNA-seq data analysis of *Srsf1*-deficient Tregs reveals that SRSF1 controls the expression of genes involved in survival, inflammatory cytokines, chemokines. mTOR pathway is activated in *Srsf1*-deficient Tregs, and expression levels of PTEN, a negative regulator of mTOR pathway, is decreased. PTEN overexpression reduces abnormal proinflammatory cytokine production from *Srsf1*-deficient Tregs. [Conclusions] SRSF1 is a novel regulator of Treg survival and function, and its deficiency in Tregs leads to fatal systemic inflammation and autoimmunity. Therefore, deficiency of SRSF1 in Tregs may represent a molecular defect that contributes to the pathogenesis of systemic autoimmune disease.

ICW16-6

Effects of IFN alpha-priming on B cell activation and actions of the FOXM1 inhibitor on activated B cells

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by aberrant B cell activation which increases autoantibody-producing plasmablasts. Type I interferon (IFN) is suggested as a trigger of SLE pathogenesis. Our previous studies found that gene expressions of cell cycle signature were elevated in plasmablasts of SLE patients and the transcription factor FOXM1 might be critical for plasmablast proliferation by microarray anlayses. Although FOXM1 plays a role in regulating cell proliferation and cell survival, studies of FOXM1 have not been reported in the field of rheumatology. Here we evaluated effects of IFNα-priming for B cell activation and actions of the FOXM1 inhibitor on activated B cells. [Methods] After peripheral B cells from healthy donors were primed with IFNα and stimulated via B cell receptor (BCR) or TLR9, effects of IFNα-priming for B cell differentiation, activation and survival were assessed by flow cytometry. Effects of IFNα-priming on FOXM1 expression of activated B cells were evaluated with quantitative real-time PCR (q-PCR). The actions of the FOXM1 inhibitor FDI-6 on activated B cells with or without IFNα-priming were examined by q-PCR analyses of FOXM1 expression and by flow cytometry analyses of cell death induction. [Results] We found that IFNα-priming promoted cell differentiation, cell enlargement, CD86 expression, cell survival and FOXM1 expression in B cells stimulated via BCR. On the other hand, we recognized that IFNα-priming promoted only cell differentiation and cell survival in B cells stimulated via TLR9. In addition, IFNα-priming increased the effects of FDI-6 on activated B cells resulting in down-regulation of FOXM1 and increased sensitivity to apoptosis. [Conclusions] Our findings can help the understanding about the significance of IFN signature for aberrant plasmablast generation in the context of SLE pathogenesis. Inhibition of IFNα-FOXM1-cell cycle/survival may be a novel therapeutic strategy in SLE.

ICW17-1

24 Weeks Safety and Efficacy of Filgotinib in Japanese Patients Enrolled in a Global Phase 3 Trial of Patients with Active Rheumatoid Arthritis and Inadequate Response to Methotrexate

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Conflict of interest: Yes

Objective: We report 24 weeks interim results of Japanese patients enrolled in the FINCH 1 study (ClinicalTrials. gov Identifier: NCT02889796) of filgotinib (FIL), an oral, selective, Janus Kinase 1 (JAK1) inhibitor in patients with RA and an inadequate response to Methotrexate. **Methods:** Patients (pts) with RA were randomized globally, in-

cluding at sites in Japan, in a 3:3:2:3 ratio to once-daily FIL 200 mg, 100 mg, adalimumab (ADA) or placebo (PBO), for 52 weeks; All arms received background MTX. The primary endpoint was the proportion of subjects who achieved an ACR20 response at Week (W) 12. **Results:** Primary endpoints at W12 were met for global population (n=1755). Overall, results in efficacy and safety were consistent between global and Jp pts (n=147; FIL200, n=40; FIL100, n=41; ADA, n=28; PBO, n=38). The primary endpoint: ACR20 response rates in Jp pts at W12 and 24 were: FIL200 77.5%, 77.5%; FIL100 65.9%, 78.0%; ADA 53.6%, 60.7%; PBO 36.8%, 47.4%; respectively. At W12, HAQ-DI LS mean changes from baseline were -0.63 (95% CI: -0.75, -0.50), -0.45 (-0.57, -0.32), -0.39 (95% CI: -0.54, -0.24) and -0.16 (95% CI: -0.29, -0.03). At W 12, the percentage of Jp pts with DAS28 (CRP) ≦3.2 was 70.0%, 56.1%, 60.7% and 18.4%. Both FIL 100 mg and 200 mg were well tolerated for 24W in both Jp and global. In Jp pts, Treatment Emergent Adverse Event rates were similar for each group (82.5%, 73.2%, 71.4% and 73.7%, respectively). Treatment Emergent Serious Adverse Event rates were few for each group (3 pts [7.5%], 2 pts [4.9%], 3 pts [10.7%] and 3 pts [7.9%], respectively). **Conclusion:** In this phase 3 study of pts with active RA and prior inadequate response to Methotrexate, treatment with FIL was associated with significant improvements in signs and symptoms of RA, with a safety and efficacy profile for 24 weeks in Jp pts consistent with that in global pts. Thus, FIL may provide a novel treatment option for Jp pts who continue to have active RA despite prior Methotrexate therapy.

ICW17-2

Rheumatoid Arthritis Treatment with Filgotinib: Week 156 Safety and Efficacy Data from a Phase 2b Open-Label Extension Study

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Conflict of interest: Yes

[Objective] Filgotinib (FIL) an oral, selective Janus kinase inhibitor, is shown to be effective and well tolerated in patients (pt) with rheumatoid arthritis (RA) and other inflammatory diseases. DARWIN3, an ongoing, open-label, long-term extension of phase 2b studies, evaluates the longer-term safety and efficacy of FIL in RA. [Methods] DARWIN3 evaluated pt outcomes for methotrexate (MTX) inadequate responders completing the 24-week DARWIN1 (FIL+MTX) and 2 (FIL monotherapy) studies. We present an interim analysis at week (W) 156 after first dose (FIL 200mg/day or 100mg/day). [Results] DARWIN3 enrolled 739 pts (497 DARWIN1, 242 DARWIN2); ~82% female, ~75% white; mean age ~53 years (y). At W156, 59.9% remained on study. Primary reasons for discontinuation were adverse events (AEs; 26.5%) and subject request (9.1%). Total FIL exposure was 2203 pt-y. For FIL+MTX and FIL monotherapy: mean (SD) FIL exposure was 3.04 (1.22) y and 2.86 (1.21) y, respectively; treatment-emergent AEs (TEAEs) occurred in 419 (84.3%) and 203 (83.9%) pts, respectively; serious TEAEs in 45 (9.1%) and 33 (13.6%) pts, respectively. AEs of special interest - herpes zoster, serious infections, malignancies (excluding non-melanoma skin cancer), deep-vein thrombosis/pulmonary embolism, tuberculosis - were uncommon (0-2 events per 100 pt-y of exposure). Grade ≧3 toxicities in >1% of pts were decreased lymphocytes (4.2/1%), decreased neutrophils (1.0/1.2%), and decreased (0/3.3%) or increased (2.2/0%) fasting triglycerides for FIL+MTX/FIL monotherapy respectively. Five deaths occurred (FIL+MTX: 2, FIL monotherapy: 3), none after W132. Clinical efficacy for FIL+MTX/FIL monotherapy at W156 (observed cases) was shown by ACR20 (87.2/89.7%)/ ACR50 (72.4/63.0)/ACR70 (45.5/40.0), DAS28 (CRP) ≦3.2 (69.0/4.7), and DAS28 (CRP) <2.6 (53.4/45.6). [Conclusions] FIL was generally well tolerated with no new safety signals or differences on FIL+MTX vs FIL monotherapy. Efficacy was sustained up to W156 in both groups.

ICW17-3

24 Weeks Safety and Efficacy of Filgotinib in Japanese Patients Enrolled in a Global Phase 3 Trial of Patients with Active Rheumatoid Arthritis and Naïve to MTX Therapy

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Conflict of interest: Yes

Objective: We report 24 weeks interim results of Japanese patients enrolled in FINCH 3 study (ClinicalTrials. gov Identifier: NCT02886728) of filgotinib (FIL), an oral, selective, Janus Kinase 1 (JAK1) inhibitor in patients with RA who were naïve to MTX Therapy. **Methods:** Patients (pts) with RA were randomized globally, including at sites in Japan, in a 2:1:1:2 ratio to once-daily FIL 200 mg + MTX, FIL 100 mg + MTX, FIL 200 mg mono, and MTX mono for 52 weeks. The primary endpoint was the proportion of subjects who achieved an ACR20 response at Week (W) 24. **Results:** Significant improvements were observed with FIL 200mg + MTX and 100mg + MTX, compared with MTX mono in terms of ACR20 at W24 for global population (n=1249). Overall, results in efficacy and safety were consistent between global and Jp populations (n=71; FIL200 + MTX, n=23; FIL100 + MTX, n=11; FIL200, n=12; MTX, n=25). ACR20 response rates in Jp pts at W12 and 24 were: FIL200 + MTX 73.9%, 82.6%; FIL100 + MTX 81.8%, 90.9%; FIL200 83.3%, 83.3%; MTX 72.0%, 80.0% respectively. At Wk 24, HAQ-DI LS mean changes from baseline were -0.94 (-1.16, -0.72), -0.95 (-1.28, -0.63), -0.97 (95% CI: -1.29, -0.66) and -1.00 (95% CI: -1.21, -0.79). The percentage of Jp pts with DAS28 (CRP) <2.6 was 69. 6%, 63.6%, 50.0% and 40.0%. Both FIL 100 mg and 200 mg were well tolerated for 24 W in both Jp and global. In Jp, Treatment Emergent Adverse Event rates were similar for each group (82.6%, 90.9%, 83.3% and 76.0%, respectively). TE Serious Adverse Event rates were few for each group (1 pts [4.3%], 0 pts [0%], 1 pts [8.3%] and 0 pts [0%], respectively). **Conclusion:** In this phase 3 study of pts with active RA who were naïve to MTX Therapy, treatment with FIL was associated with significant improvements in signs and symptoms of RA, with a safety and efficacy profile for 24 weeks in Jp pts consistent with that in the global population. Thus, FIL may provide a novel treatment option for Jp pts with active RA who are naïve to MTX Therapy.

ICW18-1

Effects of filgotinib on anaemia, thrombocytopenia and leukopenia: Results from a Phase 3 study in patients with active rheumatoid arthritis and prior inadequate response or intolerance to biological disease-modifying antirheumatic drugs

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Conflict of interest: Yes

[Objective] Cytopenias in patients with rheumatoid arthritis (RA) treated with non-Janus kinase 1 (JAK1)-selective inhibitors may occur via inhibition of JAK2. We investigated the incidence of cytopenias in patients with active RA and prior inadequate response/intolerance to biological disease-modifying antirheumatic drugs (bDMARDs) treated with filgo-

tinib (FIL), a selective JAK1 inhibitor, in the double-blind, Phase 3 trial FINCH2 (NCT02873936). [Methods] Patients (pts) were randomised 1:1:1 to oral FIL 200 mg, 100 mg, or placebo (PBO) once daily + conventional synthetic DMARDs for 24 weeks. In this subgroup analysis, we assessed haemoglobin (Hb), platelets (PLTs), neutrophils (NPs) and lymphocytes (LYMs) at baseline, Week (W) 12 and W24. [Results] A total of448 pts were treated (FIL 200 mg, 147; FIL 100 mg, 153; PBO, 148). At baseline, 319 (71%), 443 (99%), 438 (98%), and 417 (93%) pts had normal levels of Hb, PLTs, NPs and LYMs, respectively, while 129 (29%), 4 (1%), 10 (2%) and 26 (6%), respectively, had mild-moderate low levels and 5 (1%) had severe low levels of LYMs. Overall 73-74% of pts with baseline measurements also had W24 data, and of these, 86-92%, 99-100%, 96-99% and 91-98% with normal baseline Hb, PLTs, NPs and LYMs, respectively, still had normal levels at W24, while 8-14% with normal baseline Hb had mild low levels at W24. Of pts with mild-moderate low baseline Hb and W24 data, 41% receiving FIL achieved normal Hb at W24 vs. 24% receiving PBO. All pts with mild-moderate low baseline levels of PLTs or NPs with W24 data had normal W24 levels, except one pt receiving FIL 100 mg who had mild neutropenia at W24. In pts with mild-moderate low baseline LYMs and W24 data, 67% receiving FIL achieved normal levels at W24 vs. 40% receiving PBO. There were no cases of severe cytopenia at W24. [Conclusions] FIL did not influence the incidence of cytopenias in pts with active RA; Hb, PLT, NP and LYM levels remained consistent throughout the study.

ICW18-2

Pooled Safety Analyses from Phase 3 Studies of Filgotinib in Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Objective] Filgotinib (FIL) is a selective Janus Kinase 1 inhibitor in development for treatment of rheumatoid arthritis (RA) and other inflammatory diseases, evaluated in three Phase 3 studies in patients with moderate to severely active RA with inadequate response to MTX (FINCH 1; NCT02889796); or inadequate response to biological therapies and receiving conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; FINCH 2; NCT02873936); or who were MTX-naïve and initiating MTX or FIL alone or in combination (FINCH 3; NCT02886728). We present pooled safety data from the double-blind, active and placebo-controlled periods of FINCH 1-3 up to 24 weeks. [Methods] Patients in FINCH 1 and 2 who did not achieve ≧20% improvement in both swollen and tender joint counts by Week 14 discontinued study drug and switched to standard of care. Week 24 safety data from the three studies were aggregated and summarized. Key safety endpoints were treatment-emergent adverse events (TEAE), serious TEAEs, TEAEs of interest, deaths, and treatment-emergent laboratory abnormalities. [Results] 3,452 patients were assessed (2,088 received FIL). At Week 24, the frequencies of TEAEs and laboratory abnormalities were similar between patients in the FIL, placebo and active control arms of the FINCH studies. Laboratory abnormalities were mostly Grade 1-2. The proportions with TEAEs of interest were similar across groups; the most common TEAEs were infections (notably upper respiratory tract and nasopharyngitis). Major adverse cardiac events (MACE), herpes zoster virus (HZV), deep vein thrombosis (DVT) and pulmonary embolism (PE) rates were low and similar across groups (MACE: 0.2% FIL, 0.3% adalimumab, 0.5% placebo; HZV: 0.6% FIL, 0.6% adalimumab, 0.4% placebo; DVT/PE: <0.1% FIL, 0% adalimumab, 0.3% placebo). [Conclusions] These pooled data highlight the favorable safety and tolerability profile of FIL in RA both as a monotherapy and in conjunction with MTX/csDMARDs.

ICW18-3

Evaluation of potential mechanisms underlying the safety observations of filgotinib in clinical studies in RA

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Conflict of interest: Yes

[Objective] Janus Kinase (JAK) inhibitors have demonstrated efficacy in rheumatoid arthritis (RA), but differences in selectivity between JAK inhibitors may impact safety. Filgotinib (FIL) is a selective JAK1 inhibitor that did not negatively impact hemoglobin, LDL: HDL ratios, or natural killer (NK) cell counts in clinical trials. In this study we compared the *in vitro* mechanistic profiles of JAK inhibitors at clinically relevant doses. [Methods] We compared the *in vitro* profile of JAK inhibitors with different JAK selectivity profiles. FIL, FIL metabolite [GS-829845], baricitinib [BARI], tofacitinib [TOFA], and upadacitinib [UPA] were evaluated for erythroid progenitor cell expansion and maturation from human cord blood $CD34^+$ cells using a HemaTox™ liquid expansion assay, IL-15-induced NK cell proliferation (NKCP), and LXR agonist-induced cholesteryl ester transfer protein expression (LXR-CETP) in a hepatic cell line (HepG2). Target coverage at clinically relevant doses was calculated from these assays and literature derived plasma concentrations. The activity of FIL in humans was based on PK-PD modeling of FIL + GS-829845. [Results] In vitro dose-response assay results were obtained for each inhibitor. Based on these results, human exposure data, and modeled PK-PD relationships, FIL100/200mg resulted in lower inhibition of NKCP over 24 hours (39/52%) when compared to BARI2/4mg (52/79%), TOFA5/10mg (75/86%) or UPA15/30mg (74/84%); FIL also reduced LXR-CETP (17/27%) while the other inhibitors had no effect. There was no obvious difference between JAK inhibitors in their effect on erythroid progenitor cell differentiation or maturation in this assay. [Conclusions] JAK1 selectivity of FIL resulted in less inhibition of NKCP compared to BARI, TOFA and UPA. FIL also reduced CETP expression. These results provide a potential mechanistic link to the observed reduction of CETP concentration and activity following FIL treatment, and the observed reduction in LDL: HDL in RA patients.

ICW18-4

The transcriptional effects of JAK inhibitors on synovial fibroblasts from rheumatoid arthritis patients

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Conflict of interest: Yes

[Objective] Synovial fibroblasts (SFs) play a crucial role in the synovial inflammation of rheumatoid arthritis (RA) through expressing a number 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, the functional mechanisms of these novel drugs on SFs are still incompletely understood. The objective of this study is to investigate the transcriptomic effects of a selective JAK inhibitor (BARI) on RASFs, and to compare the immunological characteristics with a pan-JAK inhibitor (TOFA) or with other classes of disease modified anti-rheumatic-drugs (DMARDs). [Mehods] RASFs (n = 6) were incubated with representative inflammatory cytokines in the joints (TNF-α+IL-1β+IFN-γ) for 12 hours. Following the stimulation, DMARDs (Methotrexate, Iguratimod, TOFA and BARI) were added. After 24 hours, total RNA were extracted and RNA-sequencing was carried out (NovaSeq 6000). The analysis of differentially expressed genes (DEGs) was performed with the edgeR package. The pathway analysis was carried out with Ingenuity Pathway Analysis (QIAGEN). [Results] RASFs treated by BARI showed distinct transcriptomic patterns compared with TOFA and other DMARDs. The DEGs and pathway analysis focusing on the difference between BARI and TOFA revealed that some signal

transduction pathways (i.e., NF-κB signaling) and essential molecules for cell-cell interaction (i.e., NOTCH1) were significantly inhibited by BARI. Furthermore, RA susceptibility genes were enriched in transcriptomic changes brought by BARI compared with TOFA. [Conclusions] Our data suggested the presence of the characteristic effects of selective JAK inhibitors on RASFs in transcriptional levels. Further analysis integrated with epigenome data will facilitate our understanding of mechanistic effect of present treatments and elucidate the unmet needs in the molecular level.

ICW18-5

Effects of JAK inhibitors on immune phenotypes of peripheral lymphocytes in patients with rheumatoid arthritis, from FLOW study

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Conflict of interest: None

[Objective] We have showed biological DMARDs (bDMARDs) induced different changes in different immune cell phenotypes in the patients with rheumatoid arthritis (RA). Effects of JAK inhibitor on peripheral immune cell phenotypes is unclear. We assessed changes of peripheral immune cell phenotype before and after JAK inhibitor treatment. [Methods] Phenotypic characterization of peripheral immune cell phenotypes was defined by 8-color flow cytometric analysis for "Human Immunology Project" termed by NIH/FOCIS in 32 bio-naïve RA patients (tofacitinib n=26, baricitinib n=6). Peripheral immune cell phenotypes at baseline and 24 weeks after JAK inhibitor treatment were analyzed, and the CDAI remission (n=10) and non-remission (n=22) groups were compared. We also compared effects of treatment with various bDMARDs (TNF inhibitor n=14, tocilizumab n=13, abatacept n=13) on peripheral immune cell phenotypes. [Results] There were no significant differences in patient backgrounds between the remission and non-remission groups. Remission group had a higher proportion of T follicular helper (Tfh) cells ($p<0.01$), activated Tfh cells ($p<0.01$) and double negative (DN; $IgD^{-}CD27^{-}$) B cells ($p<0.01$) than non-remission group. After 24-week treatment, the remission group showed a significant reduction in Tfh cells (1.2±0.6% at baseline and 0.7±0.4% after treatment, $p=0.04$), activated Tfh cells (0.8±0.4% at baseline and 0.5±0.4% after treatment, $p=0.04$), DN B cells (7.3±1.9% at baseline and 6.1±1.9% after treatment, $p=0.04$). The non-remission group and treatment with TNF inhibitor did not show such changes. Treatment with tocilizumab significantly reduced the frequency of DN B cells ($p<0.01$) and abatacept significantly reduced the percentage of Tfh ($p=0.05$) and activated Tfh cells ($p<0.01$). [Conclusions] JAK inhibitor characteristically reduced the proportion of Tfh cells and DN B cells in RA. JAK inhibitor might have unique effect on peripheral immune cell phenotype like a combination of TCZ and ABT.

ICW19-1

Result of Spacing tocilizumab (TCZ) vs tapering methotrexate (MTX) study in Keio university, for rheumatoid arthritis (RA) patients In remission Phase: A Multi-center, Randomized control study

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Conflict of interest: None

[Objective] To clarify the possibility of decreasing the dose or frequency, and also discontinuation of either TCZ or MTX in RA patients who have maintained remission with combination of both drug. [Methods] Twenty-two RA patients who have maintained remission (DAS-ESR <2.6) for more than 24 weeks in the stable use of TCZ (8mg/kg, every 4 weeks) with MTX (≧6mg/week) participated in the study. They were randomly assigned to 3 groups: 1) TCZ taper, 2) MTX taper, 3) Maintenance group. In TCZ taper group, TCZ were administered twice at a 5 week and a 6 week intervals in each, and discontinued. In MTX taper group, MTX dose were reduced by 2mg/week in every 4 weeks, and discontinued. Fixed dose of TCZ and MTX at entry were continued in Maintenance group for 36 weeks. Remission rate at 12 weeks after TCZ/MTX withdrawal in TCZ and MTX taper groups, and remission rate at week 36 in Maintain group were the primary outcome. Clinical and laboratory data were compared between subgroups in which tapering TCZ/MTX resulted success and failure. [Results] Four out of 8 cases (50%) in TCZ taper group, 6 out of 8 cases (75%) in MTX taper group had maintained remission at 12 weeks after TCZ/MTX withdrawal, and all (n=6) patients in Maintain group stayed in remission at week 36. No significant clinical difference was shown between 3 groups. RA duration (49 vs 127 month) was significantly shorter, CRP at initiation of TCZ (0.86 vs 2.93 mg/day) and IL -6 level (8.7 vs 27.1 pg/ml) were significantly lower in TCZ taper success group than those in failure group (values are shown in median, $p<0.05$, respectively). Since there were few patients who failed in MTX taper (n = 2), no significant difference was shown in those patients. [Conclusions] MTX were able to be tapered and discontinued in 75% of the RA patients who maintained remission in a combined use of MTX and TCZ. There was also successful possibility of taper and discontinuation of TCZ in patients with favorable prognostic factors.

ICW19-3

Comparison of effectiveness between abatacept alone and combined with methotrexate in rheumatoid arthritis patients: from FIRST registry

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Conflict of interest: None

Objective: Biological DMARDs for rheumatoid arthritis (RA) is more effective when combined with methotrexate (MTX). While efficacy of abatacept (ABT) monotherapy is clear in clinical trials, studies in actual clinical practice are few. Here, we compared the effectiveness between ABT with and without MTX in RA patients. Methods: The efficacy of ABT plus MTX in patients with RA (n=353) was compared with ABT -alone (n=201). Selection bias was adjusted by using propensity score matching (PSM) and inverse probability of treatment weighting (IPTW). Data were analyzed by the last-observation-carried-forward method. The ABT + high-dose MTX (≧10 mg/w) (n=254) and ABT-alone (n=201) groups were also compared. Primary endpoints were the simplified disease activity index (SDAI) remission rate at 52 weeks. Results: After PSM and IPTW, there were no significant differences in patient backgrounds. The two groups showed no significant differences after PSM (n=146 each) and after IPTW (n=500 for ABT+MTX; n=501 for ABT) in SDAI remission rates at 52 weeks (ABT+MTX vs. ABT: 23% vs. 25.2% [p=0.78] after PSM and 24.4% vs. 26.6% [p=0.64] after IPTW), continuation rate, or incidence of serious adverse events (SAE). There were no significant differences after PSM (n=127 for each) and after IPTW (n=447 for ABT+MTX; n=413 for ABT) in continuation rate at 52 weeks or SAE incidence, but the ABT+high-dose MTX group had a significantly higher SDAI remission rate than the ABT-alone group (ABT+high-dose MTX vs. ABT: 29.9% vs. 17.3% [p=0.03] after PSM and 21.3% vs. 36.9% [p<0.01] after IPTW). Conclusion: Effectiveness did not differ significantly between the the ABT-alone and ABT+MTX groups, but the ABT+high-dose MTX group showed a higher effectiveness than the ABT-alone group. These results suggest ABT to be more effective when combined with MTX at a dose of ≧10 mg/w in RA patients eligible for combination therapy.

ICW19-4

Possibility of drug free remission after sustained remission in patients with RA - The two-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 possibility of drug free remission in patients with RA who achieved sustained remission. **Methods:** 427 patients who treated with combination of MTX (≧8mg) 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 dose of MTX (n=184), 3) discontinue MTX (n=24), 4) reduce bDMARDs (n=68), 5) discontinue bDMARDs (n=71). At 1-year after, 327 patients who maintained remission completely discontinued either MTX or bDMARDs in principle, otherwise continued the same treatment. The remission (DAS28-ESR <2.6) rate and associate factors at 2-year were assessed. **Results:** The remission rate at 1-year was 1) 86%, 2) 82%, 3) 79%, 4) 75%, 5) 56%, respectively, only the discontinuation of bDMARDs was significantly different from the continuation of all DMARDs (p=<0.001). Among the patients with maintaining remission after 1 year, 57 continued all DMARDs, 86 discontinued MTX, 82 discontinued bDMARDs, 13 discontinued all DMARDs. Drug free remission at 2-year was achieved in 1.6% (7/427). When comparing patients who continued all DMARDs vs. those who completely discontinued MTX, 82.5% and 77.6% sustained remission (p =0.654), respectively. Patients who continued all DMARDs had a significantly higher remission rate than those who discontinued bDMARDs (62.0%, p=0.013). In the sub-analysis comparing immediate discontinuation of bDMARDs vs. step-down tapering of bDMARDs, remission rate was higher in immediate discontinuation of bDMARDs (79.4% vs 26.3%, p=<0.001). **Conclusions:** Rate of successful drug free remission was low, because continuing treatment was preferred by shared decision making. This study indicates that the possibility of remission in half of the patients with bDMARDs-free. After sustained remission in RA patients treated with MTX and bDMARDs, MTX-free is the similar to continuing treatments.

ICW19-5

Characteristics of difficult-to-treat rheumatoid arthritis

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Conflict of interest: None

Objective: To clarify characteristics of patients with difficult-to-treat rheumatoid arthritis (RA) in real-world. Methods: We reviewed all consecutive RA patients in Keio University Hospital between 2016 and 2017 and collected medical information. We defined patients in moderate disease activity and high disease activity according to disease activity score for 28 joints (DAS28) at the last visit despite more than one year treatment for RA as difficult-to-treat RA and analyzed their clinical characteristics. Results: A total of 1693 patients with RA were reviewed, and 237 patients (14%) were included in the analysis as difficult-to-treat RA. Characteristics of difficult-to-treat RA were the mean age of 70 years old, female of 89%, and the mean disease duration of 14.8 years. The current treatments were conventional synthetic disease modifying anti-rheumatic drugs alone in 40.7%, biologic agents or janus kinase (JAK) inhibitors in 55.8%, and glucocorticoids in 29.0%. The causes of difficult-to-treat RA were unresponsiveness to several biologic agents and/or JAK inhibitors in 22.9%, comorbidities in 33.8%, and personal reasons in 39.8% (costs in 35.9%, low adherence in 4.3%, concerns about possible adverse reaction of drugs in 54.3%, and high patient global assessment in 5.4%). Patient characteristics were significantly different between the causes; age at RA onset (51 vs 61 vs 51 years, p<0.001), current age (65 vs 77 vs 66 years, p<0.001), tender joint count (3.4 vs 1.6 vs 2.1, p=0.005), swollen joint count (3.1 vs 1.6 vs 2.9, p=0.003), evaluator global assessment (21 vs 14 vs 16 mm, p=0.03), and a history of serious infection (28 vs 41 vs 13%, p<0.001). Conclusion: 14% of patients with RA were difficult-to-treat in real world in spite of intensive treatment. Their characteristics are distinct by the cause of difficulty to treat, suggesting the approach to difficult-to-treat RA should be personalized.

ICW19-6

CDAI and DAS28 in the management of rheumatoid arthritis

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Conflict of interest: Yes

Objectives: To investigate the real-world performance of clinical disease activity index (CDAI) and disease-activity score for 28 joints (DAS28) in rheumatoid arthritis (RA) Methods: We reviewed consecutive RA patients who are receiving any disease modifying anti-rheumatic drug (DMARDs) in Keio University Hospital between 2016 and 2017 and collected medical information. We focused on the patients in CDAI remission and/or DAS28 remission at the time of last visit, and analyzed their clinical characteristics. Results: A total of 1585 patients with RA were reviewed. Their characteristics were mean age of 64 years old, female of 84% and mean disease duration of 12.0 years. Current treatments were conventional synthetic (cs) DMARDs alone, TNF inhibitors, IL-6 receptor inhibitors, CTLA-4Ig, and JAK inhibitors in 39.2%, 29.0%, 22.8%, 7.1%, and 1.8% patients, respectively. Of them, 62.7% were in CDAI remission and 64% were in DAS28 remission. Among patients with CDAI remission, 16.4% did not meet DAS28 remission criteria. In contrast, among patients in DAS28 remission, 18.0% did not meet CDAI remission. Patients in CDAI remission and DAS28 non-remission had higher C-reactive protein, erythrocyte sedimentation rate, and comorbidity rates (0.37 vs 0.07 mg/dL, p<0.001; 45.7 vs 8.0 mm, p<0.001; 26.4 vs 18.0%, p=0.07, respectively), and those in CDAI non-remission and DAS28 remission had worse patient-reported outcomes including patient global assessment and health assessment questionnaire-disability index (31.1 vs 9.5 mm, p<0.001; 0.82 vs 0.41, p<0.001, respectively.). Patients in both CDAI and DAS28-ESR remission were apparently in better disease activity than those who met either criteria. Conclusion: Assessing patients with two composite measures simultaneously is important to evaluate patients' condition from view points of RA itself and comorbidities and adjust treatment appropriately.

Poster Session

P1-001

Survey on treatment of elderly RA patients in ANSWER cohort -Comparison between EORA and aging YORA -

Hideki Amuro[1,2], Yonsu Son[2], Motomu Hashimoto[3], Koichi Murata[3], Wataru Yamamoto[3,4], Tohru Takeuchi[5], Yuri Hiramatsu[5], Toru Hirano[6], Akira Onishi[7], Sadao Jinno[7], Ryota Hara[8], Masaki Katayama[9], Yoshio Ozaki[2], Shosaku Nomura[2]

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Conflict of interest: None

[Objective] To clarify the treatment of elderly RA patients in the ANSWER cohort. [Methods] RA patients enrolled in the ANSWER cohort were extracted from people over 65 years old as of March 2018. We divided into two groups: onset over 65 years old (EORA: EG) and onset under 65 years (YORA: YG), and compared complications, treatment, and disease activity at the time of registration and one year later. We used receipt data to extract complications. [Results] The extracted patients were 635 pacients in EG, 801 pacients in YG, and the average age was 76.7 years for EG and 71 years for YG. In complications, the percentage of diabetes was high in YG, but there was no difference between malignancy and heart disease. The frequency of hospitalizations in 2018-19 was significantly higher with YG (9.6% vs. 5.8% p = 0.02). In RA treatment, there was no difference between the two groups in MTX usage and dose, but PSL and biologic usage was higher in YG. The average CDAI at the time of registration did not differ between the two groups (EG 6.48 and YG 6.55). One year later, CDAI decreased with EG. (6.48 → 5.33), but there was no change in YG. [Conclusions] Elderly RA patients had different complications, treatments, and treatment responsiveness due to differences in disease duration.

P1-002

Comparison of disease activity and factors based on differences in onset age of rheumatoid arthritis at multicenter cohort study-Comparison between elderly patients (EORA) and semi-elderly patients (Pre-EORA)

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Conflict of interest: None

[Objective] EORA was defined by disease onset at 60 years over with previous reports, but the Japan Geriatrics Society defined seniors as 75 years of age or older. Therefore, we divided elderly onset RA into two groups, and compared the presence or absence of the onset factors the findings at the time of diagnosis. [Methods] We divided into three group; pre-EORA (231) as the age of onset 65 years old and younger than 74 years, EORA (70) as 75 years old and older, and AORA (878) as16 years old and older as 64 years old. We compared disease activity, bone erosion, and background factors. Clinical findings were analyzed by Mann-Whitney U-test and frequency by 2x2 Chi square test. [Results] The number of TJC and SJC was not significantly different in each group, but the CRP, ESR, and MMP-3 values were statistically significantly higher in the older age group. RA family history and stress were more frequent in the younger age group, and operation history was more frequent in the older age group. Bone erosion showed the highest frequency in the order of EORA. The female ratio was high in EORA and pre-EORA, but there was no difference between EORA and pre-EORA. [Conclusions] The cause of EORA is more likely to be attributed to complications and less related with genetic factors.

P1-004

Evaluation of biologicals use cases in the elderly-AORA registry 2018

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Conflict of interest: None

[Objectives] Although rheumatoid arthritis (RA) is improving with the advent of biologics (BIO), the elderly RA patient group has significantly higher disease activity than the younger group. The purpose of this study is to evaluateelderly RA patients over 75 years old who use BIO. [Methods] 2234 registered cases in AORA registry 2018, 131patients who were able to measure DAS28-ESR among 146RA patients over 7 years old who used BIO (DAS28-ESR<3.2) Divided into 6cases and bad group (DAS28-ESR≧3.2) 71cases, age of each group, disease duration, steinbrocker classification, biochemical examination, concomitant drugs, addiction, BIO switch, and type of BIO. [Results] The mean age of the good group and the poor group was 79.4 years and 79.6 years, respectively, and there was no significant difference between the disease durations of 220.7months and 195.9 months, respectively. Biochemical tests showed significant differences. TNF-α inhibitor 37cases, T-cell inhibitor 17cases, IL-6 inhibitor 20cases, poor group TNF-α inhibitor 35cases, T-cell inhibitor 17cases, IL-6 inhibitor 20cases In the good group, many IL-6 inhibitors were used. [Conclusions] RF and ACPA values were significantly lower in the good control group of the elderly using BIO, and IL-6 inhibitors were frequently used.

P1-005

Clinical characteristicstudy of elderly rheumatoid arthritis patients (RA) at Ogawa Red Cross Hospital

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Conflict of interest: Yes

(Purpose) To compare treatments and complications between elderly onset RA patients and young patients. (Patients and methods) The study involved 152 patients (103female, average age 70years old) in May 2019. They were surveyed their characteristics, therapeutic agents, renal function by eGFR and complications by medical records. The components were evaluated among three groups (GroupA; under 65years old, 65years old <GroupB <75years old, GroupC; more than 75years old). (Results) A: 28% (71%women), B: 34% (65%women), C: 38% (61%women). As a treatment, MTX use (59%, average 6.6mg/w) (A: 22%, 7.2mg, B; 20%, 6.6mg. C: 17%, 5.4mg). PSL use (28%, average4.9mg) (A: 8%, 4.7mg, B; 10%, 4.2mg, C: 10%, 5.9mg). Anti-TNF inhibitors (ETN, IFX, GLM) (16%) (A: 6%, B: 5%, C: 5%). Anti-IL6 inhibitors (SAR, TCZ) (10%) (A: 1%, B; 7%, C: 2%). ABT (5%) (A: 1%, C: 4%). JAK inhibitors (2%). SASP (36%) (A: 5%, B: 11%, C: 20%). TAC8% (A: 1%, B: 3%, C: 4%). MZB3% (B: 1%, C: 2%). Renal dysfunction 21cases (A: 1%, B: 4%, C: 9%), Malignancies; 4cases (56, 62, 69, 72 years old). (Conclusion) The number of elderly RA patients increased in our hospital, and the ratio of women was high by any generation. As the generation rose, the number and the amount of MTX use decreased ABT, SASP, and MZB were used frequently by the elderly. Renal dysfunction was often observed in groupC.

P1-006

The differential diagnosis of polymyalgia rheumatica (PMR) and elderly onset rheumatoid arthritis (EORA) at our hospital

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Conflict of interest: None

[Objective] To find out clinical features for the differentiation between PMR and EORA. [Methods] Among patients who were admitted to our hospital between 2014 and 2018, 38 over-sixties patients complaining of joint pain and myalgia with high inflammatory response were enrolled. Seropositive cases were excluded. There were 20 cases in the PMR group and 18 cases in the EORA group, and clinical symptoms, laboratory findings, and joint echo (US) findings were compared retrospectively. [Results] Fourteen cases of PMR and 5 cases of EORA group met the 2012 EULAR/ACR Criteria for PMR. On the other hand, none in the PMR and only 2 cases in the EORA group met the 2010 EULAR/ACR Classification Criteria for RA. The median follow-up period was 26 months. Diagnosis was changed in only 1 case from the initial diagnosis. There are significant differences for shoulder bursitis and synovitis of the small joints in US, swollen and tender small joints and myalgia at diagnosis between two groups. [Conclusions] It was suggested that the classification criteria for RA may be less useful for EORA. The presence of myalgia, small joint findings of physical examination and ultrasonography were useful for distinguishing. In particular, US synovitis of small joints was seen in all cases of RA group.

P1-007

Rheumatoid arthritis and frailty

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Conflict of interest: None

[Objective] To investigate the actual state of QOL/ADL decline and flail due to aging in patients with rheumatoid arthritis (RA), and clarify background factors including psychosocial factors. [Methods] We investigated RA patients aged 40-79 who visited university hospitals from March to July 2019 who agreed to cooperate in the survey. Out of 25 points on the basic checklist, 8 or more points were defined as flailty. [Results] During the survey period, we received 441 survey cooperation agreements, and 389 returned survey forms. Of the 371 people who could be evaluated for flail (312 women, average age 64.5±9.7 years, average age 15.8±11.8 years), 25.6% fell into flail. Age-adjusted logistic regression analysis using the stepwise method selected DAS28, HAQ-DI, and depression (BDI-2) as significant relevant factors. [Conclusions] Follow-up survey for 2 years in comparison with the survey results of general residents will disclose the effective factors to prevent RA patients from frailty.

P1-008

Profiles of quality of life and disease activity of patients with rheumatoid arthritis -multicenter prospective observational study: FRANK registry-

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Conflict of interest: None

[Objective] The control of Rheumatoid arthritis (RA) had been dramatically improved due to the development of treatment, whereas, disease activity and responce of treatment were differ among the patients. Recent several observational cohort studies have revealed many prognositic factors of disease activity and responce of treatment. [Methods] We have started the multicenter observational RA cohort study around Fukuoka city (**FRANK (F**ukuoka **R**heumatoid **A**rthritis **N**etwor**k**) registry). RA patients registered in this cohort (1571 cases, female 89%, the mean age 64.2±13.0 year-old) were analyzed the factors of disease activity and quality of life (QOL). We examined the association with the disease activity (DAS28-CRP, DAS28-ESR, SDAI, CDAI), QOL (mHAQ, EQ-5D), the status of patients (age, disease duration, sero-negative/-positive, work, complication), treatments (sDMARDs, bDMARDs, tsDMARDs, prednisone), and musculoskeletal surgery. [Results] QOL were significantly decreased according to aging and disease activity. Multivaliate analysis showed that the use of prednisone ($p=0.0460$) and disease activity ($p<0.0001$) affected with the QOL of patients. [Conclusions] This cohort for RA patients is useful, and necessory to analyze the changes of disease activity, QOL, and the status of patients.

P1-009

Investigation of rheumatoid arthritis patients with dementia

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Conflict of interest: None

[Purpose] The purpose of this study is to investigate the treatment of rheumatoid arthritis (RA) patients with dementia using our registry. [Method] We chose 1,662 patients (average 68 years old, 362 males, 1,300 females) who answered whether or not they were taking drugs for dementia at the time of the survey in our registry. RA patients with dementia were defined as “with drugs for dementia” and the rest as “without drugs for dementia” . In these two groups, (1) blood tests, (2) HAQ, (3) disease activity, and (4) the medication were examined. [Results] There were 54 patients with dementia and 1,608 patients without dementia, and the prevalence rate with dementia was 3.2%. In comparison between the two groups, CRP, erythema, MMP-3, HAQ, and disease activity were all significantly higher in the group with dementia. In the RA drugs, the prescription rate of Methotrexate (MTX) was 25.9% and that of Prednisolone (PSL) was 61.1% in the group with dementia, while the prescription rate

of MTX was 58.9% and that of PSL was 42.2% in the group without dementia. There was no significant difference between the two groups in the amount of MTX and PSL used. [Conclusion] In RA patients with dementia, blood tests, HAQ, and disease activity were all high, indicating no tight control.

P1-010

Alterations of spinal cord glia in mice with collagen-induced arthritis

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Conflict of interest: Yes

[Objective] Patients with rheumatoid arthritis complain of central nervous system symptoms such as chronic pain and mood disorders as well as joint symptoms. In order to investigate the mechanism, we observed the changes of glial activation at the spinal cord, where first receives nociception from the arthritic joints. [Methods] Collagen-induced arthritis (CIA) was induced by immunization with type II collagen. Saline was administered to the control group. mRNA expression level of microglial marker (CD11b) and astrocyte marker (Gfap) in L3-5 lumbar spinal cord was quantified by RT-PCR analysis on days 19, 24, 28, 33, 38 and 42 after the first immunization day (Day 0). Immunohistochemistry of CD11b, GFAP, and STAT3 was performed on the L4 lumbar spinal cord. [Results] Significant increase of Cd11b and Gfap mRNA was observed in mice with CIA not only after day 33, when the arthritis became apparent, but also before the onset of arthritis on day 24. Immunohistochemistry of the spinal cord showed enhanced expression of CD11b and GFAP. STAT3, a therapeutic target molecule in rheumatoid arthritis was expressed in the nucleus of the spinal cord astrocytes. [Conclusions] These results suggests that spinal cord microglias and astrocytes were activated before the onset of arthritis.

P1-011

Analysis on autophagy-related molecules and structures of the capsular tissues in periprosthetic joint infection

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Conflict of interest: None

[Objective] Autophagy in normal synovial joint is an important mechanism for cellular homeostasis. In this study, we used the autophagy marker; the PI3P-binding protein, the WD repeat proteins interacting with phosphoinositide (WIPI) to campare the expression of autophagy in PJI and OA in addition to micro structure analysis. [Methods] 1) Immunofluorescence (IF) analysis: Expression of autophagy was determined double immunofluorescence in paraffin-embedded specimens. PJI (n=8) and OA (n=8) specimens were surgically obtained from PJI and OA patients. The area of double positive cells was examined using immunofluorescence microscopy. 2) Electron microscopic observation: The specimens were observed by transmission electron microscopy. [Results] Anti-WIPI-2 clearly stained autophagy positive cells, then anti-CD68 and TEM1 also stained macrophages and fibroblasts, respectively. Furthermore, Co-localization of autophagy and CD68 was less confined to the synovial lining layer, but infiltrated into the stromal tissues. [Conclusions] The results of immunoflurorescence analysis indicating that autophagy occurs in macrophages and less in fibroblasts, and the expression of autophagy-related protein, WIPI in PJI was significantly higher than in OA.

P1-012

TNF-alpha-induced CCL2 regulates migration of RA-FLSs through transcriptional factor ROR-alpha/REV-ERB-alpha and histone acetyltransferases CBP/p300

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Conflict of interest: None

[Objective] We have reported that TNFα induced expressions of clock gene *Bmal1* through transcriptional factor *Rorα*, *Rev-erbα* and histone acetyltransferases CBP and p300 in RA fibroblast-like synoviocytes (RA-FLSs). CCL2 is regulated by RORα and REV-ERBα as well as Bmal1. In this study, we investigated the relation between RORα/REV-ERBα, CBP/p300 and TNFα-induced CCL2 expression in RA-FLSs. [Methods] RA-FLSs were treated with RORα antagonist SR1001 (20μM) and/or REV-ERBα agonist GSK4112 (20μM) in the presence of TNFα (10ng/ml). RA-FLSs were incubated with p300/CBP inhibitor C646 or transfected with p300 and CBP siRNA before stimulation with TNFα. Thereafter, *ccl2* mRNA and culture supernatant CCL2 were analyzed by qPCR and ELISA, respectively. Wound healing assay and F-actin staining were performed using C646 pretreated culture supernatant under TNFα stimulation. [Results] TNFα-induced CCL2 expression was inhibited by simultaneous treatment with both SR1001 and GSK4112. CCL2 expressions were also suppressed by treatment with C646 and silencing of both *cbp* and *p300* genes. C646 inhibited both TNFα-induced cell migration and reorganization of the F-actin. [Conclusions] We newly found that TNFα induced CCL2 regulates migration of RA-FLSs through RORα, REV-ERBα and CBP/p300.

P1-013

Differences in gene expression profiles between synovial mast cells from rheumatoid arthritis patients and osteoarthritis patients

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Conflict of interest: None

[Objective] We have reported that synovial mast cells (MCs) express FcγRI and aggregated IgG induced TNF-α production from MCs through FcγR. However, no major differences, in the FcR expression profiles or in the amounts of mediator production between MCs from RA and OA patients (RAMCs and OAMCs), were observed. The purpose of this study was to investigate differences in gene expression profiles between RAMCs and OAMCs. [Methods] DNA chip and miRNA chip was performed. The expression level of the gene that differed in expression between RAMCs and OAMCs in DNA chip or miRNA chip were measured by quantitative PCR. The correlation between miRNA and gene expression levels, differing in expression levels between RAMCs and OAMCs, was investigated. [Results] As results of the DNA chip and quantitative PCR, the expression levels of PTGS1, PTGS2 in RAMCs were significantly higher than in OAMCs. Expression of some miRNAs in OAMCs was three times higher than in RAMCs. In the miRNAs, it has reported that miR199a-3p inhibited expression of PTGS2. The negative correlation between expressions of miR199a-3p and PTGS2 in RAMCs Was found. [Conclusions] Differences in PTGS2 expression between RAMCs and OAMCs were found. It was suggested that miR199a-3p inhibited PTGS2 expression.

P1-014

Proof-of-Concept Trial of drug repositioning of metformin in rheumatoid arthritis

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Conflict of interest: None

[Objective] There have been several reports suggesting the possibility of improving autoimmune diseases by metoformin. In this study, we investigated the inhibitory effect of metformin on human osteoclasts, synovial cells and vascular endothelial cells, and examined the possibility that metformin suppresses RA activity. [Methods] First, we performed TRAP staining and bone surface resorption assay, and measured MMP-9 and cathepsin K by RT-qPCR to assess whether metformin inhibit osteoclast differentiation and function. Next, the mRNA expression of IL-6, IL-1β, MMP-3 were quantified by RT-qPCR to assess whether metformin inhibit the TNFα-induced inflammatory cytokine production in human synovial cell line (MH7A). Finally, a tube formation assay was performed to assess whether metformin inhibit angiogenesis using the HUVEC. [Results] Metformin reduced the osteoclastogenesis. Metformin suppressed TNF-α-induced inflammatory response in MH7A. Metformin inhibited the angiogenesis. [Conclusions] These results indicate the possibility that bone destruction and pannus formation are suppressed by the function of metformin in osteoclasts, synoviocytes and vascular endothelial cells. This work supports future clinical exploration of metformin in drug repositioning as a new treatment for RA.

P1-015

Peficitinib suppresses the secretion of VEGF in rheumatoid arthritis fibroblast-like synoviocytes

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Conflict of interest: None

[Objective] Peficitinib is a novel JAK inhibitor developed for the treatment of rheumatoid arthritis (RA). But elucidation of its mechanism of action in RA involving the inflammatory process is still inadequate. In this study, we evaluated the effects of peficitinib on angiogenesis in RA fibroblast-like synoviocytes (FLS). [Methods] After adding peficitinib, RA FLS were stimulated with IL-6 and IL-6 receptor (IL-6R). To examine the functional analysis of peficitinib, we performed a proliferation and chemotaxis assays with FLS using THP-1 and peripheral blood mononuclear cells (PBMC). VEGF, RANTES/CCL5, MCP-1/CCL2, MMP3, fractalkine/CX3CL1, ENA-78/CXCL5, and IL-8/CXCL8 in the cell supernatant was measured by ELISA assay. [Results] We found that peficitinib is involved in the suppression of FLS proliferation, and inhibits the chemotaxis of THP1 and PBMC through inhibition of MCP-1/CCL2 in the RA FLS supernatant. VEGF in RA FLS supernatant was suppressed after adding peficitinib when compared to that without adding. [Conclusions] Peficitinib suppressed monocyte chemotaxis and proliferation of FLS through inhibition of inflammatory cytokines. It was suggested that peficitinib suppresses VEGF production of RA FLS and suppresses angiogenesis in the inflammatory pathology of RA.

P1-016

The novel action of JAK inhibitor (Baricitinib) in human fibroblast-like synoviocytes by gliostatin production

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Conflict of interest: None

[Objective] Baricitinib is a novel oral JAK inhibitor and it has demonstrated high efficacy in rheumatoid arthritis (RA). Aberrant gliostatin (GLS) production has been observed in the synovial membranes of RA patients. We have previously reported that GLS induced the extracellular secretion of matrix metalloproteinase (MMPs) in cultured fibroblast-like synoviocytes (FLSs). The suppression of GLS production might be an effective therapy in RA. The purpose of this study was to investigate the inhibitory action of baricitinib in RA-FLSs. [Methods] RA-FLSs were cultured from synovial specimens of patients with RA and stimulated by IFNγ with or without treatment of baricitinib. The expression levels of GLS were determined using RT-PCR, western blotting and immunocytochemistry. [Results] In cultured RA-FLSs, GLS mRNA and protein were significantly induced by stimulation with IFNγ and these GLS inductions were significantly suppressed by treatment of baricitinib in dose-dependent manners. [Conclusions] Our data demonstrated that JAK/STAT signal pathway is involved in the induction of GLS in RA-FLSs. Suppression of GLS production in inflamed synovia has been suggested as one of the anti-inflammatory effects of baricitinib.

P1-017

Raloxifene augments the expression of IL-1beta induced by TNF alpha in SW982

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Conflict of interest: None

[Purpose] When SW982, which is a cell line of synovial cells, was cultured in the presence of TNFa and raloxifene, IL-1b expression of SW982 was increased by raloxifene. This time, this mechanism of action was investigated. [Method] After SW982 was cultured in serum free for 24 hours, phosphorylation of NF-kB pathway, AP-1 pathway, and PI3K pathway-related proteins, which are implicated in IL-1b expression under the stimulation of TNFα, was measured with or without raloxifene. In addition, IL-1b expression is compared with raloxifene using inhibitors and activators in pathways and we examined whether this action is either estrogen receptor alpha (ERa) or beta (ERb). The patient's synovial membrane was used to compare the expression of ERa and ERb with SW982. [Result] Phosphorylation of Akt was inhibited by raloxifene, and phosphorylation of Fox01 downstream thereof was inhibited. The Fox01 inhibitor AS1842856 and the Akt promoter Akt activator II suppressed IL-1b expression and Akt inhibitor IV enhanced Il-1b expression. The IL-1b expression enhancing effect on SW982 was reduced by ERb inhibitor PHTPP. [Conclusion] Raloxifene augments the expression of IL-1b induced by TNFa through inhibiting phosphorylation of Akt via ERb in SW982.

P1-018

Amino acid transporter Slc7a5 provides a novel strategy to regulate human B-cell activity

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Conflict of interest: None

[Objective] Recent studies have revealed that in certain types of cancer cell and immunocyte, an amino acid transporter Slc7a5 accelerates L-leucine influx and mTORC1 signaling, facilitating cellular activity. Although B cells play important roles in autoimmune diseases, expression and roles of Slc7a5 in B cells are poorly investigated. This is the first study to demonstrate critical involvement of Slc7a5 in B-cell responses. [Methods] Peripheral blood $CD19^+$ B cells were obtained from healthy adults and stimulated by a toll-like receptor 9 ligand, CpG-ODN. Expression of Slc7a5 and L-leucine uptake were evaluated by flow cytometry and radioisotope assay. Next, effects of Slc7a5 inhibition on mTORC1 signaling and production of IgG and inflammatory cytokines were assessed. [Results] Slc7a5 expression was significantly upregulated in CpG-stimulated B cells. Inhibition of Slc7a5 abrogated L-leucine influx and mTORC1 signaling, resulting in suppression of IgG and cytokine production. Once B cells have differentiated to plasmablasts, Slc7a5 expression is downregulated, which indicates Slc7a5 serves exclusively in the process of B-cell activation. [Conclusions] Slc7a5 critically regulates inflammatory activity

of human B cells. Slc7a5 may become a novel therapeutic target in autoimmune diseases.

P1-019

The nociceptive pain control of oxytocin in the hypothalamo-neurohypophisial/-spinal pathway in the knee osteoarthritis model rats

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Conflict of interest: None

[Objective] To evaluate the neurological reaction of oxytocin (OXT) with knee osteoarthritis (OA) model rats. [Methods] The right knee osteoarthritis was induced by intra-articular injection of 1mg/0.05mL mono-iodoacetate. First, male Wistar rats were used, and the nociceptive thresholds were measured. These rats were perfused or decapitated at 28 days after injection for immunohistochemistry or *in situ* hybridization. Next, male OXT-mRFP1 transgenic rats were used, and these rats were perfused at 28 days after injection for evaluation of OXT-mRFP1 appearance in the hypothalamus and spinal cord. [Results] The nociceptive thresholds were significantly decreased in the OA rats. The number of the FosB-LI positive cells in the supraoptic nucleus, paraventricular nucleus (PVN), and L4 ipsilateral lamina I-II of the dorsal spinal cord were significantly larger in the OA rats. In addition, the gene expression of OXT mRNA and the fluorescent intensity of OXT-mRFP1 in the dorsal-parvo PVN were significantly higher in the OA rats. Further, the number of OXT-mRFP1 positive granules in the L4 ipsilateral lamina I-II was significantly larger in the OA rats. [Conclusions] The haypothalamo-spinal, not hypothalamo-neurohypophysial, pathway of OXT was activated by the nociceptive stimulation of the knee OA.

P1-021

Monocyte activation in SLE and RA murine models

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Conflict of interest: None

[Objective] Monocytes consist of heterogeneous populations with functional differences. Accumulating evidence showed that monocyte activation is associated with the disease progression in SLE and RA. In this study, we examined the pathogenic role of monocyte subsets in SLE and RA based on our current studies. [Methods] We examined the relationship between monocyte subset and disease severity in SLE-prone B6. Fcγ-RIIB-/-. Yaa and RA-prone B6/129. FcγRIIB-/- mice. [Results] In both strains, the activated monocyte subset was increased. These activated monocytes expressed high levels of B cell-stimulating cytokines. In RA mice, these monocytes were also involved in osteoclastogenesis. [Conclusions] Activate monocyte subset plays an essential role in the pathogenesis of SLA and RA.

P1-022

Cytokine gene polymorphisms in Japanese patients with autoimmune disease

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Conflict of interest: None

[Objective] Production of autoantibody is important for autoimmune disease. Cytokines play a key role in its pathogenesis. The analysis of cytokine gene polymorphisms is important factor of pathophysiology and treatment. [Methods] This study subjects consisted of Japanese with autoimmune disease, rheumatoid arthritis (n=48), systemic lupus erythematosus (n=31), immune thrombocytopenia (n=68), others (n=19), and healthy controls (n=30). We analyzed TNFα, TGFβ$_1$, IL-6, IL-10 and IFNγ polymorphisms. [Results] IL-10 (-819 C/T) revealed that there was significant decrease in the frequency of IL-10 (-819) CC genotype as compared to controls. And IL-10 (-592 C/A) revealed that there was significant decrease in the frequency of IL-10 (-592) CC genotype as compared to controls. Genotyping of IL-10 showed that there was significant decrease ACC/ACC genotype. No significant differences in TNFα, TGFβ$_1$, IL-6 and IFNγ genotypes and alleles frequency were observed between the patients with any groups and controls. [Conclusions] The results show that IL-10 (-819 C/T, -592 C/A) polymorphism is associated with RA in Japanese population.

P1-024

Study of convolutional neural network for classification of two-dimensional array images generated from clinical information in rheumatoid arthritis

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Conflict of interest: None

[Objective] In diagnosis of rheumatoid arthritis (RA), there has been no definite criteria nor direct marker. Rheumatologists use ACR/EULAR classification criteria for diagnosis, however many cases do not satisfy the criteria. This research aimed to study use of convolutional neural network (CNN) for diagnosis of rheumatoid arthritis (RA). [Methods] Our novel idea was that converting several clinical information to simple images. We semi-quantitatively converted each clinical information to four color square images and arranged them as one image. Single rheumatologist (JF) added some modification to clinical information in each patient to increase tuning data (one nonRA data to four artificial data, one RA data to five artificial data). Totally 300 images (100 RA, 200 nonRA) were used to fine-tune one of the pretrained CNNs, AlexNet. The fine-tuned AlexNet classified testing images generated by the clinical data (5 RA, 10 nonRA) that were independent of the tuning data. [Results] The fine-tuned AlexNet classified tuning data with accuracy of 97%. The fine-tuned AlexNet classified testing images that were independent of the tuning data with accuracy of 87%. [Conclusion] The CNN classification of images generated from clinical data could support RA diagnosis.

P1-025

The case which Cytoplasmic positiveness in indirect fluorescent antibody in our hospital

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Conflict of interest: None

[Objective] Autoantibody founded in collagen disease such as anti ARS antibody is a cytoplasm antibody. On the one hand, Cytoplasmic positiveness are often seem in indirect fluorescent antibody of anti-nuclear antibody test. We study the case which Cytoplasmic pattern positiveness in our hospital. [Methods] Among 11100 patients which examined indirect fluorescent antibody in 2003/9/1-2019/6/30 in our hospital, and 500 examples which became Cytoplasmic positiveness were studied. [Results] Other Staining pattern Additionally are Homogeneous 83 patients (16.6%), Speckled 256 (51.2%), Discrete 28 (5.6%), Nucleolar 42 (8.4%) and is 7 (1.4 %). In disease peculiar antibody, anti-mitochondrial antibody positive 48.3% (42 in 87), anti-mitochondrial M2 antibody 33.3% (4 in 12) and anti-ARS antibody 30.4% (49 in 161). Matter for the disease name of disease, 242 of interstitial pneumonia, 103 Rheumatoid Arthritis and 26 systemic sclerosis, 35 Sjogren syndrome, 17 inflammatory myositis, and 22 of Primary biliary cholangitis. [Conclusions] The positive rate of the anti

ARS antibody, the anti-mitochondrial antibody and the anti-mitochondrial M2 antibody is highly positive inn a Cytoplasmic positive case in indirect fluorescent antibody, and the measurement is beneficial.

P1-026

Matrix metalloproteinase-3 (MMP-3) for the diagnosis of rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] We investigated the usefulness of MMP-3 in the diagnosis of RA. [Methods] One hundred and seven patients, who were referred to our hospital from January to June in 2018 due to arthralgia, were included in this study. We measured MMP-3, anti-CCP (cyclic citrullinated peptide) antibody (ACPA) at the first visit and investigated whether these patients were diagnosed with RA at one year. [Results] At one year, 66 patients were diagnosed with RA. Twenty-six patients were ACPA-negative RA. In RA patients, MMP-3 were significantly higher (117.6 (65.2-274.5) vs 59.0 (45.1-76.4) ng/mL, $p<0.001$) than in those who were not diagnosed with RA (non-RA). In ACPA negative patients, MMP-3 were higher than in non-RA patients (170.8 (68.9-293.4) ng/mL vs 59.0 (45.1-76.4) ng/mL, $p=0.001$). ACPA negative patients were older than non-RA patients (68 (58-75) vs 49 (59-69) years old, $p=0.019$), but there was not a significant difference in eGFR ((84.2 (67.5-93.3) vs 84.2 (66.4-93.1) mL/min. /1.73m^2, $p=0.723$). In comparison between ACPA negative RA and non-RA, the cut-off value of MMP-3 that could be diagnosed with RA was 114.7 ng / mL (sensitivity 88%, specificity 62%), and AUC was 0.75. [Conclusions] MMP-3 might be a useful biomarker for diagnosis of RA especially in case of ACPA-negative patients.

P1-027

Presepsin levels are suppressed in patients with rheumatoid arthritis treated with biological disease-modifying anti-rheumatic drugs and Janus kinase inhibitor

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Conflict of interest: None

[Objective] Presepsin, a soluble N-terminal fragment of CD14, is released from the immune cells through shredding following cellular phagocytosis. Because dysregulation of innate immunity is related to not only the defence against infection but also pathological mechanisms of autoimmune diseases, including rheumatoid arthritis (RA), we aimed to investigate the implication of innate immune status in patients with RA without infection by evaluating presepsin levels. [Methods] We enrolled 105 patients with RA without infection. Their presepsin levels were determined using PATHFAST® Presepsin. [Results] In multiple regression analysis, presepsin level was not associated with DAS28. On the other hand, the estimated glomerular filtration rate (eGFR) and the use of biological disease-modifying anti-rheumatic drugs (bDMARDs) or Janus kinase inhibitor (JAKi) were negatively independently associated with presepsin level. Neither methotrexate nor prednisolone use influenced the presepsin levels. [Conclusions] These findings suggest that treatment with bDMARDs/JAKi might induce opportunistic infections in patients with RA by suppressing innate immunity; however, it remains unclear how the suppression of innate immunity influences RA activity.

P1-028

Examination of outcome of polymyalgia rheumatica

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Conflict of interest: None

[Purpose] A diagnosis of polymyalgia rheumatica (PMR) should only be considered after excluding other diseases, including rheumatoid arthritis (RA), with similar symptoms. Treatment for some PMR patients may change after a change in diagnosis. We retrospectively studied the outcomes of PMR cases. [Methods] We analyzed serological data and the treatment of 24 patients initially diagnosed with PMR at our hospital from 2014 to 2018. [Results] The diagnosis of seven patients was changed because of resistance to prednisolone (PSL) therapy (5, RA; 1, scleroderma with pseudo-gout; 1, relapsing polychondritis). No significant difference was found in age, gender, or serological data at initial visit (CRP, ESR, MMP-3, RF-positive, ANA-positive, and ANCA-positive) for 17 patients with a final diagnosis of PMR. Five patients were finally diagnosed with RA. Rates of wrist arthritis at first visit and an ANA-positive result were significantly higher in RA than PMR patients (arthritis, 80.0% vs. 23.5%; ANA, 80.0% vs. 17.6%). PSL was discontinued for seven patients with PMR (41.2%) vs. none with RA (0%). [Discussion] The diagnoses of PMR cases showing peripheral arthritis at first visit, resistance to PSL therapy and with sera positive for autoantibodies should be carefully re-examined.

P1-029

Peripheral vascular disturbance associated with pulmonary hypertension in connective tissue diseases -disparity of nailfold temperature as its index-

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Conflict of interest: None

[Objective] Connective tissue diseases (CTD) involve peripheral circulatory disturbance and pulmonary hypertension (PH). The possible parallel development of the two is examined, and an early sign of the former is searched. [Methods] Three CTD-PH patients were examined for ten nailfold temperatures from before to 30' after cold load (hands immersion in 10° C water for 10'') by thermography. Coefficient of variation (CV, SD/mean temperature) was adopted as the index of temperature disparity. Maximal CV (CVmax) was compared to those in CTD patients without peripheral vascular disease or PH. Estimated pulmonary artery pressure (PAP) was by echocardiography. [Results] Case 1. 76-yr male, systemic scleroderma (SSc) with Raynaud. CVmax: 0.105→0.088, PAP: 74→56 mmHg after PGI2, ERA, & PDE5. Case 2. 71-yr male, SSc with finger cyanosis. CVmax: 0.067. PAP: 40→39 after PGI2, ERA, & PDE5. Case 3. 59-yr female, SSc with Raynaud. CVmax: 0.086. PAP: 44→44after PGI2. CVmax in 8 controls was 0.043±0.015. [Conclusions] All three CTD-PH patients showed increased CV. In a case with available data before and after therapy, both PAP and CV improved. The disparity might indicate disturbance and remodeling of small vasculature both in peripheries and in lungs.

P1-030

Comparison of BioPlexTM ANA screen test and individual kits in measuring autoantibodies in patients with connective tissue diseases

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Conflict of interest: Yes

[Objective] To compare BioPLexANA™ screen test and individual kits in measuring autoantibodies in patients with connective tissue diseases [Methods] Patients with connective tissue diseases and rheumatoid arthritis in our hospital were enrolled in the study. Anti-dsDNA, ant-RNP, anti-Sm, anti-SS-A/Ro, anti-SS-B/La, anti-Scl-70, anti-centromere and anti-Jo-1 antibodies were measured with BioPLexANA™ screen tests and individual Stacia MEBLux™ tests. The concordance rates and the correlation of titers were investigated. [Results] One hundred six patients (28 systemic lupus erythematosus, 20 Sjogren syndrome, 14 systemic sclerosis, 16 polymyositis/dermatomyositis, 13 mixed connective tissue disease, 15 rheumatoid arthritis) were enrolled in the study. The concordance rates of the autoantibodies were 83.0% for anti-dsDNA, 95.3% for ant-RNP, 93.4% for anti-Sm, 93.4% for anti-SS-A/Ro, 98.1% for anti-SS-B/La, 98.1%for anti-Scl-70, 98.1% for anti-centromere and 99.1% for anti-Jo-1 antibodies. Correlations of titers were R>0.7, P<0.001 for all antibodies. [Conclusions] The BioPLexANA™ screen test showed highly concordant results with conventional individual kits.

P1-031

The safety and usefulness of open muscle biopsy in rheumatic diseases

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Conflict of interest: None

[Objective] To clarify the usefulness and safety of open muscle biopsy in the diagnosis of rheumatic diseases. [Method] We retrospectively examined all cases of muscle biopsy performed from 2012 to 2018 in our department. [Results] 211 cases of muscle biopsy were extracted. The purposes of the biopsy were diagnosis of vasculitis in 116 cases and of myositis in 86 cases. Significant histopathological findings were obtained in 39 / 116 cases (33.6%) for vasculitis diagnosis and 58 / 86 cases (67.4%) for myositis diagnosis. In 61 cases with ANCA ≧ 10 U/ml, vasculitis was observed in myopathology in 34 cases (55.7%). Complications included minor wound dehiscence (11 cases) and subcutaneous hematoma (7 cases). In the group with wound dehiscence, albumin tended to be low (p = 0.06). Serious complications included anaphylaxis due to local anesthesia (1 case), compartment syndrome (1 case), hematoma requiring resuming wound (1 case), and hypotension with arterial bleeding (1 case). Latter three hemorrhagic cases were all on antiplatelet drugs. [Conclusion] Open muscle biopsy is useful for diagnosis and the safety profile is acceptable. Serious adverse events rarely occur, but should be performed carefully when patients are taking antiplatelet drugs.

P1-032

Consideration of the relationship between CRP at diagnosis of rheumatoid arthritis and the number of involved joints, duration of disease, ACPA titer, age of onset

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Conflict of interest: None

[Objective] To investigate the relationship between CRP at diagnosis of the first visit of RA patients, age at onset, duration of disease, number of involved joints (small or large joint), and ACPA. [Method] Regression analysis was performed using the age of onset, the period from onset to first visit, the number and location of involved joints (large or small joints), and ACPA titer as explanatory variables and the CRP of RA patients who were not treated with MTX or biologics at the first visit as objective variable. [Results] The average CRP of 319 RA patients (238 women) was 2.1 mg/dl, the mean age at onset was 58.2 y. o (18-91 y. o). The average number of involved (small/large) joints was 1.4 / 5.5 joints. As a result of single / multiple regression analysis, the age of onset (correlation coefficient 0.036 *p<0.001)* and the number of affected large joints (correlation coefficient 0.77 *p<0.001*) were correlated with CRP. When CRP was compared with the presence or absence of major joint disease, the value of the major joint disease group was significantly higher (3.15 vs 0.79 mg /dl *p <0.001*). [Conclusion] From these results, patients with a high inflammatory response are likely to have large joints, and CRP is low in patients with only small joints without large joints.

P1-033

Sensitivity and specificity of RF and ACPA in outpatient department for rheumatic disease

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Conflict of interest: None

In a classification standard of the rheumatoid arthritis, RF, ACPA and CRP are adopted. This time, I report those real clinical on-side sensitivity and specificity. In 286 cases of the RA outpatient department, 107 cases had a diagnosis of RA. In RA patients, the positive example of CRP, ACPA, MMP3 and RF were 78.5%, 76.8%, 75.6%, 72.9% each. The sensitivity and the specificity were 76.6% and 91.1% in ACPA, 72.9% and 79.9% in RF, 78.5% and 6.9% in CRP, and 75.7% and 81.6% in MMP3. In addition, I had a diagnosis of RA in 98.2% when all CRP and ACPA and MMP3 were positive. On the contrary, in the case of negative, 97.4% were not all RA. ACPA had high sensitivity, specificity in comparison with RF together.

P1-034

Objective evaluation and digitization for stress and fatigue in patients with rheumatoid arthritis ~Analysis by a device~

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Conflict of interest: None

[Objective] Stress and fatigue was evaluated by patients' subjectivity. We used the device that was able to quantify the stress and investigated the correlation of VAS and questionnaire, and relationship of disease activity. [Methods] We used the date from prospective observational study (CHIKARA study). 84 RA patients entered. We calculated the physical (S-physical ST), mental (S-mental ST), and total stress score (S-total ST). We also performed the questionnaire by Perceived Stress Scale (PSS) 10, and VAS of stress (stress-VAS) and fatigue (fatigue-VAS). We investigated the relationship between the stress, fatigue and disease activity. [Results] Mean age was 68.6 years, disease duration was 8.8 years, DAS28ESR was 3.24 and HAQ was 0.5. S-physical ST was correlated with fatigue-VAS, and S-mental ST was also correlated with stress-VAS. However, there was no correlation between PSS10 and objective stress parameters. DAS28ESR was correlated with fatigue-VAS (R=0.223 p=0.041) and S-total ST (R=0.329 p=0.002). The higher the disease activity was, the bigger the ratio of heavy stress became. [Conclusions] Stress score by objective measuring device was correlated with stress- and fatigue-VAS. We reveled that fatigue-VAS and objective stress score were high in bad disease control.

P1-035

Associations between environmental factors and presence of autoantibodies in general population

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Conflict of interest: None

[Objective] Blood sampling and dietary questionnaires were conducted to investigate whether specific lifestyle, food or nutrition affected the

appearance of autoantibodies (Abs). [Methods] 900 general residents in Ishikawa Prefecture were interviewed and a meal survey was conducted using dietary questionnaires. Serum ANA, RF, ACPA, and anti-SSA abs were measured, and statistically analyzed whether specific food or nutrient relate to ab appearance. [Results]: 23 were positive for ANA, 69 for RF, 13 for ACPA, and 31 for anti-SSA ab. Urinary Na/Cr ratio was positively correlated with ACPA positivity (OR 1.261 95% confidence interval (CI) 1.017-1.655). Fatty fish intake positively correlated with RF positivity (OR 1.013, 95% CI 1.001 to 1.025). Smoking history negatively correlated with anti-SSA abs positivity (OR 0.207, 95% CI 0.206-0.994), and energy, protein, and polyunsaturated fatty acid intake negatively correlated with ANA positivity (OR 0.999, 0.965, 0.837, 95% CI 0.998-1.000, 0.939-0.994, 0.752-0.958, respectively). [Conclusions] The urinary salt excretion correlated with ACPA positivity, suggesting an association between salt intake and the onset of RA. On the other hand, results of such as smoking and fish oil intake were not consistent with the previous reports.

P1-036

Relationship of appendicular skeletal mass index and fracture in patients with rheumatoid arthritis analyzed by the CHIKARA study three years data

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Conflict of interest: None

[Objective] We reported the related factors for falls in RA patients. The predictors for fractures were investigated over 3-year periods by the longitudinal study. [Methods] We used the 3-years follow-up date from prospective observational study (CHIKARA study). The survival rate was calculated by fracture as endpoint. We investigated the relationship between fracture and baseline data and change of the 3-years periods. [Results] 100 patients (78 women, 68 years) enrolled. 12 patients had fractures and the survival rate was 86.9%. That with locomotive syndrome (Locomo) at baseline was lower than without Locomo (81.3%, 91.9%: P=0.134). ΔmHAQ, Δweight, Δmuscle mass, Δbone mass, Δbasal metabolic rate, and Δappendicular skeletal muscle index (ASMI) were predictors for fracture. Body composition, disease activity, and sarcopenia do not correlate. ΔASMI was an independent predictor by multivariate analyses (odds ratio: 0.015, P=0.026). When ΔASMI decrease over 0.14kg/m^2 by ROC analysis, the odds ratio of fracture increased 9.8-hold (P=0.001). [Conclusions] The survival rate was 86.9% from 3-years periods. It was difficult to predict fracture from baseline data. The reduction of ASMI was an independent predictor for fracture. The notice of muscle mass loss may lead the prevention of fracture.

P1-037

Three cases of Rheumatoid arthritis associated with Kartageners' syndrome

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Conflict of interest: None

Kartageners' syndrome (KS) is a rare disease with three main symptoms: situs inversus, chronic sinusitis, and bronchiectasis, and is a type of primary ciliary dyskinesia (PCD). Case 1: An 82-year-old female at the time of death. Rheumatoid arthritis (RA) onset was in 1984, referred in 2006. Rheumatoid factor (RF) and anti-CCP antibody (ACPA) were positive and KS was observed. Despite etanercept (ETN) treatment, nephrotic syndrome was observed with gradual aggravation in systemic symptoms leading to death in 2014. An autopsy revealed systemic AA amyloidosis. Case 2: A 76-year-old female with RA onset in 2003, referred in 2013. RF and ACPA were positive and KS was observed. Bacterial pneumonia resulted in repeated hospitalization; however, this ceased with the start of regular procaterol inhalation. Case 3: A 79-year-old female with RA onset in 2004, referred in 2009. RF and ACPA were positive and KS was observed. She has been treated with ETN since 2010, after which her activity of RA has been stable. Conclusion: All cases were positive for ACPA, and the chronic inflammatory environment of the respiratory tract associated with PCD may have affected the onset of RA. Since there have been no reports of multiple cases of RA associated with KS in a single institution, we report here.

P1-038

Search for genes associated with elderly-onset rheumatoid arthritis

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Conflict of interest: None

[Objective] The number of elderly-onset rheumatoid arthritis (EORA) patients is increasing with the aging of society. As the one of causes of EORA, it seems that genetic factors affect the onset age of rheumatoid arthritis (RA). In this study, we searched for SNPs associated with EORA. [Methods] The subjects were 655 Japanese female patients (≧ 17 years old) of RA. They were categorized into two groups: EORA (≧ 60 years old, n = 113) and younger-onset rheumatoid arthritis (YORA, < 60 years old, n = 542). Illumina HumanHap300K, Human610-Quad or HumanOmniExpress chip were used for genotyping. SNPs used in this study were common among these 3 chips and were 302,814 SNPs. Case-control study was carried out between EORA and YORA using Chi-Squared test in Recessive Model. [Results] As the result of GWAS, rs1001594 (p = 10) on *PCLO* (Piccolo) was found among SNPs with comparative lower P value. Odds ratio for the minor allele was 35.7 (95% CI 4.4-293). [Conclusions] To our knowledge, our study is the first to analyze the relationship of genetic factors with EORA. It has been reported that PCLO is associated with various psychiatric disorder. PCLO may affect the age of onset of RA because a lot of EORA patients is accompanied by depression.

P1-039

Analysis of oral microbiota focusing on Rheumatoid Arthritis and Anti-CCP Antibodies in Health Checks for Residents

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Conflict of interest: None

[Objective] It has been reported that ACPA is observed in several organs prior to the onset of RA. Oral mucosa is considered to be one of the important tissues. Nagasaki University has intervened in residents health

check-ups in Nagasaki prefecture and have accumulated data regarding to the development of rheumatoid arthritis. [Methods] We have recruited residents who come to health check-ups and asked them to write a medical interview sheet, take a blood test to examine ACPA, HTLV-1, HLA genotyping and saliva. The oral microbiota composition is determined the operational taxonomic unit (OTU) analysis by using 16SrRNA gene by next-generation sequencing. For the alpha diversity within the specimen for each research subject, the difference between groups was tested by the Wilcoxon test for ACPA positive/negative and for the presence or absence of RA. [Results] Samples were collected from 1385 individuals between 2018 and 2016. The study included 191 women (61%), 42 samples positive for ACPA, and 34 patients are diagnosed RA. In OTU, no difference between ACPA positive and negative groups was detected. There was a significant difference in the presence or absence of RA ($p<0.05$). [Conclusions] We discuss how oral mucosa contribute to ACPA production and RA development.

P1-042

Study on cause of death of rheumatoid arthritis complicated with interstitial pneumonia using ANSWER cohort database

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Conflict of interest: None

[Objective] We examine the causes of death and factors related to death of rheumatoid arthritis-related interstitial pneumonia. [Methods] Using the ANSWER cohort database, 26 patients who followed the turning point of interstitial pneumonia (IP) were identified from May 1, 2011 to July 31, 2019, and examined the cause of death and clinical factors. [Results] Mean age 77.7 ± 6.6 years, 18 males, 8 females, mean morbidity 20.5 ± 30.8 years, ACPA positive 16 cases, negative 4 cases, RF positive 19 cases, negative 6 cases, mean diagnosis KL-6: 930.9 ± 143.8 U / ml, smoking rate is 10 smoking, 9 non-smoking, 7 unknown, mean steroid dpses at death was prednisolone 5.7 ± 1.1 mg, methotrexate at death 1 case 4 mg. The cause of death was lung infection in 9, IP exacerbation in 6, lung cancer in 2, and other 9. In KL-6 of IP-related death and other diagnoses, the former was 1146.1 ± 305.5 U / ml, and the latter was 859.2 ± 164.1 U / ml. For IP-related deaths and other cases, the former averaged 7.4 years and the latter averaged 14.3 years. [Conclusions] Pulmonary infection was the most common cause of death of rheumatoid arthritis-associated IP, followed by a lot of IP exacerbation. Deaths from IP exacerbation were common in relatively short cases of rheumatoid arthritis.

P1-043

Our case reports of rheumatoid arthritis in our hospital, which already had malignant lymphoma at the time of diagnosis of rheumatoid arthritis

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Conflict of interest: None

[Objective] Although cases with malignant lymphoma are often seen during the course of rheumatoid arthritis, there are few reports of cases in which malignant lymphoma preceded rheumatoid arthritis. To investigate the clinical features of rheumatoid arthritis preceded by malignant lymphoma. [Methods] In our hospital, clinical characteristics were examined in a total of 5 cases in the past 10 years, which were associated with malignant lymphoma at the onset of rheumatoid arthritis, or who were likely to have malignant lymphoma. [Results] The histological types of malignant lymphoma are DLBCL 3 cases, Hodgkin lymphoma 1 case, follicular lymphoma 1 case. Therapies for malignant lymphoma are chemotherapy 3 cases, radiation treatment 1 case, follow-up 1 case. The treatment of rheumatoid arthritis is csDMARDs 2 cases, follow-up 2 cases, rituximab 1 case. [Conclusions] All patients who underwent chemotherapy showed improvement in rheumatoid arthritis symptoms with the start of chemotherapy. Although csDMARDs did not improve sufficiently, malignant lymphoma treatment improved rheumatoid arthritis. However, because all chemotherapy uses high-dose steroids, it was not possible to determine whether the improvement in joint pain was due to steroid effects or antitumor effects.

P1-044

Association of RA patient background with pharmacist intervention in the use of biologics and JAK inhibitors

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Conflict of interest: None

[Objective] In our hospital, rheumatoid arthritis (RA) medical care was started in August 2017. In this study, we evaluated the significance of pharmacist intervention at the start of biologics and JAK inhibitors. [Methods] Subjects are RA patients who initiated treatment with biologics or JAK inhibitors between Aug 2017 and March 2019. The patient's background, DAS28-CRP, VAS-GH, and HAQ-DI were evaluated with an observation period of 12 weeks after the pharmacist intervention. [Results] There were 81 patients who met the conditions, consisting of male / female ratio was 15/66, average age was 70 years. The 12-week continuation rate was 89%, and the discontinuation group was due to primary resistance. The change in the continuation group were -1.18 ($p<0.01$) in DAS28-CRP, -13.86 ($p<0.01$) in VAS-GH, and -0.018 ($p=0.85$) in HAQ-DI. [Conclusions] In pharmacist intervention cases, the efficacy of biologics and JAK inhibitors were shown. None of them were discontinued due to side effects, indicating the importance of pharmacists taking medication instructions. Based on this study, pharmacists' participation in the RA clinical team not only improves patient treatment satisfaction (Patient Reported Outcome) but also contributes to the quality of treatment (Treat to Target).

P1-045

Estimation of the blood concentration in infliximab after 14 weeks at the initial therapy (RemiQ study)

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Conflict of interest: Yes

Objectives: Infliximab (IFX) is the only biological agent that can measure the blood concentration by using commercial kit (RemicheckQ). However, there are not enough for the issues for the results in RemicheckQ. In the present study, we measured RemicheckQ at 14 week after the start of IFX to evaluate its usefulness as a therapeutic predictor. **Methods:** We evaluated the clinical responses, retention rate, and whether dose escalation with IFX of 15 patients with rheumatoid arthritis (RA) at 6 and 12 months by using RemicheckQ. **Results:** After 14 weeks, RemicheckQ

measured 6 positive and 9 negative. Within 6 months after the start of treatment, 2 patients who were discontinued were negative for RemicheckQ at 14 weeks. The patients who were treated the dose-escalation of IFX increased within 6 and 12 months after the start of IFX treatment was significantly higher in RemicheckQ negative cases. There was no significant difference in retention rate, and there was trend to decrease in DAS28-ESR change at 6 months in RemicheckQ positive cases. At 12 months, DAS28 clinical remission rate was 66.7% for positive and 14.3% for negative in RemicheckQ. **Conclusions:** The results of RemicheckQ measurement 14 weeks after the introduction of IFX could be a predictor of treatment.

P1-046

Clinical features of difficult-to-treat Rheumatoid arthritis

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Conflict of interest: None

[Objective] We investigated the clinical features of difficult-to-treat RA (DT-RA). [Methods] This retrospective study analyzed data obtained from 404 patients with RA who visited our hospital between April 2011 and July 2017. DT-RA was defined as the presence of RA (DAS28>3.2) activity, despite prior treatment with at least one csDMARD and at least two b/tsDMARDs. [Results] Twenty-two patients (5.4%) fulfilled the criteria for DT-RA, and 382 patients were classified as not having DT-RA. There were no significant between-group differences in age, sex, disease duration, and the positivity of RF and anti-CCP antibody. The activity of RA at the start of treatment for RA was higher in the DT-RA group, especially the number of tender joints, and the visual analog scale scores of patients and doctors. The number of patients with concomitant interstitial pneumonia was higher in DT-RA. [Conclusions] Previous reports have shown that DT-RA has high activity, especially regarding the count of tender joints and VAS scores. This study showed similar results. On the other hand, our results indicated that interstitial pneumonia may be a risk factor for DT-RA. But in this study, the number of patients enrolled was small, and this study was retrospective; thus, further studies are needed.

P1-047

Subjective symptoms in patients with rheumatoid arthritis who achieved clinical remission; Retrospective analysis of the IORRA database

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Conflict of interest: Yes

[Objective] To explore patient-reported outcomes (PROs) related to quality of life (QOL) in patients (pts) with rheumatoid arthritis (RA) who achieved clinical remission. [Methods] In IORRA dataset that was collected in April 2017, RA pts aged 18 years or older who met SDAI remission criteria were enrolled for this analysis. As PROs, pain-VAS [0-100 mm], pts general assessment VAS (PtGA) [0-100 mm], J-HAQ, duration of morning joint stiffness (MJS), and fatigue (Checklist Individual Strength 8R (CIS)) were evaluated. To evaluate each PROs in contribution to variance in EQ-5D-5L score, variance analysis was performed by ANOVA. [Results] Among 2443 pts who met remission criteria, mean age was 61.9 years; 84.6% were female; mean DAS28 and SDAI was 2.0 and 1.3, respectively. Mean EQ-5D-5L was 0.9; mean pain VAS and PtGA were 7.2 and 7.4, respectively; mean J-HAQ was 0.3. MJS was reported in 18.8% of pts with a mean duration of 38.4 minutes. Mean CIS was 24.1. Factors that significantly contributed to EQ-5D-5L were pain-VAS (48.8%), CIS score (18.1%) and PtGA (15.6%), and 82.5% of variance in EQ-5D-5L was explained with those three PROs. [Conclusions] This study demonstrated that the contribution factors on EQ-5D score in RA pts who met SDAI remission were pain-VAS, CIS and PtGA.

P1-048

Clinical factors that correlate with being Boolean remission during rheumatoid arthritis treatment

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Conflict of interest: None

[Objective] Clinical factors that correlate with being Boolean remission during rheumatoid arthritis (RA) treatment was investigated. [Methods] Patient has been treated under treat to target strategy since August 2010. In these, a group who attained Boolean remission and at the same time, attained remission with clinical disease activity score (CDAI) just previously (CDAI-R), a group who could not attain CDAI remission (CDAI-F), and a group who could not attain Boolean remission despite attaining CDAI remission (Boolean-F) were picked up. Patients' clinical factors during treatment are compared with ANOVA technique, statistically. [Results] In 608 patients, 255 CDAI-R, 161 CDAI-F, and 28 Boolean-F were recruited. Significant higher mean age, lower education level, higher modified Health Assessment Questionnaire at remission, higher CDAI score and higher EugoQol 5th Dimension-5L score before remission demonstrated in the Boolean-F than in the other groups. The pain score in the CDAI-R demonstrated significantly more improvement than in the CDAI-F group. The other factors demonstrated no significant difference between any pair of the groups. [Conclusions] Some conditions were suggested to attain Boolean remission. Initial target before attaining Boolean remission is to attain CDAI remission.

P1-051

Validity and precaution for evaluation of patients with rheumatoid arthritis based on GLFS-25 score

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Conflict of interest: None

[Objective] The purposes of this study are to check validity and to clarify precautions for evaluation of RA patients based on GLFS-25 score. [Methods] GLFS-25 score, standing up test and 2 step test for locomotive syndrome (LS) and HAQ-DI and DAS28-CRP for RA are mesured on RA patients who visited our specialized outpatient for LS. [Results] 11 patients are analyzed. All are female, the mean age was 70±7.1 y.o., the mean duration of disease was 9±5.3 years, the mean HAQ-DI was 0.352±0.470 and the mean DAS28 was 2.2±1.05 (7 were remission, 1 was LDA and 3 were MDA). The mean GLFS-25 score was 16.4±12.4. 2 were grade 1 and 9 were grade 2 of LS. Both HAQ-DI and DAS28 significantly correlated with GLFS-25 ($r=0.89$ $p=0.0003$ and $r=0.70$ $p=0.017$ respectively by Pearson's correlation). GLFS-25 scores were relatively high compared to HAQ-DI and DAS28 with 2 patients, who were HAQ-DI: 0, DAS28: 1.43, GLFS-25: 16 and HAQ-DI: 0.125, DAS28: 1.45, GLFS-25: 21. Both got remission of RA but had extra-articular pains such as low back pain, which made GLFS-25 higher than expected from HAQ-DI and DAS28. [Conclusions] GLFS-25 significantly correlated with HAQ-DI and DAS28 on RA patients as previously reported. It should be noted that a patient with extra-articular may has high GLFS-25 score even got remission.

P1-052

Analysis of joint destruction in rheumatoid arthritis patients treated with biologics

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Conflict of interest: None

[Objective] We aimed to investigate factors predictive of structural remission one year after Tumor Necrosis Factor (TNF) inhibitor or non-TNF inhibitor administration in patients with rheumatoid arthritis (RA). [Methods] In the patients treated with TNF inhibitor (Infliximab 60, Etanercept 65, Adalimumab 48, Golimumab 4) or non-TNF inhibitor (Abatacept 24, Tocilizumab 44), modified Total Sharp Score (mTSS), DAS28-ESR, mHAQ, MTX, NSAID, PSL, RF, ACPA, and MMP-3 before and one year after administration were examined to explore the baseline factors predictive of structural remission ($\Delta mTSS \leqq 0.5$). [Results] 53.1% of all patients completed the structural remission. There was no significant difference between TNF inhibitor and non-TNF-inhibitor. Multivariate analyses revealed that stageI-II was the only factor predictive of structural remission. Receiver operating characteristic analysis revealed that stageII was the cut-off value with sensitivity 0.69 and specificity of 0.55. The 1-year structural remission rates of patients with stage less than or equal to II and in those with stage greater than II at baseline were 57.1% and 32.8%, respectively ($p < 0.01$). [Conclusions] The results of our study indicated that a baseline stage I-II might be a predictive factor for structural remission.

P1-054

Analysis of lung involvement in patients with human T-cell leukemia virus type 1 (HTLV-1)-positive rheumatoid arthritis (RA): a retrospective observational study

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Conflict of interest: None

[Objective] The aim of this study is to clarify the lung involvements of HTLV-1-positive patients with RA. [Methods] All participants in this study had already registered in Miyazaki HTLV-1 RA Registry study. One-hundred sixteen RA participants who had evaluated the lung involvements by the high-resolution computed tomography (HRCT) were enrolled in this study. To compare the clinical characteristics and the findings of HRCT, these participants were divided into two group as follows: 86 HTLV-1-negative and 30 HTLV-1-positive RA participants. [Results] There were no differences in the prevalence of lung involvements in HTLV-1-negative and positive RA groups (48% and 47%, respectively). There were also no differences in that age, sex, duration of RA, history of smoking, and prevalence of autoantibodies-associated with RA. The pattern of interstitial lung disorders according to HRCT was not differ between two groups. However, the prevalence of respiratory tract involvement such as bronchiolitis and bronchiectasis was higher in HTLV-1-positive group than in HTLV-1-negative group ($P = 0.0012$). [Conclusions] HTLV-1 infection may be involved in the lung involvement of patients with RA such as bronchiolitis and bronchiectasis.

P1-055

Pulmonary MAC infection complicated with airway disease by longitudinal sequential chest HRCT in RA patients

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Conflict of interest: None

[Objective] Air way disease of rheumatoid arthritis is extra-articular manifestation and is related with pulmonary ACPA. RA air way disease is developed to pulmonary cystic lesions mimicking honeycombing lung. [Methods] We assessed pulmonary MAC infection with RA airway disease by sequential long-term followed-up chest HRCT. Pulmonary MAC was diagnosed as 21 of 618 RA patients (mean age 73 years old, RA duration 11year). [Results] Following periods of bacteriological confirmed pulmonary MAC was 59 months, and mean sequential CT observation was 72 months. Seven of 21 MAC patients with RA airway disease were developed to multiple cystic lesions. High titer RF (237 U/mL) and ACPA (237 U/mL) were shown, but anti-MAC antibody was positive at 43%. RA patients developed to cystic bronchiectasis with MAC infection could not achieve adequate RA therapy. Pulmonary MAC patients consisted with middle lobe syndrome were treated by MTX or biologics (ABT, TCZ, GLM). Anti-MAC therapy by CAM, RFP, EB, STFX was underwent 14 patients. Four of 7 patients with pulmonary cystic lesions were dead, but 3 were negative sputum culture for long term, and without administered MTX or biologics. [Conclusions] Adequate RA therapy may be regulated progressive developed MAC infection and RA airway disease.

P1-057

Multiple intracranial or pulmonary rheumatoid nodules in the patients with rheumatoid arthritis treated with biological agents: two case reports

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Conflict of interest: None

[Case presentation] The first case was a 75-year-old woman, who was diagnosed as rheumatoid arthritis (RA) in 2007, being treated with Golimumab. In May 2017, computed tomography (CT) revealed a nodule in the right lower lobe. She was diagnosed as having rheumatoid nodules (RN) after video-assisted thoracic surgery (VATS) biopsy in April 2019. Since June 2019, she became to behave abnormally. Cranial CT revealed a mass in the left occipital lobe. We diagnosed it also as RN after tumorectomy. She was treated with predonisolone and improved immediately. The second case was a 75-year-old woman, who was diagnosed as RA in 1995, being treated with Abatacept. She experienced hemosputum in January 2019. CT revealed multiple nodules in bilateral lung. She was diagnosed as having RN after VATS biopsy. Despite strengthen treatment for RA, they tended to increase. As blood culture revealed MRCNS and chest contrast-enhanced CT revealed them presented as ring-enhancing lesions, she was treated with vancomycin as lung abscess. However, they remained increasing in size. Then she was treated with predonisolone and improved immediately. [Discussion] Recently there are few reports of RN except of subcutaneous. Here, we report two cases of having multiple RN, with showing impressive pictures.

P1-058

A case of accelerated progressive RA-IP

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Conflict of interest: None

A 70-year old male was came to my department of our hospital because of seronegative arthritis. The diagnosis of RS3PE was made and steroid therapy was started. The arthritis was cured successfully. About a year after, arthritis recurred, This time, ACPA and RF were positive. The diagnosis of RA with IP was made. Because IP finding was rather subtle, MTX was started. Several months after he complaint short of breath, respirator physician noticed exacerbation of IP. Steroid therapy was started and MTX was stopped, but IP was still progressed and RF was remarkably elevated. Strengthened steroid therapy was and finally calm down the activity to the plateau state. Etiology of RA-IP was multifactorial, this case showed many suggestions of pathological process of RA-IP.

P1-059

KL-6 is a useful marker to monitor the progression of RA-ILD, but not to diagnose or predict the development of ILD

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Conflict of interest: None

Objective: To determine whether KL-6 elevation is useful to diagnose ILD, to predictnewly developing/worsening ILD, and to monitor the progression of ILD. **Methods:** A retrospective cohort study. Subjects were 129 consecutive RA patients and received HR-CT examination before and during biologics therapy and serum KL-6 levels were measured before the therapy. Chest radiography was taken before biologics. When KL-6 levels were above 400 U/ml, KL-6 was judged as elevated. A sequential KL-6 examination was carried out in 86 cases. CT findings were accepted gold standard for the existence of ILD. **Results:** Subjects were M/F; 44/85, mean age; 51.6 year old, disease duration; 7.9 years, and RF-positivity; 83%. ILD was found in 48 patients (37%). KL-6 elevation was found in 10/81 (11.3%) of non-ILD patients and in 23/48 (48%) of ILD ones. The sensitivity and specificity of KL-6 elevation for ILD were 0.48 and 0.87, respectively. KL-6 at the entry failed to predict newly emerging/worsening of ILD. On the other hand, increasing KL-6 levels during the observation period was associated with newly emerging/ worsening of ILD. **Conclusion:** KL-6 is a useful marker to monitor activity of ILD, but not to diagnose and predict it.

P1-060

An unusual case of subclinical alveolar hemorrhage as the first manifestation of rheumatoid arthritis

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Conflict of interest: None

A 69-year-old woman who presented with polyarthralgia predominantly in her hands and wrists with leg edema. Laboratory studies demonstrated high-positive ACPA and RF. ANA, ANCAs, anti-SSA/anti-SSB antibodies were all negative. Although she had no respiratory symptoms, a chest CT scan showed ground-grass opacities and reticular shadows in bilateral lungs. Her bronchoalveolar lavage fluid findings indicated alveolar hemorrhage. She was diagnosed as alveolar hemorrhage associated with rheumatoid arthritis. She was treated with corticosteroidA (PSL0.6mg/kg) and MTX, her arthritis and lung lesions improved. Few studies have reported cases of alveolar hemorrhage associated with rheumatoid arthritis. To our knowledge, this is the first case report of alveolar hemorrhage as the first manifestation of RA. We consider that subclinical alveolar hemorrhage may occur as complication of rheumatoid vasculitis.

P1-061

Risk of Biological DMARDs (BIO) for worsening interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] To investigate the risk factors for worsening ILD/AD in RA patients under the BIO therapy. [Methods] There were 22 RA-ILD/AD patients using BIO between April 2012 and December 2018 in our hospital. Subjects were M/F: 8/14, mean age M/F: 69/76 y.o., and 7 patients had smorking history. Among the 22 patients, 20 had ILD (NSIP pattern: 8, OP pattern: 8, UIP pattern: 4, 2 had ILD+AD), and remain 2 had AD. 11 patients received abatacept (ABT), 5 received tocilizumab (TCZ), 7 received etanercept (ETN), 6 received adalimumab (ADA), 1 received golimumab (GLM). [Results] After BIO therapy initiation, among 22 patients, 4 patients showed ILD exacerbation, 1 patient showed improvement, 17 were unchanged in X-ray/HRCT. 4 excavation cases were M/F: 3/1, 3 patients had smoking history; 1 had NSIP pattern and 3 had UIP pattern; 2 received ABT, 1 received TCZ, 1 received ETN. [Conclusions] Just like previous reports, men and smoking history are considered risk factors for exacerbation of ILD. The UIP pattern tended to be worse than the NSIP pattern. Although AD have been reported as a risk factor for worsening of ILD/AD, in this study no exacerbations were observed in patients with AD. There was no consistent trend for worsening ILD/AD by BIO, but the only case that improved was ABT user.

P1-062

Autoantibody profiles in rheumatoid arthritis associated interstitial lung disease

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) is often complicated with rheumatoid arthritis (RA) as an extra-articular manifestation. Acute exacerbation of ILD also occurs in patients with RA. RA associated ILD (RA-ILD) and acute exacerbation of ILD in RA influence the prognosis of RA. Acute exacerbation of ILD is frequently observed in dermatomyositis patients with anti-MDA5 antibodies. However, no autoantibodies were reported to be associated with RA-ILD or acute exacerbation of ILD in RA. In the present study, we investigated autoantibodies associated with RA -ILD or acute exacerbation of ILD in RA. [Methods] Sera from RA patients with or without ILD were collected. Sera from RA patients with acute exacerbation of ILD were also collected on admission, and in the stable state. Autoantibodies in the sera were comprehensively analyzed by ProtoArray; selected autoantibodies were validated by ProtoPlex and GST capture ELISA methods. [Results] The results from ProtoArray analyses were not confirmed bv ProtoPlex or GST capture ELISA. [Conclusions] We tried to reveal autoantibodies associated with RA -ILD or acute exacerbation of ILD in RA. However, we were not able to detect them in the system used.

P1-063

Analysis about the combination effect of the steroid drug in the primary treatment for rheumatoid arthritis

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Conflict of interest: None

(Objective) After announcement of EULAR2016 recommendations, positioning of the steroids in the RA initial treatment have been changed. However, there is not enough evidence for the benefits of steroids combined with initial RA treatment for Japanese patients. Therefore, we tried to verify the effects of steroids in the initial treatment of RA in Japanese patients. (Methods) Among patients who introduced MTX as an initial RA treatment in our hospital between 2014 and 2018, 30 patients in the PSL combination group (P group) and 26 patients in the non-combination group (N group) were selected for the analysis. And we retrospectively examined RA disease activity from their medical record. (Results) Comparison of the time course of SDAI (0w/6w/12w/24w/52w) when RA treatment start was 0w, the P group showed a significantly lower SDAI score only at 6w. The number of SDAI remission cases at 6w was higher in the P group. When the components of SDAI at 6w were compared, there were no significant differences in the number of tender joints, PtVAS, MDVAS, and CRP, but the number of swollen joints tended to be small in the P group. (Conclusions) Our results suggest that the combination of ste-

roids in the initial treatment of RA may contribute to the early remission of RA.

P1-064

The efficacy of glucocorticoid combination treatment for newly diagnosed rheumatoid arthritis

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Conflict of interest: None

Objective: In EULAR recommendation (2016), it is recommended MTX or csDMARD treatment with short term and low dose glucocorticoid (GC) after diagnosis of rheumatoid arthritis (RA). The aim of study is to evaluate GC combination treatment for newly diagnosed RA. Method: In this retrospective study, we evaluated 54 untreated RA patients (63.0% of women, average age 62.7 years old, and average disease duration 4.6 months) newly diagnosed in our clinic after 2017. Clinical course compared GC combination (GC+) or not (GC-) for 1 year. Result: GC+ and GC- cases were 37 (68.5%) and 17 cases (31.5%). The average age, disease duration, and MTX combination rate were 64.7, 58.3 years old, 4.4, 5.0 months, and 73.0, 100% in each group. First GC average dose was 6.9 mg/day. Discontinuation rate was 48.6% at six months and 70.3% at 1 year. Combination rate of bDMARD or JAKi were 34.6%, 55.6%, and 17.6% each in GC discontinuation, continuation, and GC-. Serious adverse event was seen in two cases of GC+ (perforation of duodenal ulcer and acute appendicitis). Conclusion: GC+ suffers from control of the disease activity, and it is often needed combination of bDMARD or JAKi and GC. Long term treatment plan for RA is important to consider GC combination with taking adverse event in future.

P1-065

Influence of intraarticular injection with triamcinolone for rheumatoid arthritis patient

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Conflict of interest: None

[Objective] Influence of intraarticular injection with triamcinolone (TCN) for rheumatoid arthritis (RA) patient was reviewed retrospectively, and evaluated statistically. [Methods] RA patients who were injected intraarticularly with TCN from April 2014 to March 2019 were picked up. Their clinical parameters are compared before to after injection with one sample T-test. Patients were classified according to number of injection. Change of clinical parameters including bone mineral density (BMD) were compared between pair of the groups with one Tailed T-test. [Results] 1020 times for 208 patients with 53 male and 155 female were injected as 70.3 as mean age. All components of simplified disease activity index and pain score with visual analog scale demonstrated significant reduction after injection, although no significant change of modified Health Assessment Questionnaire demonstrated. No significant difference demonstrated any pair of the groups, while BMD in lumbar spine tended to increase in single injection group than in other more injected groups, yet no statistical significance. [Conclusions] Intraarticular injection is useful for disease activity and pain control, however did not improve activity in daily living. There remains some debate about influence by number of injection.

P1-066

Management of liver impairment and gastrointestinal symptoms in patients on MTX treatment~Usefulness of daily administration of Foliamin 1mg/day~

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Conflict of interest: Yes

[Background] From February 2012, use of MTX up to 16 mg/week became possible. However, dose-dependent adverse events such as liver impairment and gastric disorders posed challenges. Interventions such as increased foliamin dose were routinely applied. [Objective] Clinical efficacy of changing foliamin dose from 5 mg/week to 1 mg daily for liver impairment and gastric disorders in MTX-treated patients was investigated at the author's institution. [Methods] Among rheumatoid arthritis (RA) out-patients on MTX, 156 with liver impairment and 48 with gastric disorders were studied. Mean age was 57.2years, mean MTX dose 11.0 mg/week, mean AST (GOT) at the change was 53, and mean ALT (GPT) 80. Changes in symptoms were assessed up to 3 months. [Results] 1) Liver impairment symptoms improved significantly at 1 month, and continued uneventfully up to 3 months. MTX dose decrease was needed for 27patient while an increase was possible for 7. 2) Gastric symptoms disappeared in 30 patients after 1 month, in 14 after 2 months, 1 after 3 months, and 3 after 4 months with no decrease in MTX dose. [Conclusions] Changing the foliamin dose to 1 mg daily was shown to be an effective intervention option for such gastric and liver adverse reactions of MTX

P1-067

The effects of methotrexate (MTX) are related not only to the MYX dose but also area under curve (AUC)

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Conflict of interest: None

[Objective] We have reported that the dose of MTX is significantly less in RA patients of more than 75 years than those less than 75 years. However, SDAI at the final observation was not different and speculated relation to the reduced renal excretion of MTX. The effects of MTX is mediated by MTX-PG in cells, and the concentration of MTX-PG is related to AUC. Here we calculated the AUC of MTX and studied the relation to clinical effects. [Methods] Subjects were 318 patients with RA on MTX with the mean age of 64 years. The average dose of MTX was 8.5+/-3.2 mg. AUC was calculated referring the report by Suzuki et al. (TDM study, 1998), and the following parameters were used; absorbance 0.7, V/f 0.665 (L/kg), Kel 0.365 (/hr) when CCr is 100ml/min, and Tmax 1.1 hr. [Results] The calculated mean AUC was 738 (mcg/ml * hr) +/- 286. AUC correlated well with the dose of MTX (rs = 0.71), but 3 times difference was found in patients with 10 mg of MTX. The dose of MTX was significantly less in patients more than 75 years than those less than 75, but the AUC the same (743 vs 737). The difference of DAS28ESR between the first visit and the last visit correlated significantly not only with the MTX dose but also with AUC. [Conclusions] Calculation of AUC seems to be useful.

P1-068

Prospective multicenter study of MTX reduction in patients with RA patients maintaining low disease activity

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Conflict of interest: None

(Objective) We prospectively examined whether bone destruction progressed 48 weeks after declining or discontinuing MTX and treatment continuity (UMIN000028875). (Methods) The subjects were RA patients with DAS28-CRP following low disease activity for 24 weeks or more after MTX administration, and having no joints of PDUS Grade 2 or more by bilateral hand sonography. The presence or absence of joint destruction progress was evaluated by the joint X-ray evaluation by the mTSS method at 1 year after the start of MTX reduced dose administration. Evaluation of clinical indices and the continuation rate after MTX reduction were also evaluated. (Results) The subjects were 78 (17 males, 61 females). Age average 60.9 years, disease duration 4 years 4 months, MTX dose 8.43 mg / w, DAS28-CRP 1.52, DMARDs (24.3%), ACPA 192.7 U / ml (70.5%), RF 55.6 IU / ml (65.4%). MTX was reduced from an average of 8.43 mg / w before study to 5.46 mg / w one year later. In the treatment evaluation, DAS28-CRP increased from 1.52 to 1.84. 89.7% did not progress joint damage. The one-year continuation rate was 78.2%. (Conclusion) Patients

with continuation of low disease activity and finger and wrist joint echo PDUS grade 0-1 satisfy almost no joint destruction even after MTX reduction.

P1-069

Factors related to the continuation rate of iguratimod in our hospital

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Conflict of interest: None

[Objective] To clarify the factors related to withdrawal or reduction of iguratimod (IGU) due to adverse events (AE) in our hospital. [Methods] There were 209 patients of rheumatoid arthritis who were adiministered IGU from July 1, 2013 to January 31, 2019. Patients we could not follow more than three months were excluded. [Results] Of 209 cases 168 were women, the mean observation period was 26.8 ± 21.1 months, 63.2 ± 13.1 years of age, and body weight was 54.9 ± 11.6 kg. 65 cases (31.1%) showed withdrawal or reduction. There were 43 cases (20.6%) of withdrawal or reduction due to AE. Gastrointestinal symptoms were 17 cases, nephropathy: 5 cases, hepatic disorder: 6 cases, cytopenia: 4 cases, skin symptoms: 4 cases, infection: 3 cases, other AE: 4 cases, inadequate response: 14 cases, symptom improvement: 5 cases, and other 3 cases. Univariate analysis did not reveal any risk factors for withdrawal or reduction by AE. Stepwise logistic regression analysis showed that DAS28-ESR (OR: 1.37, 95%CI: 1.003-1.885, p=0.0449) is a significant risk factor. [Conclusion] There is a high possibility of withdrawal or reduction of IGU due to AE when patients are in high disease activity at the time of oral start.

P1-070

Efficacy of iguratimod for rheumatoid arthritis in elderly patients

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Conflict of interest: None

[Objective] We compared the efficacy of IGU in elderly group (75 years or older; Group A, 57 patients) with the non-elderly group (younger than 75 years; Group B, 133 patients). [Methods] 190 patients who were able to continue IGU more than 3 months were included. Their background, the change of CRP, the use of MTX and glucocorticoid, and the DAS28-ESR (before, 6, 12, and 24 months) were compared. [Results] The averaged age at the beginning of IGU was 79.9 yrs. in Group A, and 59.9 yrs. in Group B. The averaged disease duration was significantly longer in Group A than in Group B (14.8 vs. 8.5 year). Although the averaged doses of MTX were not statistically different, the rates of MTX use were significantly fewer in Group A (28.1 vs. 56.4%). The rate of glucocorticoid use was significantly higher in Group A (56.1 vs. 36.1%), but the averaged dosage did not show a difference. The CRP level was significantly higher in Group A at the beginning of IGU (2.0 vs. 1.2 mg/dl), but no difference was found after 6 months. The DAS28-ESR showed that more than 60% of cases were low disease activity or remission in both groups, and there was no difference between 2 groups. [Conclusions] The efficacy of IGU for elderly patients did not show differences with non-elderly people.

P1-072

Iguratimod is particularly effective in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To examine the short-term outcomes of iguratimod (IGU) and related effective factors in patients with rheumatoid arthritis (RA). [Methods] We examine retrospectively changes in disease activity from 0 to 12 weeks, EULAR good response rate in 61 RA patients who continue IGU for 12 weeks or more. [Results] Patient background: 17 males, 44 females, average age 65.4 years, disease duration 6.5 years, use of MTX 38 cases, MTX dosage 7.0 mg, use of biologic agents 8 cases, use of PSL 9 cases, and PSL dose 0.5 mg. Number of tender joints, number of swollen joints, patient VAS, DAS28-CRP, and SDAI improved significantly from 2.33, 3.59, 44.1, 3.51 and 15.2 at 0 week to 0.98, 2.36, 31.9, 2.52 and 9.2 at 24 weeks. EULAR good response was 21 cases, moderate response was 13 cases, and no response was 27 cases. The age was 70.5 in good response group (G), 62.7 in moderate and no response group (MN) (P=0.02), number of tender joints was 3.2 in group G, 1.9 in group MN (P=0.03), DAS28-CRP was 3.86 in group G, 3.33 in group MN (P=0.02), there were significant differences. In multiple logistic regression analysis, elderly was extracted as an independent factor related to good response. [Conclusions] IGU was effective at 12 weeks in RA patients. Elderly was a factor related to good response.

P1-073

The efficacy and safety of iguratimod for rheumatoid arthritis patients who were resistant to DMARD therapy

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Conflict of interest: None

[Purpose] We evaluated the efficacy and safety of IGU for DMARD-resistant RA. [Methods] Of 71 RA patients in whom IGU had treated September 2012 through March 2017, 52 patients who were followed up at least 12 months at our hospital were examined. Prognostic factors for IGU efficacy were determined by comparing clinical factors between the groups with and without SDAI≦11 after 6-month IGU treatment. [Result] Average age 70.5 ± 10.5 years (9 males, 42 females), disease duration 9.1 ± 11 years, CRP 1.7 ± 2.0mg/dL, ESR 5 ± 32mm/hr, MMP3 248 ± 425ng / ml, RF 172 ± 309U/ ml, SDAI 13.2 ± 8.37. IGU was added on other DMARD-treatment, including biologics in 3, csDMARDs in 35 (MTX in 28, SASP in 6, and 1 BUC). All patients had a history of other csDMARDs use. PSL dose 2.1±2.6 mg/day in 26 patients. IGU had been continued over 6 months in 50% of the patients. The mean values of SDAI before administration in the groups with and without SDAI≦11 were 10.5 and 16.4 (P: 0.02), respectively. The disease durations were 8.2 and 10.1 years, MTX combinations 73.0% and 61.5%, and PSL combinations were 52.9 and 50%. [Conclusion] These results suggest that IGU may be more effective for RA patients who insufficiently respond to other DMARD therapy than those with active RA.

P1-074

Efficacy of add-on iguratimod in patients with rheumatoid arthritis who inadequately respond to either tocilizumab or tumor necrosis factor alpha inhibitors

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Conflict of interest: None

[Objective] This study aimed to evaluate the efficacy of add-on iguratimod (IGU) in patients with rheumatoid arthritis (RA patients) who inadequately respond to either tocilizumab (TCZ) or tumor necrosis factor alpha inhibitors (TNFi). [Methods] Twenty-three RA patients treated with TCZ (the TCZ group) and 17 RA patients treated with TNFi (the TNFi group) were enrolled in this 24-week retrospective study from our multicenter registry. All inadequate responders to either TCZ or TNFi received add-on IGU. Baseline demographics and disease activity at 24 weeks after initiating add-on IGU were compared between the two groups. [Results] Baseline clinical disease activity index (CDAI) values in the TCZ group

and TNFi group were 14.1 and 13.0 (p=0.52 between the two groups). At 24 weeks, CDAI values in the TCZ group and TNFi group were 5.15 and 8.18 (p=0.002 and 0.001 compared to baseline, respectively) and ΔCDAI values were -8.92 and -4.81 (p=0.023 between the two groups). Multiple linear regression analysis revealed that add-on IGU in the TCZ group was associated with greater improvement in CDAI relative to the TNFi group. [Conclusions] Add-on IGU was more effective in inadequate responders to TCZ than in inadequate responders to TNFi.

P1-075

Analysis of biologics from the viewpoint of age of patients at initiation

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Conflict of interest: None

[Purpose] In elder rheumatid arthritis (RA) cases, the frequency of complications is high, and powerful drug therapy may be a concern. RA cases introduced with biologics (BIO) were analyzed from the age of introduction. [Subjects and Methods] We examined 527 patients who had introduced BIO to naive patients by the end of 2018 from the viewpoint of age of patient introduction. [Results] The breakdown of 527 cases was 110 males and 417 females (79.1%). The age at introduction was 11 to 83 years, with an average of 58.2 years. By age group: 10 years: 3 cases, 20 years: 14 cases, 30 years: 43 cases, 50 years: 124 cases, 60 years: 163 cases, 70 years: 103 cases, 80 years: 14 cases. The 60s were the most common. The number of drugs used and the average age were: infliximab: 174, 54.6, etanercept: 94, 61.5, tocilizumab: 92, 58.3, adalimumab: 80, 58.6, abatacept: 60, 63.4 Golimumab: 20 cases, 62.1, Certolizumab pegol: 4, 54.5, and JAK inhibitor 3, 58.0. [Discussion] In elderly patients, abatacept, etanercept, and golimumab were often used. In addition, subcutaneous injections were often used rather than intravenous infusion. Even in elderly RA cases, it is considered that BIO treatment can safely elicit efficacy if conditions are met.

P1-076

Treatment for elderly RA patients in Kitasato University Hospital

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Conflict of interest: None

[Objectives] In this study, we examined the clinical features of elderly RA patients in this hospital in order to clarify the treatment contents for elderly RA patients. [method] We created a database of RA patients undergoing Kitasato University Hospital, evaluated DAS28ESR, SDAI, and CDAI, and collected and analyzed the treatment content and complications of infection during the past year. [Results] There were 569 cases: 334 under 70 years and 235 over 70 years old. The administration rate of MTX was 73.05% under 70 years old, 57.87% over 70 years old, and the usage rate was significantly lower in the group 70 years old and over. The average dose of MTX was 9.14 ± 2.92 mg / week for those under 70 years old, and 8.60 ± 2.55 mg / week for those 70 years of age and older. MTX usage was significantly lower in the 70 years and older group. The usage rate of csDMARD tended to be high in the group over 70 years of age, and there was no significant difference in the usage rate of bDMARDs. There was no significant difference between the two groups in DAS28ESR, SDAI, and CDAI. [Conclusions] The treatment of elderly RA patients showed a tendency to use MTX at a low rate or amount, but it was confirmed that disease activity could be controlled by concomitant use of other DMARDs.

P1-077

Proper use of the biological DMARDs which made an index of the degree of nursing

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Conflict of interest: None

What can we do for decrease of the social security expenses? For nursing costs is expected to squeeze medical costs, we have to regard medical costs together with nursing costs. Biological DMARDs (bDMARDs) for rheumatoid arthritis (RA) suppress disease activity, bone destruction and improve ADL and IADL. But when complication is worse, ADL may not always rise. The bDMARDs cannot continue forever expensively. Proper use of the bDMARDs was considered from the point of view regarded as medical treatment together with nursing by used degree of nursing. When compare of continuation of bDMARDs use in RA 129 patients in our hospital, 54 out of 86 patients in no degree of nursing, 16 out of 24 patients who need support, but only 2 out of 17 patients who need nursing. Actually, use of bDMARDs by a need of nursing was cut down. The most reason of cancellation of bDMARDs is hospitalization beside of RA. The disease which damages ADL, disuse atrophy and dysfunction of RA origin because of bDMARDs loss during hospitalization rise to the degree of nursing. We suggest that bDMARDs are used aggressively until to need nursing for suppression of rising degree of nursing. Conversely, bDMARDs had to cancel into 1 degree of nursing for decrease of the social security expenses.

P1-078

Usefulness of weekly subcutaneous tocilizumab treatment in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We examined the usefulness of switching from biweekly to weekly subcutaneous tocilizumab (TCZ) treatment in patients with rheumatoid arthritis (RA) for 9 months. [Methods] Ten patients (average age= 60.8 years, disease duration=16.6 years) were examined. Six patients concomitantly used methotrexate (MTX) and 7 used prednisolone (PSL). Disease activity (DAS28-ESR) and dose change of these medications were evaluated in these patients retrospectively. [Results] 1) In comparison with DAS28 in biweekly TCZ (3.38±1.08), DAS28 was decreased in 3 month after switching to weekly TCZ (1.76±0.93, $p<0.05$). None achieved SDAI remission in biweekly TCZ treatment, but 4 patients were in remission after 9 months. In 2 patients, TCZ was discontinued because of insufficient response and economical reason. 2) ESR was improved in 3 months (16.7→5.6 mm/h, $p<0.05$), but average value of CRP was not different between before and after switching to weekly TCZ. 3) Both MTX (10→6 mg/week, $p<0.05$) and PSL (7.5→2.8 mg/day, $p<0.005$) doses can be reduced in 9 months after switching to weekly TCZ. [Conclusion] Although CRP value is well controlled by biweekly TCZ, switching to weekly TCZ treatment should be considered for patients who will achieve SDAI remission and/or reduce dose of PSL or MTX.

P1-081

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 (4.73mg/day) /13 (1.94). Bio-naïve: 6/11. [Methods] Efficacy of ABT and GLM was evaluated by DAS28, CDAI and SDAI for 312 weeks. [Results] 1) Mean DAS28 at the

baseline (ABT/GLM): 5.87/5.80, CDAI 25.47/23.42, SDAI 28.64/27.48. Disease activity was significantly decreased in both groups. The ratio of LDA + remission increased significantly until 24 w and maintained until 260 w in both groups. No significant difference in both groups. 2) Adherence rate at 52 w showed more than 80% in both groups and that at 104 w 69.2%, at 156 w 61.5%, at 208 w 46.2%, at 260 w 42.3% in ABT, 56.0%, 40%, 36%, 32% in GLM. No significant difference in both groups.3) HAQ-DI was significantly improved after 12 w in ABT. 4) Both levels of CRP and MMP-3 were significantly reduced in GLM after 12 w, while the only CRP level in ABT after 52 w.5) Drop-out reasons (ABT/GLM); inadequate response 5/7, cancer1/1, organizing pneumonia 0/1, pneumonia 1/1, EBV reactivation 1/1, remission1/0 and so on. [Conclusion] Efficacy and adherence of ABT and GLM were similar.

P1-082

The evaluation of Akita Orthopedic Group on Rheumatoid Arthritis registry 2019 patients who received adalimumab

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Conflict of interest: None

[Objectives] The aim of this study is investigating of the profiles of rheumatoid arthritis patients who received adalimumab (ADA). [Methods] We evaluated 95 patients in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry (mean age, 64.2 years) who received ADA. [Results] The average age of initiation was 58.2, and the mean disease period was 130 months. The cases had Steinbrocker classification stages I/II/III/IV (26/18/22/29 patients), classes 1/2/3/4 (42/36/15/2 patients). Eighty-two patients (86.3%) received methotrexate (MTX; mean dosage, 8.25 mg/week); and Fifty-five (57.9%), prednisolone (3.25mg/day). Biologics naïve patients are 83 and continued therapy provide in 48 patients (50.5%) in 2019 registry. The mean CRP was 3.98 mg/dl and MMP-3 was 205.3 ng/ml in the first ADA administration. The mean follow-up period was 96 weeks (Maximum 106 Months). Forty-seven patients had failure of ADA administration. The therapy was discontinued because of primary failure and changing hospital in 12 cases respectively and secondary failure in 8, Clinical remission and cessation and Pneumonia in 4. [Conclusion] The patients who received ADA had a high combination rate with MTX, high continuation rate, and good results, and were therefore appropriately selected and treated.

P1-084

A case of resuming etanercept during pregnancy and continuing to delivery

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Conflict of interest: Yes

A 34-year-old woman was diagnosed with rheumatoid arthritis at age 24. She was treated with Methotrexate (MTX), but she stopped taking medicine with hope of pregnancy and gave birth to her first child when she was 30 years old. After normal delivery, joint symptoms worsened, followed by immediate restart of MTX and additional introduction of etanercept (ETN) 3 months. At the age of 32, MTX was withdrawn with the hope of raising a baby again, followed by and withdrawal of ETN after confirming pregnancy, but she had stillborn baby at the 16th week of pregnancy. Although ETN was resumed but the disease was strong, the patient switched to subcutaneous injection of tocilizumab (TCZ). DAS28CRP 5.11, at the time of pregnancy confirmation, PSL 5mg / day was started at 6 weeks of pregnancy, ETN was resumed at 12 weeks of pregnancy, and tacrolimus (TAC) was started at 20 weeks of pregnancy. ETN 50 mg / week + TAC 2 mg / day + PSL 5 mg / day resulted in DAS28CRP 1.28, normal delivery at 38 weeks of gestation while maintaining low disease activity, and the child was healthy. Although ETN is considered to have relatively little placental migration, there are few reports of continuing ETN until delivery. If disease activity is high, continuing ETN during pregnancy is also an option.

P1-085

Etanercept therapy outcome in elderly rheumatoid arthritis patients: an investigation of the Akita Orthopedic Group on Rheumatoid Arthritis registry

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Conflict of interest: None

[Objective] We aimed to investigate the continuation rate for ETN therapy, reasons for discontinuation, and therapeutic effects among elderly RA patients. [Methods] Among 245 AORA-registered patients starting ETN therapy between January 2009 and August 2018, data for the 19 patients who were ≧80 years old at the initiation of therapy were evaluated. We evaluated the 1-year cumulative continuation rate for ETN therapy, and investigated the characteristics of patients who discontinued treatment. We evaluated efficacy in 15 patients based on EULAR criteria. [Results] The 1-year cumulative continuation rate for ETN therapy was 78.9%. Fourteen patients discontinued treatment. The reason for discontinuation was 6 adverse events and 4 lack of efficacy. A mean age of 82.2 years at the start of treatment, with a mean disease duration of 9.2 years, 21.1% of patients switching from another biologic agent, and a comorbidity rate of 73.7%. Efficacy was noted for 53.3% of all patients with 52 weeks of ETN therapy. [Conclusions] Retention rate and efficacy were considered satisfactory in elderly RA patients receiving ETN therapy. The risk of adverse events was suggested to increase with increasing age, declining ADL, and presence of comorbidities.

P1-086

A case of systemic lupus erythematosus developed during administration of a TNF inhibitor for rheumatoid arthritis

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Conflict of interest: None

A 70 years old female was diagnosed rheumatoid arthritis (RA) because of polyarthritis, CCP antibody and RF positive in June three years before. She was administered of MTX 10 mg, PSL 5 mg, and BUC 200 mg, but her moderate disease activity persisted, so etanercept (ETN) 50 mg / week was started in May two years before. Thereafter, remission was achieved, and the dose of MTX was reduced to 8 mg, and PSL was stopped. She presented nail circumference erythema in January this year, erythema on the cheek in May, and nail bed bleeding in June. A blood test showed an increase in antinuclear antibody (ANA) 320 times (homoge-

neous and speckled type), anti-DNA antibody 15.6 IU / ml. It was thought that systemic lupus erythematosus (SLE) developed during the use of TNF inhibitor for RA, so ETN was discontinued, and hydroxychloroquine (HCQ) was introduced in anticipation of effects on SLE and RA. Thereafter, the CRP level tended to decrease again, and erythema on the cheek was also improved. It has been well known that TNF inhibitor treatment for patients with RA is associated with ANA development. The effects of cytokines by TNF inhibitor administration have been suggested, and the usefulness of JAK inhibitors has recently been studied. We report on the pathophysiology and treatment of this case.

P1-087

Safety and efficacy of the injection-interval compression for subcutaneous tocilizumab therapy in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We evaluated safety and efficacy of the injection-interval compression for subcutaneous tocilizumab (TCZ-SC) therapy in RA patients. [Methods] 29 RA patients who received TCZ-SC therapy with injection-interval compression due to inadequate efficacy to TCZ therapy were reviewed in our hospital. [Results] Age: 67.7±12.5 years, disease duration: 15.4±14.2 years, stage1.2: 28%, class1.2: 97%, Biologics use: 79.3%, PSL dosage: 5.7±1.9mg/day, PSL use: 24.1%, MTX dosage: 7.3±3.9mg/week, MTX use: 20.7%, CRP: 0.6±2.2mg/dl, SDAI: 17.8±10.3, and HAQ-DI: 0.7±0.5. After 2.5 years, the continuation rate of the injection-interval compression for TCZ-SC therapy was 73.1% by Kaplan-Meier curves. SDAI at 0, 4, 12, 24, and 52 weeks were 17.8, 12.1, 9.7, 8.1, and 7.6. SDAI at 4, 12, 24, and 52 weeks were significantly lower than SDAI at 0 week. Disease activity (remission/low/moderate/high) at 0, 4, 12, 24, and 52 weeks were (0/32/46/21), (11/36/50/4), (22/44/30/4), (26/43/30/0), and (29/48/24/0). 9 patients who discontinued the injection-interval compression for TCZ-SC therapy because of ineffectiveness (n=2), safety issues (n=3), remission (n=3), and others (n=1). [Conclusions] The injection-interval compression for TCZ-SC therapy in RA patients was well tolerated and effective in daily practice.

P1-089

Comparison of safety and efficacy between Sarilumab (SARI) and Tocirizumab (TCZ) in our hospital

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Conflict of interest: None

[Objective] To investigate the comparison of efficacy and safety between SARI and TCZ [Methods] 22 patients of SARI prescription and 23 patients of TCZ prescription (IV: 15patients, SC every 2 weeks: 8 patient) are the subject which has passed for more than 24 weeks after prescription starting in our hospital. Two group were compared about persistency rate, reason of dropout, background at the prescription starting time, and ΔCDAI, ΔMMP3 and ΔHAQ at the 24 weeks. [Results] The backgrounds at baseline were impartial intentionally by two groups. Persistency rate is SARI group/TCZ group: 72.7%/73.9%. Reason of dropout are 2 patients: side effect, 2 patients: invalidity, 1 patient: economical reason in SARI group and 2 patients: side effect, 2 patients: invalidity, 1 patient: economical reason in TCZ group. Each index were SARI group/TCZ group: (comparative p value between two groups) CRP: 2.04→0.19/1.52→0.01 (0.307), ΔCDAI: -5.74/-7.80 (0.718), ΔMMP3: -123.9 ng/ml /-125.8 ng/ml (0.765) and ΔHAQ: -0.06/-0.244 (0.205). [Conclusions] Persistency rate of two groups was impartial, and significant improvement was indicated at 24 weeks, but the significant difference wasn't admitted by SARI and TCZ by comparison between the group.

P1-090

Treatment with Tocilizumab for elderly patients and non-elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To assess the safety and efficacy of tocilizumab (TCZ) in patients with RA. [Methods] We conducted a retrospective study of TCZ use in 28 RA patients in our hospitals between 2010 and 2016. These patients were divided into 2 groups by the age of 65 years old. They were evaluated at January 2019. [Results] In elderly group (n=12) who were ≧65 years old, TCZ had been started at 67±7.6 years old, and mean age at the evaluation was 75±8.3. In non-elderly group (n=16) who were <65 years old, TCZ had been started at 47±12 years old, and mean age at the evaluation was 54±11. TCZ retention was 66% in elderly group and 63% in non-elderly group at 5 years after the initiation of treatment. The rate of CDAI remission was 33% in elderly group and 31% in non-elderly group at 5 years after the initiation of treatment. Six arthroplasty were performed in six patients of elderly group, and two arthroplasty were performed in two patients of non-elderly group. There was one adverse event discontinuation of TCZ that was suture abscess at total hip arthroplasty in elderly group, and there was two adverse event discontinuation of TCZ in non-elderly group that were one pneumonia and one septic arthritis in the shoulder. [Conclusions] TCZ efficacy was same in elderly group and non-elderly group.

P1-091

Long-term use of tocilizumab in our hospital in an aging region

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Conflict of interest: None

[Purpose] The status of using TCZ was judged by Kaplan-Meier method. We also compared elderly patients (over 70) and non-elderly (under 70) and examined the transition of medications. [Cases] Number of cases 48 (10 males, 38 females), mean age at introduction 69.2 years (23 to 89), mean disease duration 16.3 years (0.5 to 45), 17 cases with MTX at introduction (average 9.4 mg / week, 4-16 kg), stage1:1 2:12 3:5 4:30, class1:6 2:36 3:6 4:0, 27 cases are ongoing: 1st: 4 2nd: 12 3rd: 13 [Results] The survival rate of 48 cases was 64%, up to 113.2 months, compared with 63.8% for use and 63.5% for non-use at the start of MTX. In addition, the comparison between 70 and older was 64.2% under 70 was 66.9%. Changes in MTX and PSL in 27 cases, the starting average doses were 9.8mg and 3.2mg, but at the survey, it was reduced to 2.4mg and 0.7mg. [Discussion] If DA was got worse, the biologics will have to be changed if the DMARDs don't work. A high survival rate can be considered to maintain DA. In addition, MTX / PSL was able to be reduced in continuation cases, and there was no difference in effect even by age, so TCZ was able to reduce the amount of other DMARDs while continuing, and it was aged without side effects. It is highly likely that it will be possible to continue for the elderly.

P1-092

The efficacy of Tocilizumab therapy in rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy in tocilizumab therapy with rheumatoid arthritis (RA) and tapering of methotrexate. [Methods] This study comprised 36 patients with rheumatoid arthritis intolerant to biologic DMARDs. Patients received tocilizumab therapy with methotrexate for 12 months. The outcomes were assessed with the disease activity during 12 months study period, using the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate (DAS28 ESR) and Clinical Disease Activity Index (CDAI). [Results] DAS28ESR (from 3.5 to 1.4) and CDAI (from 5.5 to 0.6) decreased significantly from baseline to Week 52.

DAS28ESR Remission achieved in 30 cases at Week 52. Tocilizumab monotherapy was also effective with RA patients of in adequate response to antiTNF inhibitor therapy. The retension rate of tocilizumab at 52 weeks was 90%. The average dose of methotrexate tapered from 8.1mg to 5.0mg. The average dose of glucocorticoid also tapered from 7.2mg to 2.6mg. [Conclusions] These results suggested that tocilizumab therapy is effective in patients with RA of an inadequate response to other biologic DMARDs.

P1-093

To evaluate the short-term efficacy and safety of Salirumab in 15 cases of high-activity rheumatoid arthritis with high MMP-3 in our clinic

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Conflict of interest: None

[Objective] To evaluate the short-term efficacy and safety of 15 cases over 12 w after administration of SAR. [Method] 15 patients (3male, 12female) with RA with high MMP-3 (average: 387.5ng/L) who visited our clinic from Aug 2018 to July 2019 (average 65 y, disease duration 0.8years, ACPA250.9 RF43.9 DAS28-CRP5.26 JHAQ2.07, PSL combined 5 cases, MTX combined 8 cases, Bio naive 9 cases) SAR and echo guided steroid local joint injection combined therapy is performed and the short-term treatment effect and safety are evaluated. [Results] At 12 w, functional remission occurred in 10 of 15 cases, and MMP DAS HAQ, articular echo showed significant improvement in GS PD and 5 cases achieved functional remission within 6w. In comparison with 10 patients in functional remission group and 5 patients in non-remission group Bio naïve rate, RA disease duration, RA Stage, MMP before administration Significant difference was observed. Non-serious infection and moderate rash, Mild cytopenia, Liver damage was observed in 3 cases, and 2 cases in the non-remission group were discontinued due to infection and rash. [Discussion] It is suggested that SAR is effective as First Bio in highly active early RA patients with high MMP levels, and it is hoped that long-term effects will be sustained in the future.

P1-094

Clinical short-term results of Sarilumab for long standing RA patients with severe complications

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Conflict of interest: None

[Objective] To evaluate efficacy and safety of sarilumab for patients with difficult RA (inadequate response to DMARDS) and severe complications. [Methods] 23patients received subcutaneous sarilumab 200mg every 2 weeks. Efficacy measurements included Clinical Disease Activity Index (CDAI), the drug survival rates with Kaplan-Meier methods, C-reactive protein (CRP)<0,1mg/dL and Adverse events (AE). Baseline data as above, Age 70.4±9.9, Duration RA 18.3±14.0 years, ACPA-positive: 22 (91.7%), RF-positive: 20 (83.3%), Prior biologic DMARD exposure: 20 (83%), CDAI baseline HDA (14) / MDA (6) / LDA (4) Medical history was 6malignant (included MTX-LPD), 5renal failure, 5pulmonary disease. [Results] CDAI was 21.5±9.7 (baseline) 15.9±8.7 (4w) 13.4±7.7 (8w))10.6±7.6 (12w). The drug survival rate at 1 year of Kaplan-Meier methods was 91.7%. The rate below CRP<0,1mg/dL was 100% (21/21). 2patients dropped within 3months reason of Primary failure. 10 minor AEs was complicated, but none led to discontinuation like serious infectious disease. [Conclusions] Treatment of difficult RA (inadequate response to DMARDS or Biologics, long duration, elderly, severe cimplication) with Sarilumab resulted early and durable efficacy outcomes, safety profile, the stable drug concentrations by negative CRP at 12 week.

P1-095

The efficacy of sarilumab at 6 months in patients with rheumatoid arthritis in our institution

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Conflict of interest: None

[Objective] To assesse the efficacy and safety of sarilumab (SAR) in patients with rheumatoid arthritis. [Methods] Twenty second RA patients were initiated SAR in our institution from June 2018 to September 2019, and 15 of them were continued SAR over three months. DAS28-ESR and CDAI were assessed at the point of 0,1,2,3,6months. And we investigated about adverse events within the 6 months. [Results] DAS28-ESR / CDAI after initiation of SAR decreased as follows; DAS28-ESR/CDAI 0month: 5.13/20.90, 0.5month: 3.62/13.60, 1month: 3.16/11.20, 2months: 2.36/7.04, 3months: 2.03/5.88, 6 months: 1.80/5.09, with significant difference (respectively, $p<0.01$/$p<0.01$) after the first month. Remission rate of DAS28-ESR/CDAI was as follows; 0month: 6.7%/0%, 3months: 67%/27%, 6months: 80%/47%, and under low disease activity rate was as follows; 0month: 6.7%/13%, 3months: 87%/87%, 6months: 87%/87%. The incidence of adverse events (AEs) rate were 86% and 70% of them were some kinds of infectious disease and 3 cases had severe infections needed administration. There were no dead case because of AEs. [ConclusionsThese data indicate that SAR therapy is safe and effective from the early phase. Infectious diseases should be cautioned as much as other biologics.

P1-096

Safety and Efficacy of Sarilumab in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] In recent years, the treatment of rheumatoid arthritis (RA) is drastically improved, and we can choose many therapeutic modalities against RA. Tocilizumab, one of biological agents, is the first anti IL-6 receptor antibody that is approved in Japan in April 2008. The second anti IL-6 receptor antibody, Sarilumab is approved in Japan in September 2017. We surveyed safety and efficacy of Sarilumab in patients with rheumatoid arthritis. [Methods] Involved in this study were 6 patients who received Sarilumab at Saitama Medical University Hospital or Ogawa Red Cross Hospital from March 2019. Their clinical characteristics, such as CDAI, HAQ-DI, CRP, ESR, RF, MMP-3, and adverse events were evaluated. [Results] Mean age 65y.o. Four females. Disease duration; 11 years. Two PSL users. Six MTX users. Mean CRP; 1.34mg/dl. RF positive; 67%. Median CDAI; 42. Median HAQ-DI; 0.73. The patients included four TNF inhibitor failures, one ABT failure and one TCZ failure. ESR and CRP decreased at 4 weeks in all patients. CDAI significantly decreased at 4 weeks. HAQ-DI did not change in 12 weeks. Dose of MTX and PSL did not change. [Conclusions] There were no biologics-naïve patients, but CDAI improved in 4 weeks after initiating Sarilumab. No critical adverse events in the observation period.

P1-097

Real-world retrospective study of rheumatoid arthritis patients treated with sarilmab

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Conflict of interest: None

[Objective] This study aimed to assess the real-world efficacy and safety of sarilmab (SAR) in rheumatoid arthritis (RA) patients by studying the clinical cases retrospectively. [Methods] 35 patients received SAR were enrolled. Background information, treatment responsiveness and adverse reactions were evaluated retrospectively. The features of SAR in the therapy of RA were discussed. [Results] Mean age was 63.3 year-old (18-82 year-old, median: 67 year-old). 63% achieved low disease activity (LDA) of SDAI. 26% were treated with methotrexate (MTX). SAR were effective with MTX in 56% and without MTX in 85%. In 97% SAR were switched from other bDMARDs; 57% were from tocilizumab (TCZ). TCZ was switched due to secondary failure (57%) and partial effectiveness

(14%). In them, 57% and 100% achieved LDA respectively. 3 cases ≧ 80 kg achieved LDA. Adverse reactions were mouth ulcer (4), administration site reactions (3), and rash (2). SAR was discontinued in a case with rash. [Conclusions] SAR was effective and tolerated in a real-world setting. SAR was useful in the cases without MTX, and cases switched from TCZ. While biweekly s.c. TCZ can be less effective in cases with high body weight, SAR was effective in them. This study suggests selection criteria of IL-6 inhibitor therapy for RA.

P1-098

Analysis of Sarilumab Use: Single Center Experience

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Conflict of interest: Yes

[Objective] Sarilumab is the second anti-interleukin 6 inhibitor approved for rheumatoid arthritis in Japan. It has become available for clinical use since Feburary 2018. There have not been enough data for real-world use in Japan. This study aims to describe our experience of Sarilumab use. [Methods] The charts of patients on Sarilumab at St. Lukes International Hospital were reviewed retrospectively and clinical information was analyzed. [Results] Total 22 patients were identified. Twenty-one patients (95.5%) were female and the median age was 62 years. The median duration of disease was 7.5 years and rheumatoid factor/anti-CCP antibody were positive 81.8% respectively. The half of the patients used methotrexate concomitantly and 40.9% used glucocorticoids. Ten (45.5%) patients used two or more biologics or targeted synthetic disease modifying agents (tsDMARDs) prior to Sarilumab use. The average days of Sarilumab used observed were 194+-157 days. No serious adverse event was observed. The continuation rate and factors associated with discontinuation of Sarilumab were analyzed via Kaplan Meier Survival curves. [Conclusions] Sarilumab showed relatively good continuation rate and no serious adverse event was observed despite being used for treatment refractory cases.

P1-099

Efficacy of sarilumab therapy in patients with rheumatoid arthritis: retrospective single-center study

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Conflict of interest: None

[Objective] The aim of our study was to examine efficacy of sarilumab therapy in the patients with rheumatoid arthritis (RA). [Methods] Twenty-seven patients with RA who underwent sarilumab treatment in our hospital between April 2018 and May 2019 were examined. [Results] Twenty-four patients were females, the average age was 66.7 ± 14.4 years, and the mean disease duration was 10.8 ± 10.7 years. The mean CRP was 1.52 ± 2.11 mg /dL, ESR 31.2 ± 22.3 mm/h, HAQ 1.15 ± 0.97 and MMP-3 269.7 ± 352.7 mg/dL. Methotrexate was used as concomitant therapy in 9 patients, tacrolimus in 5 patients, salazosulfapyridine in 15 patients, and prednisolone in 4 patients. Four patients were naïve to bDMARDs, and 10 patients were failed to one bDMARDs. The mean DAS28-ESR at baseline was 4.63 ± 1.16. DAS28-ESR was significantly improved to 2.81 ± 1.12 at 4 weeks, to 2.90 ± 0.85 at 12 weeks, and 2.13 ± 1.24 at 24 weeks ($p<0.0001$, $p<0.0001$, and $p<0.0001$, respectively). At 24 weeks, achievement of DAS28-ESR < 2.6 in bDMARDs naïve or failed to one bDMARDs patients were significantly higher than that in failed to two or more failed bDMARDs patients. [Conclusions] These results suggested that salirumab may effective in bDMARDs naïve or failed to one bDMARDs patients.

P1-100

The efficacy and the safety of sarilumab for patients with rheumatoid arthritis in University of Tsukuba hospital

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Conflict of interest: None

[OBJECTIVE] To clarify the clinical features of patients with rheumatoid arthritis (RA) treated with sarilumab (SAR), and its efficacy and safety profile. [METHODS] Seven cases with RA treated with SAR in University of Tsukuba hospital from February 2018 until July 2019 were included in this study. We retrospectively evaluated 1) characteristics, 2) efficacy, and 3) safety of SAR. [RESULTS] 1) Mean age and disease duration were 54.7±16.6 years old and 9.7±7.3 years, respectively. Four cases exhibited moderate or severe disease activity. Methotrexate was concomitantly used in 4 cases. All patients had been treated with one or more biologics, of which tocilizumab (TCZ) had been used in 3 cases. 2) SAR improved CDAI to low disease activity or remission in 4 cases including 2 cases refractory to TCZ at 6 weeks. Three cases assessed with ultrasonography showed improvement of synovitis within 10 weeks after initiation of SAR. SAR was discontinued in 3 cases, of which discontinuation due to ineffectiveness was only one case. 3) Adverse events were occurred in 2 cases (injection site erythema and infusion reaction). [CONCLUSION] SAR was effective for RA patients refractory to prior biologics including TCZ and may lead to rapid improvement of disease activity.

P1-101

Experience with Sarilumab Therapy at Our Clinic

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Yu Family Clinic

Conflict of interest: None

[Subjects] Eight patients with rheumatoid arthritis (RA) [Methods] We administered sarilumab 200 mg subcutaneously to 5 RA patients (2 with concomitant methotrexate [MTX] use) naive to biologics and 3 RA patients (2 with concomitant MTX use) who switched from tocilizumab. We examined changes in C-reactive protein (CRP) levels, 28-joint Disease Activity Score-erythrocyte sedimentation rate (DAS28ESR), Simplified Disease Activity Index (SDAI), patient global visual analog scale (VAS) scores, and Health Assessment Questionnaire Disability Index (HAQDI). [Results] In all patients, CRP levels decreased from week 4 and remained at 0.3 mg/dL or lower from week 8. DAS28ESR also started decreasing in week 4. At week 8, DAS28ESR was <2 in 6 patients, indicating remission, while 2 patients had low disease activity. Six patients achieved SDAI-defined remission by week 8. Global VAS scores improved by 50% or more by week 4. HAQDI was significantly lower from week 8. The mean HAQDI was 0.5 or less, indicating remission. Patients who switched from tocilizumab responded adequately to sarilumab. [Discussion] Sarilumab therapy was clinically effective from week 4 and throughout follow-up. No adverse events occurred. Sarilumab is comparable to other biologics and may be a useful first-line biologic.

P1-102

The effect of sarilumab in a rheumatoid arthritis patient with previously treated methotrexate -associated lymphoproliferative disorder

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Conflict of interest: None

It is reported that a part of rheumatoid arthritis (RA) patients receiving methotrexate (MTX) develop lymphoproliferative diseases. Nevertheless, treatment methods for RA patients who had previously treated methotrexate-associated lymphoproliferative disorder (MTX-LPD) was still controversial. We report a case of a patient of 84-years-old female who was administrated sarilumab as a RA treatment after treatment for MTX-LPD. The patient had mass lesion of the tongue. The biopsy specimen revealed that it was a diffuse large B-cell lymphoma and was positive for Epstein-Barr virus-encoded RNA. Mediastinal lymphoma was found by the chest CT. High level of sIL-2R and LDH values in blood were also showed. Therefore, we suspected MTX-LPD and discontinued MTX. From 3 month after MTX discontinuation, the mediastinal lymphoma started to regress and the mediastinal lymphoma disappeared on the CT image at 6 months. Followed by mass regression, high level of sIL-2R and LDH values started to decrease and return to normal at 12 months. Whereas, RA disease activity gradually increased at 6 months after MTX discontinuation and were not controlled by salazosulfapyridine. So sarilumab was administrated after mass regression and has been successfully effective without recurrence of lymphoma.

P1-103

Perioperative management in RA treated with JAK inhibitors

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Conflict of interest: None

[Objective] Currently, three JAK inhibitors (JAKi) are available in Japan. : Tofacitinib (TOF), Baricitinib (BAR), and Peficitinib (PEF). As the number of surgeries in RA treated with JAKi increases, adverse events such as delayed wound healing (DWH), surgical site infection (SSI), and flare up of rheumatic symptoms during drug withdrawal are a concern. The purpose of this study is to investigate SSI and flare up of the disease in patients with RA to make useful perioperative guideline. [Methods] Between January 2015 and November 2019, we experienced 31 operations in RA patients treated with JAKi. The breakdown of that was 28 cases of TOF, 2 cases of BAR, and 1 case of PEF. Regarding the subject cases, we investigated perioperative withdrawal period, frequency of DWH / SSI, flare up of RA symptoms during perioperative period. [Results] Only 2 DWH cases were found in postoperative wound healing. RA symptoms flare up after withdrawal of the drug was observed in TOF / BAR / PEF 11/1/1 cases, and on average 13.5 / 16.0 / 15.0 days after withdrawal, symptoms were observed. [Conclusions] We require further investigation about surgical site infection and the flare up of rheumatic symptoms during perioperative period in RA treated with JAKi, aiming to establish perioperative management.

P1-104

Orthopaedic procedures without discontinuation of Baricitinib during the perioperative period in patients with Rheumatoid Arthritis. Case reports

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Conflict of interest: None

[Purpose] Perioperative discontinuation of JAK inhibitor has a risk of disease flare-up due to its short half-life. We retrospectively examined the cases underwent orthopaedic procedures without discontinuation of Baricitinib (BARI). [Methods] We investigated blood sampling data, surgical site infection (SSI), and wound healing delay (DWH) in 2 cases and 4 operations of RA patients. [Case 1] A woman in her 40s, thumb CMj and MPj arthroplasty were performed simultaneously. At another time, a tendon transfer operation for EPL rupture and revision surgery for the artificial finger joint of index finger MPj were performed. After that, recurrent rupture occurred and tendon transfer was performed again. [Case 2] A woman in her 60s underwent thumb MPj fusion and thumb CMj arthroplasty. [Results] Removal of the needles was carried out on average 13 days after surgery, and DWH and SSI were not observed in all operations. In one operation, the lymphocyte count decreased (520 / μl) on the day after the operation, but then recovered. [Conclusion] At present, the results of the current reports might provide useful information that a particular population of patients might undergo orthopaedic surgery safely without discontinuation of BARI.

P1-105

Denosumab may delay bone healing in joint-preserving foot arthroplasty

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Conflict of interest: Yes

[Objective] Denosumab is used to treat osteoporosis and to suppress the progression of bone erosion associated with rheumatoid arthritis (RA). Although denosumab strongly inhibits bone turnover, its effects on fracture healing have not been fully elucidated. In this study, we investigated the effect of denosumab on bone healing in joint-preserving foot arthroplasty. [Methods] We included 170 feet of 47 patients who underwent distal metatarsal osteotomy for hallux valgus and/or metatarsophalangeal joint-preserving foot arthroplasty for lessor toes from January 2013 to December 2018. The time when callus formation and bone fusion were observed by post-operative X-ray was evaluated. [Results] Denosumab was used in 28 feet of 7 patients. At 95 days after surgery, 75% of the denosumab group and 82% of the non-denosumab group had callus formation. On day 180 after surgery, 57% of the denosumab group and 72% of the non-denosumab group showed bone fusion, and the denosumab group required significantly longer days for bone fusion. Bone union was obtained in 93% in the denosumab group and 94% in the non-denosumab group at the final follow-up, which showed no significant difference. [Conclusions] The use of denosumab may delay bone union in joint-preserving foot arthroplasty.

P1-106

Eight cases of biologic-naïve rheumatoid arthritis initiated with abatacept newly

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Conflict of interest: None

[Objective] The aim was to evaluate the clinical aspect for 8 RA cases used with abatacept in the biological-naïve cases. [Results] Total 8 cases of RA were 2 males and 6 females, and average age was 68.9±17.1 [31-88] years (6 cases are over 65 years). All cases were used csDMARDs and duration of RA was 39.9±34.4 [6-79] month. Three cases were newly treated with RA in our hospital, and 5 cases are transmitted from other hospital for the administrating with comorbidities or social reasons. The averaged value of DAS28-ESR was 5.27±1.11 [3.14-6.76], and disease activity were 6 cases of HDA, 1 case of MDA, and 1 case of LDA. Comorbidities were included with 3 cases of kidney disease and 3 cases of lung disease. Six cases of 8 were examined the clinical course after initiating with abatacept. One case reached remission and 2 cases were reached LDA. The case of remarkably high value of CCP or MMP-3 were obtained with good response, despite the cases of high dose of MTX users were poor outcomes. [Conclusions] Abatacept might be a candidate for the treatment in active RA cases with elderly, cases with many comorbidities, or cases without using MTX.

P1-107

Patient-reported Outcomes from RAJ4, A Randomized, Double-blind, Placebo-controlled Study of Peficitinib (PEF, ASP015K) in Patients with Rheumatoid Arthritis (RA) with An Inadequate Response to Methotrexate (MTX)

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Conflict of interest: Yes

[Objective] To analyze health-related quality of life (HRQoL) of Japanese patients with RA and an inadequate MTX response. [Methods] Multicenter, double-blind, placebo (PBO)-controlled study. Patients with active RA (<10 years) and inadequate MTX response were randomized to PEF 100 or 150 mg/day (PEF100 or PEF150) or PBO once daily + MTX. Patient- and physician-reported outcomes at Week 12/early termination were mean change from baseline in Short Form Health Survey 36 questions (SF-36v2) and Work Productivity and Activity Impairment Questionnaire (WPAI). [Results] 519 patients were treated. For PEF100 and PEF150 vs PBO, there were significant improvements in SF-36v2 physical component (6.60 [p<0.001], 9.02 [p<0.001], vs 0.57), mental component (3.28 [p<0.001], 2.50 [p=0.036] vs 1.07) and role/social component (2.30 [p=0.099; ns], 3.90 [p=0.002] vs -0.09). For WPAI, there were significant improvements for PEF100 and PEF150 vs PBO in % impairment while working due to problem (-11.71 [p=0.007], -15.96 [p<0.001] vs -2.42), % overall work impairment due to problem (-11.58 [p=0.010], -16.91 [p<0.001] vs -2.75]) and % activity impairment due to problem (-13.98 [p<0.001], -19.35 [p<0.001] vs -2.50). [Conclusions] PEF100 and PEF150 were associated with significant improvements in HRQoL vs PBO.

P1-108

Serious Infection Rates in Japanese, Korean and Taiwanese Adult Patients with Rheumatoid Arthritis (RA) Treated with Peficitinib (ASP015K), a Janus Kinase (JAK) Inhibitor: Pooled Safety Findings up to 6 Years of Treatment

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Conflict of interest: Yes

[Objective] To analyze rates of serious infections in RA patients treated with peficitinib (PEF). [Methods] Serious infections were monitored using 2 pooled safety data sets from 4 clinical studies of RA patients treated with PEF; 1) Phase 3 (P3) studies (RAJ3, RAJ4) and 2) P2/3 studies (P2b study RAJ1; extension study RAJ2, RAJ3, RAJ4). Pooled data from 3 overseas P2b studies (RA21, RA22, RA25) in RA patients were evaluated. [Results] Pooled P3 and P2/3 studies included 1025 and 1052 patients, respectively. In pooled P2/3 studies, during 2336.3 patient-years (PY) and with a maximum follow-up of 73.4 months, serious infections occurred in 57 patients taking PEF. The most common serious infections were pneumonia and herpes zoster. The incidence of serious infections (95%CI) per 100 PY in pooled P3 studies was higher for PEF 100mg (2.8 [1.3-5.9]), 150mg (3.2 [1.6-6.3]) and etanercept (2.0 [0.8-5.5]) than for placebo (no serious infection reported). For pooled P2/3 studies, the incidence was 2.5 (1.9-3.2), compared with 1.7 (1.1-2.7) for pooled P2b overseas studies. [Conclusions] In pooled P3 studies (overall period), the incidence of serious infection was higher for PEF than placebo, but no apparent dose-dependent increase was noted.

P1-109

Herpes Zoster-Related Disease Rates in Japanese, Korean and Taiwanese Adult Patients with Rheumatoid Arthritis (RA) Treated with Peficitinib (ASP015K), a Janus Kinase (JAK) Inhibitor: Pooled Safety Findings up to 6 Years of Treatment

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Conflict of interest: Yes

[Objective] To analyze rates of herpes zoster (HZ)-related disease in RA patients treated with peficitinib (PEF). [Methods] HZ-related diseases (HZ, varicella) were monitored using 2 pooled safety data sets from 4 clinical studies of RA patients treated with PEF; 1) Phase 3 (P3) studies (RAJ3, RAJ4) and 2) P2/3 studies (P2b study RAJ1; extension study RAJ2, RAJ3, RAJ4). Pooled data from 3 overseas P2b studies (RA21, RA22, RA25) in RA patients were evaluated. [Results] Pooled P3 and P2/3 studies included 1025 and 1052 patients, respectively. In pooled P2/3 studies, during 2336.3 patient-years (PY) and with a maximum follow up of 73.4 months, HZ-related diseases occurred in 140 patients receiving PEF. The incidence of HZ-related disease (95% CI) per 100 PY in the pooled P3 studies was higher for PEF 100mg (7.4 [4.7-11.8]) and 150mg (4.0 [2.1-7.4]) than for placebo (2.3 [0.6-9.4]) and etanercept (2.6 [1.1-6.2]). It was also higher for pooled P2/3 studies (6.5 [5.5-7.7]) than for pooled P2b overseas studies (1.4 [0.9-2.4]). The incidence of HZ-related diseases did not tend to increase with longer treatment periods. [Conclusions] In pooled P3 studies, the incidence of HZ-related disease was higher for PEF than placebo or etanercept; however, no dose dependency was observed.

P1-110

Malignancy Rates in Japanese, Korean and Taiwanese Adult Patients with Rheumatoid Arthritis (RA) Treated with Peficitinib (ASP015K), a Janus Kinase (JAK) Inhibitor: Pooled Safety Findings up to 6 years of treatment

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Conflict of interest: Yes

[Objective] To analyze malignancy rates in RA patients (pts) treated with peficitinib (PEF). [Methods] Malignancies (excluding non-melanoma skin cancer [NMSC]) were monitored using 2 pooled safety data sets from 4 clinical studies of RA pts treated with PEF; 1) Phase 3 (P3) studies (RAJ3, RAJ4) and 2) P2/3 studies (P2b study RAJ1; RAJ3, RAJ4, and extension study RAJ2), and pooled data from 3 overseas P2b studies (RA21, RA22, RA25). [Results] Pooled P3 and P2/3 studies included 1025 and 1052 pts, respectively. In pooled P2/3 studies, over a total of 2336.3 pt-years (PY) and a maximum follow up of 73.4 months, malignancies occurred in 22 pts receiving PEF (including 2 pts of NMSC, colon and gastric cancers [each 3 pts], and adenocarcinoma gastric and bladder cancer [each 2 pts]). Malignancy rates (excluding NMSC) (95%CI) per 100 PY showed no major difference in pooled P3 studies across PEF (0.6 [0.2-1.6]), placebo (1.2 [0.2-8.3]), and etanercept (0.5 [0.1-3.6]), or between pooled P2/3 studies (0.9 [0.6-1.3]) and pooled overseas P2b studies (0.4 [0.1-1.0]). In pooled P2/3 studies, malignancy rate (excluding NMSC) did not tend to increase with longer treatment periods. [Conclusions] Malignancy rates for RA pts treated with PEF were consistent with those treated with placebo or etanercept.

P1-111

Improvements in Disease Activities (LDA and Remission) in Rheumatoid Arthritis Patients Treated with Baricitinib Compared to Adalimumab or Placebo

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Conflict of interest: Yes

[Objectives] Time to achieve low disease activity (LDA) and remission (REM) was evaluated in MTX-IR RA patients (pts) treated with BARI compared to placebo (PBO) and adalimumab (ADA). [Methods] In a multi-country phase 3 study (RA-BEAM), MTX-IR RA pts were randomized 3:3:2 to PBO, BARI 4 mg, or ADA 40 mg. This post hoc analysis estimated the time to achieve LDA (CDAI ≦10) and REM (CDAI ≦2.8) in overall population, Japanese subset, and the subset of high baseline disease activity (HDA) defined as CDAI >22. Cumulative incidence of LDA and REM over 24 weeks were estimated. [Results] Median time to LDA with BARI (12 weeks) was 2 weeks shorter than ADA (14 weeks) while PBO pts never reached the median time to LDA during 24 weeks. Neither pts reached the median time to REM during 24 weeks. In Japanese subpopulation, median time to LDA were 12 weeks with both BARI and ADA. In overall, BARI treated pts were 1.1 (95%CI 0.9-1.3) and 1.4 (1.0-1.9) times more likely to achieve LDA and REM than ADA; 2.3 (1.9-2.8) and 3.5 (2.4-5.1) times compare to PBO. Consistent results were obtained in pts with HDA. [Conclusions] BARI pts were more likely to achieve LDA and REM, and at a faster pace, than ADA or PBO; Japanese subpopulation showed a similar trend.

P1-112

The clinical efficacy and safety of Baricitinib treatment in patients with RA experienced bDMARDs or tsDMARDs treatment in the TBC registry: 24-week outcomes

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Conflict of interest: None

[Objective] The aim of this study was to assess the 24-week outcome of Baricitinib (Bari) therapy in patients with RA experienced bDMARDs or tsDMARDs treatment in clinical routine practice. [Methods] RA patients who underwent Bari at TBCR study group were enrolled in this study. We compaired disease acrivities. Furthermore, discontinuation due to inadequate responses (IRs) and adverse events (AEs) were evaluated. [Results] Previous treatment was as follows; TNF inhibitor (TNF-i): 38 (44.2%), IL-6 inhibitor (IL6-i): 23 (26.7%), Abatacept (Tcell-i): 11 (12.8%) and JAK inhibitor (JAK-i): 13 (15.1%). The retension rate were similar between naive and switch group. In Switch group, we confirmed no differences in clinical responses and retention rate among the prior therapy. [Conclusions] This study demonstrated short term efficacy and safety of Baricitinib in clinical routine practice. Our results suggest that Bari would be beneficial for patients failed to prior bDMARDs or tsDMARDs.

P1-113

Efficacy of low-dose Baricitinib in Japanese elderly rheumatoid arthritis

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Conflict of interest: None

[Objective] Baricitinib (BAR) is a Janus kinase inhibitor with adjustable dosage according to the estimated glomerular filtration rate (eGFR). eGFR tends to be overestimated in the elderly versus younger individuals due to decreased muscle mass. The appropriate dosage of BAR in elderly rheumatoid arthritis has not been validated. We examined the efficacy and safety of low-dose BAR (2 mg) in active elderly rheumatoid arthritis. [Methods] Single-center, retrospective study involving Japanese patients aged ≧65 years with eGFR ≧60 ml/min/1.73 m^2. CDAI, HAQ-DI, safety and tolerability were evaluated after administration of low-dose BAR. [Results] The study included consecutive 34 patients (82% females; median age: 79 years; median eGFR: 76.7 ml/min/1.73 m^2; median disease duration: 60 months). Low-dose BAR significantly improved CDAI (from 27.4±13.4 to 3.8±4.0) and HAQ-DI (from 1.8±0.8 to 0.2±0.3). At week 52, 63% of the patients continued this study. CDAI remission was achieved by 14 patients (41%). Herpes zoster infection was observed in 5 patients. There were no serious adverse events observed. [Conclusions] In Japanese eldrely rheumatoid arthritis, low-dose BAR (2 mg) may be an effective option for the treatment of active RA even in patients with eGFR ≧60 ml/min/1.73 m^2.

P1-114

Efficacy and safety of baricitinib treatment in patients with rheumatoid arthritis including who switched from tofacitinib treatment

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of baricitinib (Bari) treatment in RA. [Methods] 56 patients with RA who were treated with Bari were enrolled. Clinical disease activity and AEs were evaluated during 24 weeks. In addition, the factors contributed to achievement of remission at 24 weeks were investigated. [Results] The mean age was 62.5 years old and mean disease duration was 11.9 years. 46 patients had been treated with biologics prior to Bari (mean number of previous use of tsDMARDs was 2.6). The mean DAS28-ESR decreased from 5.19 to 3.92 at 24 weeks. 15 patients archived remission defined by DAS28-ESR at 24 weeks. Multivariable logistic analysis showed that DAS28-ESR (low) at baseline and concomitant oral steroid use (no) were independently associated with achievement of remission. 12 patients experienced AEs and herpes zoster were most frequently seen. 14 patients were switched from tofacitinib (Tofa), and the Δ values of DAS28-ESR were -0.90. In the concomitant MTX (+) and (-), the Δ values of DAS28-ESR were -1.59, -0.86, respectively. [Conclusions] Although Bari treatment was less effective in the patients who switched from Tofa and without MTX-concomitant use, bari treatment was effective and the safety profile is comparable with other tsDMARDs during 24 week.

P1-115

Musculoskeletal Ultrasound examination (MSUS) revealed the early efficacy of Baricitinib treatment to rheumatoid arthritis patients

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Conflict of interest: None

[Objective] We evaluated the early efficacy of Baricitinib (BAR) by measuring Disease activity score and MSUS scores. [Methods] Between October 2017 and March 2019 in our institution, twenty-six RA patients under the first treatment of BAR were enrolled. Twelve among 26 patients were retrospectively analyzed at 4weeks BAR-treatment by evaluating TJC, SJC, patient VAS, physician VAS, CRP, DAS28-CRP, SDAI, and MSUS scores (GS and PD). [Results] Baseline patient characteristics (n=12) were as follows; Mean age: 59.3±16.1 years old, Median disease duration: 25 months, ratio of male to female (M: 3, F: 9). After 4weeks treatment in all patients, TJC was 5.1±5.6 vs 1.3±3.4 (pre. vs post., *p=n.s.*), SJC was 8.1±6.4 vs 3.8±4.5 (*p= n. s*), Patient VAS was 50.3±26.5 vs 30.9±26.4mm (*p=n. s*), Physician VAS52.3±26.8 vs 16.7±24.3mm (*p=0.003*), DAS28-CRP3.7±1.2 vs 2.2±1.1 (*p=0.005*), SDAI25.4±16.1 vs 10.2±11.7 (*p=0.015*), MSUS-GS2.3±0.5 vs 1.5±0.8 (*p=0.0097*), MSUS-PD2.1±0.7 vs 0.83±1.0 (*p=0.0019*), respectively. Correlation coefficient between Patient VAS, DAS28-CRP, SDAI and MSUS-PD were r=0.8, r=0.84, r=0.77 respectively. [conclusions] BAR treatment for RA patients was significantly improved VAS, Disease activity score and MSUS scores in 4 weeks. There were good correlations between Patient VAS, DAS28-CRP, SDAI and MSUS-PD.

P1-116

Effective of baricitinib on radiographic progression of structural joint damage at 1 year in patient with rheumatoid arthritis

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Conflict of interest: None

[Objective] We evaluated efficacy of baricitinib (bari) for RA patients who have inadequate response to csDMARDs or bDMARDs in clinical practice. [Methods] We included 39 Japanese patients with RA [female; 28 cases, bio-naïve (BN) 26 cases, bio-switch (BS) 13 cases]. Patients were scheduled to receive bari 4mg or 2mg once daily dose. We evaluated Δ modified total sharp score (ΔmTSS), Δ erosion score (ΔERN), Δ joint space narrowing score (ΔJSN). In addition, we assessed predictors for suppression of joint destruction at 1year after the treatment with bari. [Results] At baseline, mean age and disease duration were 67.9±10.9 years and 6.1±7.2 years, respectively. Twenty one and 19 patients were treated with baticitinib by a dose of 4mg/day and 2mg/day, respectively. Thirty six patients (79.5%) were in structural remission (mTSS≦0.5). Mean scores (ΔmTSS, ΔERN and ΔJSN) of all patients were (0.26, 0.13, 0.13), respectively. There were no significant differences in ΔmTSS between 2mg/day and 4mg/day of bari dose or between BN group and BS group. MMP-3 within standard value at 12 week was associated with the predictor (logistic regression analysis; OR=14.7, 95%CI: 1.6-136.2, P=0.018). [Conclusions] Bari has a favorable effect of structural joint damage in clinical practice.

P1-117

Guselkumab, an Anti-interleukin-23p19 Monoclonal Antibody, in Patients with Active Psoriatic Arthritis Who Were Biologic-Naive or Prior TNFa Inhibitor-Treated: Week 24 Results of phase 3, Randomized, Double-blind, Placebo-controlled Study (DISCOVER-1)

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Conflict of interest: Yes

[Objective] Guselkumab (GUS), an anti-IL-23p19 monoclonal antibody, is approved for psoriasis, psoriatic arthritis (PsA), generalized pustular psoriasis, etythrodemic psoriasis, and palmoplantar pustulosis in Japan. We assessed GUS efficacy and safety in DISCOVER-1 for PsA. [Methods] DISCOVER-1 is a Phase 3 trial in patients with active PsA who were biologic-naïve or prior TNFi-treated. Approximately, 30% of patients previously have received TNFi. Patients were randomized 1:1:1 to GUS 100mg every 4 weeks (Q4W); GUS 100mg at W0, W4, every 8 weeks (Q8W); or PBO. The primary endpoint was ACR20 at W24. Major secondary endpoints included; IGA response at W24; changes in HAQ-DI and ACR50/70 at W24. [Result] 381 treated patients were analyzed. Significantly more Q4W (58.6%) and Q8W (52.8%) vs PBO (22.2%) achieved ACR20 at W24. Significantly greater improvements in HAQ-DI were seen in GUS vs PBO at W24. Among patients with ≧3% BSA and IGA ≧2 at W0, significantly more GUS vs PBO achieved IGA response. Higher proportions of patients achieved ACR50/70 at W24. Serious AEs, serious infections, and death occurred in 2.4%, 0.5%, and 0.3% patients, respectively. [Conclusion] GUS significantly improved joint and skin symptoms and QOL for PsA. Observed AEs were consistent with GUS safety for PsO.

P1-118

Guselkumab, an Anti-interleukin-23p19 Monoclonal Antibody, in Biologic-naïve Patients with Active Psoriatic Arthritis: Week 24 Results of Phase 3, Randomized, Double-blind, Placebo-controlled Study (DISCOVER-2)

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Conflict of interest: Yes

[Objective] Guselkumab (GUS), an anti-IL-23p19 monoclonal antibody, is approved for psoriasis (PsO), psoriatic arthritis (PsA), generalized pustular psoriasis, etythrodemic psoriasis, and palmoplantar pustulosis in Japan. We assessed GUS efficacy and safety in DISCOVER-2, Phase 3 trials for PsA. [Methods] In DISCOVER-2, biologic-naïve patients with active PsA were randomized (1:1:1) to GUS 100mg every 4 weeks (Q4W); GUS 100mg at W0, W4, every 8 weeks (Q8W); or placebo (PBO). The primary endpoint was W24 ACR20. Major secondary endpoints at W24 were IGA response, changes in HAQ-DI, and modified vdH-S (mvdH-S). [Results] 739 treated patients were analyzed. Significantly more Q4W (63.7%) and Q8W (64.1%) vs PBO (32.9%) achieved ACR20 at W24. Among patients with ≧3% BSA &IGA ≧2 at W0, significantly more GUS vs PBO achieved IGA response at W24. Significantly greater improvements from baseline in HAQ-DI were seen with GUS vs PBO at W24. Mean changes in total mvdH-S at W24 were significantly lower for Q4W (0.29) and numerically lower for Q8W (0.52) vs. PBO (0.95). Serious AEs and serious infections occurred in 2.4% and 0.7%, respectively through W24. [Conclusion] GUS significantly improved joint and skin symptoms and QOL for PsA. Observed AEs were consistent with GUS safety for PsO.

P1-120

The clinical results of Lelièvre procedure for forefoot deformity with rheumatoid arthritis

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Conflict of interest: None

[Objective] We examined long-term results after Lelièvre proccedure. [Methods] 44 feet of 27 patients who underwent Lelièvre proccedure for forefoot deformity with rheumatoid arthritis between 1999 to 2009 were included in this study. The average age at surgery was 62.7 years and the follow-up period averaged 10.4 years. We examined AOFAS score, satisfaction, hallux valgus angle, MTP2 angle and M1M5 angle before and 5 years after surgery and at the final survey. [Results] The AOFAS score was 26.6 preoperatively, 65.8 postoperatively, and 69.9 at the final survey, which was significantly higher than before surgery ($P < 0.05$). Satisfaction at the final survey (3.05) decreased significantly compared to preoperative level (3.63). The hallux valgus angle improved significantly to 39.3 before surgery and 15.4 at 5 years after surgery, and was 12.2 at the time of the final survey. The MTP2 angle was 13.1 before surgery, 5.22 after surgery, and 8.33 at the time of the final survey. The M1M5 angle was 32.7 before surgery, 30.6 after surgery, and 26.3 at the final survey. [Conclusions] Lelièvre procedure achieved relatively good results and patient satisfaction even after 10 years of operation.

P1-121

Evaluation after total ankle arthroplasty (TAA) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Background] The results of total ankle arthroplasty (TAA) cannot be said to be stable. [Objective] The purpose of this study was to compare the clinical results of the Revision and non-Revision groups of RA patients who underwent TAA using the FINE Total Ankle System (Nakashima Medical Co., Ltd.) and the HAQ of the lower limbs. [Methods] At Osaka City University Hospital from 2001 to 2008, 14 patients who were able to follow up to 2019 with RA patients using FINE did. The changes in the lower limb HAQ of 4 Revision groups and 10 non-Revision groups were examined, and the sinking angle over time in X-ray evaluation was compared between groups by Mann-Whitney U test. [Results] Regarding the HAQ, both the Revision group and the non-Revision group worsened before and after surgery, but the non-Revision group was more satisfactory after surgery. There was no obvious significant difference at each initial installation angle and even at the time of the last follow-up between the two groups. [Discussion] Although there was no significant difference in the installation angle, the revision group tended to have a larger change in the implant installation angle. Although this time it was a small survey and we could not identify factors related to sinking, we would like to clarify the cause.

P1-122

Joint-preserving surgery for hyperextension of the hallux interphalangeal joint in patient with rheumatoid arthritis _ Case Report

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Conflict of interest: Yes

[Objective] The hyperextension of the interphalangeal (IP) joint is one of the major hallux deformity in RA patients; however, the surgical method for this deformity is not established. We here presented a case of RA patient in which the hyperextension of IP joint was successfully treated with combination of osteotomies. [Case] 69 y, F, RA disease duration of 45 years, Stage IV, Class 3. Remission with pharmacological treatment using biological agent. Chief complaint was painful callosity under the hallux. Physical findings revealed the hyperextension of the IP joint, callosity underneath, rocker bottom deformity, and contact with the ground at the IP joint. Lateral WB radiograph of the foot revealed 1) severe destruction of mid- and hindfoot joint and collapse of the medial arch, 2) elevation of the first metatarsal, 3) plantar deviation of the proximal phalanx, 4) hyperextension deformity of the distal phalanx. Several procedures were performed as follows; opening wedge osteotomy of the medial cuneiform for 2), plantar and proximal translation of the metatarsal head for 3), and tenotomy of the extensor hallucis longus for 4). At the follow-up of 3 and a half years after surgery, the patient is satisfied with the treatment without the recurrence of deformity and callosity.

P1-123

Treated with external fixation for peri-implant fracture After Total Ankle Arthroplasty in a rheumatoid arthritis patient

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Conflict of interest: None

[Purpose] Periprosthetic fractures after total ankle arthroplasty (TAA) are uncommon. In this report, we present a case of a 62-year-old female with rheumatoid arthritis who underwent external fixation for a periprosthetic ankle fracture. [Case] A 62-year-old female with rheumatoid arthritis onset in 1986 (steinbroker classification Class 2 stage 4), she underwent bilateral total elbow/hip/knee arthroplasty in the past. And then, she underwent TAA in 2013 and can walk with cane. In 2018 she fell down and periprosthetic ankle fracture (above the tibia implant) was observed with a blister around ankle, but the prosthesis was not loose in CT image. ORIF was very difficult, so external fixation was performed and continued for 3 months. We removed external fixation in 12 weeks after surgery because callus formation was seen in CT image and there is no instability in the fracture, and she started to walk. Bone union was seen in 4 months after surgery and she can walked with walker. [Discussion] Periprosthetic fractures after TAA are uncommon, but this treatment has not been established. The incidence of this fracure may increase with aging in the society, we think that the treatment by external fixation is one of the surgery option for a periprosthetic ankle fracture after TAA.

P1-124

A Case Report of Ankle Arthrodesis for Severe Valgus Foot Deformity with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We report a good result of joint fixation using retrograde intramedullary nail for advanced valgus deformity associated with dislocation of the talocrural joint caused by rheumatoid arthritis (RA). [Case] At age 36, he was diagnosed with RA and started treatment. From 56 years of age, he became aware of swelling and deformation of his right ankle joint, and his gait disturbance gradually progressed. The patient was admitted to our hospital at the age of 65 for surgery. A severe valgus deformity and swelling were observed. Surgery was performed using a retrograde intramedullary nail for the talocrural joint fusion. After the operation, full load was started with a cast from 4 weeks, and full load walking was permitted in about 2 months using a plastic short leg brace. At present, bone union is recognized, and it is possible to walk for a short distance by touching the sole. [Conclusions] Although the number of cases of joint deformity is decreasing due to the progress of treatment for RA, we still encounter a case of severe joint deformation. This time, there was a significant valgus deformity with dislocation, and tarsal bone fusion was also observed. Good results were achieved by valgus correction and joint fusion using retrograde intramedullary nails.

P1-125

Destructive arthritis with cutaneous polyarteritis nodosa requiring surgical intervention

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Conflict of interest: None

[Clinical significance] We report a case of cutaneous polyarteritis nodosa (CPN) patient associated with destructive arthritis of the right foot, accompanied by seronegative arthritis in the right ankle. A 63-year-old woman had been mediated with cyclosporine and prednisolone, due to livedo reticularis in the lower limbs, foot numbness and arthritis in the right ankle and midfoot. X-ray and CT revealed progressive joint destruction in the right talonavicular joint, and MRI demonstrated severe synovitis of the right tibiotalar joint. She had undergone arthrodesis of the talonavicular

joint combined with arthroscopic synovectomy of tibiotalar joint. Postoperatively, joint symptoms were completely resolved, together with the synovitis of the right foot and ankle. At the time of 4 years after surgery, no recurrence of the joint disease has been observed. Radiographs demonstrate good tarsal bone alignment, with bone union in the right talonavicular joint. This case represents the first description of presentation with surgical intervention for the foot and ankle, which are the most common sites for CPN-associated arthritis. Rheumatologists and orthopaedic surgeons should be aware of potential complications such as destructive arthritis when treating patients with CPN.

P1-126

A Mobidity of peri-prosthetic joint infection of RA patients post TKA operation

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Conflict of interest: None

[Objective] We tried to clarify the morbidity of PJI of the patients with rheumatoid arthritis (RA) post TKA operation and suspected the related factors of which. [Methods] The Patients with RA who was done TKA operation from January 2001 to December 2008, total number is 109, were included in this study. The ages at operations, gender, the durations of observations, medications at the time when infections occurred or the most recent visiting to our hospital, hemi lateral TKA or bilateral TKA, with or without PJI, and the times when PJI occurred were recorded from charts. Uni-variated regression analysis was done to select the related factors of PJI. P<0.05 was defined as statistically significance. [Results] Eight patients had suffered from PJI, that had occurred in 5 of them 5 years or more post TKA operation. The cumulative morbidity was 7.4 percent, 4 patients of who had been prescribed biological disease modified anti-RA drugs (bDMARDs), and 6 had been prescribed glucocorticoids. Cox hazard ratio of uses of bDMARDs were 1.84 (p=0.339), and that of glucocorticoids were 4.07 (p=0.087). [Conclusions] We clarified that the cumulative morbidity of PJI of the patients with RA 10 years or more post TKA operation was 7.3%. It may occur in relations with uses of glucocorticoid.

P1-127

Ultrasound assessment, not tenderness, at entheses reflects inflammatory condition in patients with psoriatic arthritis

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Conflict of interest: None

[Introduction] We reported that ultrasound (US) and clinical assessments were completely different when assessing enthesitis in patients with psoriatic arthritis (PsA). We investigated enthesitis as assessed clinically and by US in patients with PsA. [Methods] Forty-seven patients with PsA underwent US examination of the bilateral humeral medial epicondyles and insertions of the triceps, distal quadriceps, proximal/distal patellas, Achilles tendons, and plantar fascia. These 14 entheses were also clinically evaluated by tenderness. The associations between US and clinical enthesitis with disease activity (DAPSA, DAS28-CRP, PASE, PASI), inflammatory markers (CRP, MMP-3), radiographic damage (mTSS), functional status (HAQ), and axial involvement were investigated. [Results] Among 47 patients with PsA, 79% had US enthesitis (3.8±2.3 sites) and 49% had clinical enthesitis (3.5±2.8 sites). US and clinical enthesitis counts showed no correlation (r=0.15, p=0.30). The US enthesitis count correlated with the MMP-3 level (r=0.41, p=0.007), whereas the clinical enthesitis count correlated with the DAPSA, DAS28-CRP, HAQ, and PASE (r=0.50, p<0.001; r=0.44, p=0.002; r=0.41, p=0.008; r=0.54, p<0.001, respectively). [Conclusions] US enthesitis reflects the inflammatory condition.

P1-128

The investigation of the efficacy of biological agents for Psoriatic arthritis (PsA)

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Conflict of interest: None

[Objectives] We investigated the therapeutic effects of the biological preparations (Bio) in patients with PsA of our institute. [Methods] 12 cases with PsA were treated with Bio from 2007 to 2018, and the disease activity and Bio-persistence rate were investigated. [Results] The average age at onset of osteoarthritis in 12 cases was 38.1 years on average, 39.2 at diagnosis, and 42.6 at Bio induction. The follow-up was 56m (12-144). Peripheral arthritis was observed in all cases, and spondylitis was in 3. First Bio was ADA in 4 cases, IFX in 6 and ixekizumab in 2. On the use of first Bio, DAS28-CRP was decreased from 3.4 at the induction to 1.7 at 48w and 2.4 in the last follow. In 3 ADA cases and one IFX case, Bio was switched to IFX and ADA respectively due to secondary failure in 58m (36-76). The initial bio could be continued in 8 cases (67%). In a case who switched to INF, tuberculous pleurisy (suspected) occurred, and INF was stopped in 13m. The remaining 3 cases were able to continue 2nd-Bio. The dermatitis worsened in 2 cases with secondary failure, but in the remaining cases disappeared or improved. [Conclusion] Bio to PsA gave a marked improvement of disease activity at one year, but secondary failure or tuberculosis occurred in one thirds of cases with long-term use.

P1-129

A retrospective study of drug survival rate for Psoriatic arthritis (PsA)

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Conflict of interest: None

[Objective] To clarify the trend of treatment of PsA, we examined the continuation rate of treatment arms including newly appeared drugs. [Methods] PsA patients, who visited our clinic between 2008 and 2018 and who met the CASPER criteria, were included. Clinical information was retrospectively collected. The transition of therapy, average duration of continuation, drug survival rate were examined. [Results] Forty-five cases were included. Mean age and disease duration were 45.5 and 3.7 years, respectively. Of these, 60% were male, 22% on prednisolone (PSL). All were bio-naïve. As for the trend of usage, the number of each drug was increased in order of market launch. Interestingly, the increase rate of csDMARDs was not affected by the emergence of new drugs. Mean durations of drug survival (months) were 46 for csDMARDs, 39 for TNF inhibitors, 6 for a PDE4 inhibitor, 9 for IL-17 inhibitors, 7 for a IL-23 inhibitor. Continuation rate at 1 year was 76% for csDMARDs, 75% for TNF inhibitors, 50% for a PDE4 inhibitor, 43% for IL-17 inhibitors, and 0% for a IL-23 inhibitor. The main reason for cessation was inadequate response. [Conclusions] Our data suggest that the duration of the continuation of each drug was shortened because of the emergence of various agents and quick response.

P1-130

Characteristics of patients with psoriatic arthritis requiring medication

Koji Mandai[1], Kentaro Inui[2], Tadashi Okano[2], Yutaro Yamada[2], Shohei Anno[1,2], Tatsuya Koike[3,4], Chiharu Tateishi[5], Daisuke Tsuruta[5], Hiroaki Nakamura[2]
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Conflict of interest: None

[Objective] Determination of the start of treatment for psoriatic arthritis (PsA) is sometimes difficult. We investigated the course of PsA cases that did not require therapeutic intervention. [Methods] Overall, 205 patients with psoriasis (PSO) were referred to our department to assessSpondyloarthritis (SpA) from dermatology. Diagnosis of PsA was performed using the CASPAR criteria, assisting with ultrasound. The patients were evaluated for Psoriatic Arthritis Screening and Evaluation (PASE), DAS28-CRP. [Results] Patients (PsA; n=118), (PSO; n=87) were diagnosed. The mean age was 55.9±13.8 years in PsA, 60.1±14.3 years in PSO, mean DAS28-CRP was 3.13±1.27 in PsA, 1.87±0.83 in PsO ($p<0.001$). Of the 93 PsA patients who met CASPAR criteria, 69 patients needed treatment immediately after diagnosis. 7 cases out of cases did not initiate treatment therapy is needed later. There was no significant difference in DAS28-CRP in the group that required treatment compared to the group that did not require treatment ($p=0.53$). In the group that needed treatment, inflammation was significantly detected by ultrasound at the baseline ($p=0.026$). [Conclusions] PsA with inflammation detected by ultrasound may require treatment during the course.

P1-131

The assessment of the effect of IL-17A inhibitor for the treatment of Psoriatic arthritis with comparing TNF-alpha inhibitor

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Conflict of interest: None

[Objective] Compared to TNF-α inhibitors (TNF-αi), IL-17A inhibitors (IL-17Ai) have the same effectiveness of the treatment of skin and joint lesion and the lower risks of severe complications. We examined the treatment effect of IL-17Ai comparing with TNF-αi in patients with psoriatic arthritis (PsA). We also examined whether the patients who achieved the remission by TNF-αi could be maintained after switching to IL-17Ai. [Method] We retrospectively investigated 17 patients treated with IL-17Ai and 10 patients treated with TNF-αi from February 2015 to June 2019. Seven cases had achieved remission at the start of IL-17Ai (remission group). The number of swollen joint counts (SJC,0-66), the number of tender joint counts (TJC,0-68), Visual Analog scale (VAS), DAS28-CRP, DASPA, ACR20 achievement rate, and HAQ were used for the assessment at baseline, 12, 24 and 52 weeks after treatment. [Results] Four patients were dropped out due to poor treatment response, however there were no adverse events. All assessment items showed the same effects in both treatment groups. ACR20 achievement rate indicated higher tendency in TNF-αi group. In the remission group, 6 of 7 patients maintained remission. [Conclusions] IL17-Ai treatment might be an effective alternative for PsA patients.

P1-132

Pitfall of psoriatic arthritis: Importance of skin biopsy

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Conflict of interest: None

<introduction> Mycosis fungoides is one of the cutaneous T cell lymphoma, and it's incidence is 6 in 1,000,000. We report a case of mycosis fungoides mimicking psoriatic arthritis. <case> 45 years-old man with a past medical history of gout presented to our department with joint pain. He had 10 years history of nail pitting and nail bed thickening. 1 year prior to referral to our hospital, he was diagnosed psoriasis. 5 months prior to referral to our hospital, he noticed pain and swelling of finger and toes, so he visited our department. Physical exam and ultrasound revealed synovitis in IP and DIP joint, sausage finger, and erythema with scales on his trunk. Serological test was negative for rheumatoid factor and anti-CCP antibody. At first, we diagnosed him psoriatic arthritis, and planned to treat him with biologic agent. However, skin biopsy revealed mycosis fungoides, so we started salazosulfapyridine. <conclusion> Mycosis fungoides sometimes mimic psoriasis, and there is a 3 years delay of diagnosis. Pathological findings play an important role in order to differentiate them. We need to know that some mycosis fungoides patient mimic psoriatic arthritis, so we emphasize the importance of skin biopsy for psoriatic arthritis patient before initiating tumor-inducive medications.

P1-133

Clinical importance of dactylitis in patients with psoriatic arthritis

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Conflict of interest: None

[Objective] Patients with psoriatic arthritis (PsA) often show a decrease in QOL as seen in those with rheumatoid arthritis, requiring early diagnosis and appropriate medical treatment. We investigate a relationship between dactylitis and joint destruction in PsA patients. [Methods] We retrospectively reviewed medical records of PsA patients who had been treated in our hospital between April 2016 and September 2019. [Results] Six patients were enrolled in this study (3 men and 3 women, mean onset age 32 years). Dactylitis with finger joint destruction was seen in 3 patients, and of these 2 showed active inflammation with bone destruction in sacroiliac joints. The remaining 3 patients without dactylitis did not show obvious bone destruction in either peripheral or axial joints. There was no obvious relationship between CRP and joint destruction. [Conclusions] Dactylitis may be a predictor of bone destruction in PsA. We should consider early treatment after checking bone destruction in joints in PsA patients with dactylitis irrespective of inflammatory reactions.

P1-135

Examination of reason for discontinuation and continuation rate of oral bisphosphonate in female patients with autoimmune diseases

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Conflict of interest: Yes

[Objective] The aim of this study was to examine the reason of for discontinuation and continuation rate of oral bisphosphonate in female patients with autoimmune diseases. [Methods] We analyzed the 114 female patients with autoimmune diseases in treated with oral bisphosphonate from January 2016 through December 2016 at our hospital. [Results] The two-year continuation rate of oral bisphosphonate was 68%. The rate of change to the stronger anti-osteoporosis drug such as denosumab and romosozumab was 12%. And the rate of drug withdrawal was16% due to reduction of corticosteroid dose. [Conclusions] It is necessary to consider continuing oral bisphosphonate according to the individual bone mineral density and symptoms.

P1-136

Clinical features in rheumatoid arthritis (RA) patients with osteoporosis (OP): comparison with non-OP RA patients

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Conflict of interest: None

[Objective] Advances in pharmacotherapy have changed not only profile of RA patients but also OP pathology. We investigated the clinical features of RA patients with OP. [Methods] 48 RA patients were divided into 23 patients with OP (OP+) and 25 patients without OP (OP-). Age, disease duration, Stage, HAQ-DI, laboratory data (CRP RF MMP-3), disease activity (SCAI CDAI), pain VAS, lumbar spine and femoral T-score were compared. [Results] In the OP+ and the OP- group, the age (years) were 75.1, 65.3 ($P=0.0048$), disease duration (years) were 18.3, 10.1 ($P=0.0063$), Stage 3 and 4 ratio (%) were 69.2, 22.7 ($P=0.0013$), HAQ-DI were 1.5, 0.5 ($P= 0.00035$), CRP (mg/dL) were 1.5, 0.6 ($P=0.13$), RF (U/

mL) were 168.5, 80.2 (P=0.14), MMP-3 (ng/mL) were 93.7, 94.6 (P=0.97), SDAI were 7.4, 4.3 (P=0.16), CDAI were 5.9, 3.7 (P=0.25), pain VAS (/100) were 29.4, 14.9 (P=0.038), lumbar T-score (SD) were -0.6, 0.3 (P=0.21), femoral T-score (SD) were -2.1, -0.6 (P=0.0030). [Conclusions] the OP+ group were significantly older, had longer morbidity, had severe joint destruction, and were physically impaired, had lower femoral T-score. In the treatment of OP, it is considered important to manage pain by appropriate exercise, orthosis, and analgesics to prevent physical dysfunction and bone loss as well as OP drug therapy.

P1-137

Femoral neck fracture in patient with rheumatoid arthritis without the history of trauma

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Conflict of interest: None

[Introduction] Osteoporosis is an important complication in the rheumatoid arthritis. The incidence of femoral neck fracture has recently increased with the aging of the rheumatoid arthritis patients. We report our experience with one case of femoral neck fracture in patient with rheumatoid arthritis without the history of trauma. [Case] Patient was 75-year-old woman who was treated for rheumatoid arthritis. She consulted our hospital because of thigh pain. On radiography, femoral neck fracture with transposition was accepted. We chose to perform total hip replacement with dual mobility cup. In addition, we started osteoporosis treatment after surgery. There is no pain of the patient and the everyday life of the patient has become independent. [Conclusion] When we treat the rheumatoid arthritis, attention is necessary for osteoporosis. We expect that total hip arthroplasty with dual mobility cup will provide good hip functional outcome in patient with femoral neck fracture with rheumatoid arthritis.

P1-138

Contralateral femoral fracture during denosumab therapy in a patient on hemodialysis with a history of atypical femoral fracture

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Conflict of interest: None

[Case report] A 75-year-old woman was being treated with steroids for myasthenia gravis. For osteoporosis, alendronic acid was started in 20XX. Left femoral pain began in April 20XX+3 and resulted in left atypical femoral fracture in June 20XX+3. Osteosynthesis was performed. We discontinued alendronic acid and prescribed calcitonin. Hemodialysis was introduced for worsening renal function in 20XX+4. After starting denosumab in January 20XX+5 because of multiple thoracolumbar vertebrae compression fractures, right thigh pain developed in July 20XX+6. Due to right atypical femoral fracture diagnosed in October 20XX+6, we performed osteosynthesis. [Clinical significance] We describe a relatively early contralateral atypical femoral fracture during denosumab therapy in a patient on hemodialysis with a history of atypical femoral fracture. Most anti-osteoporosis drugs are contraindicated or require careful administration in patients with renal insufficiency, but denosumab, which suppresses the expression of RANKL, can be used while being careful about hypocalcemia. When there is a history of atypical femoral fracture, thorough examination and careful follow-up are necessary.

P1-139

Incidence of fragility fractures in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) have a greater risk of osteoporosis and fracture than the general population. To examine the clinical fractures of vertebral and non-vertebral fractures in patients with rheumatoid arthritis. [Methods] We retrospectively studied 149 out patients with RA (mean age 65.7 years, Female 76.2%) for 2 years from september 2017. Information on fractures occurrence was obtained from medical records in this study. [Results] There were 10 fractures in 9 patients during the 2-years follow-up period. The vertebra fracture occurred at 7 times, each fracture of the tibia, femur and humerus occurred once. All fractures were fragilily fractures. [Conclusions] The incidence of fractures was 3.05 per 100 patient-years in this study.

P1-140

The investigation of 11 romosozumab cases in our hospital

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Conflict of interest: None

[Objective] fractures caused by osteoporosis is an important problem that often leads to irreversible motor dysfunction and a decrease the independence of life. In particular, RA patients are a group with a high risk of fracture, and thus there is a need for osteoporosis treatment. Romosozumab, an anti-sclerostin antibody, is a novel drug expected to have a strong bone mineral density (BMD) increasing action. To date, the efficacy and safety of patients with RA have not been clarified. [Methods] Evaluate patient background, pre-treatment drugs, BMD, bone metabolism markers, fractures during administration, adverse events, treatment continuation rate [Results] All patients were female, 7 RA, 4 non-RA patients, age 77.0 ± 7.33, BMD (T-score) lumbar spine -2.88 ± 0.93 and femur-2.76 ± 0.34. At the time of abstract registration, 3 persons completed the evaluation after 6 months. The increase rate of lumbar BMD in the first 6 months was 10.97 ± 7.66%. The increase rate of femur BMD was -1.57 ± 1.16%. To date no new fractures or serious adverse events have been treated [Conclusions] In our hospital, romosozumab is mainly used for patients with severe osteoporosis. There are cases of increased lumbar bone density at 6 months after administration.

P1-141

Risk factors of fragile fractures in RA patients

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Conflict of interest: None

[Objective] RA is known to cause paraarticular and systemic osteoporosis and have a high risk of fracture. Purpose of this study is to investigate the risk factors of fragile fractures in RA patients. [Methods] 72 patients (19 males, 54 females, average age 72.1 years) were enrolled in this retrospective study. We evaluated fracture site, mechanism (vulnerable fracture, traumatic, etc.), duration of disease, Stage / Class, DAS28CRP, administration of steroid, medication for RA and osteoporosis. And we compare between two groups: the fragile fractured group (FG) and the none fragile fractured group (NFG). [Results] Fractures occurred in 22cases. Fagile fractures occurred 11 cases (15.3%). The fragile fracture sites were 8 vertebral bodies, 4 lower limb, and 1 forearm. The average age was 79.7 years for the FG and 70.7 years for the NFG. There was no difference in disease duration, and the proportion of patients with advanced stage was high in the FG. DAS28CRP was 3.16 in the FG and 2.59 in the NFG. The proportion of steroid administration was 81.8% in the FG and 56.5% in the NFG, which was significantly higher in the FG. [Conclusions] The risks of fracture were age, stage, disease activity, and steroid administration.

P1-142

Clinical characteristics of patients with rheumatic diseases and low alkaline phosphatase

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Conflict of interest: Yes

[Objective] Hypophosphatasia is caused by mutations in the tissue nonspecific alkaline phosphatase (TNSALP) gene and characterized by defective mineralization of bone and low serum ALP levels. Due to the varieties of its severity, there are cases, particularly adult cases, with only non-specific clinical features such as pain and fractures who need to be differentiated from rheumatic diseases. We aimed to clarify the clinical characteristics of patients with rheumatic diseases and low ALP. [Methods] Studied were 112 patients who visited our department between October 2018 and September 2019 and whose serum ALP levels were below normal range. [Results] 55 and 18 patients were on bisphosphonate and denosumab, respectively. Among underlying diseases, SLE was the most prevalent (n=37), followed by myositis (n=18) and rheumatoid arthritis (RA, n=10). All RA patients were on bone resorption inhibitors (p=0.01). A 60-year-old woman with RA exhibited an extremely low serum ALP level (33 IU/L) and newly had a diagnosis of hypophosphatasia with increased urinary phosphoethanolamine (330.5 μmol/gCr) and TNSALP gene mutation (1015G>A [Gly339Arg] hetero mutation). [Conclusions] Bone resorption inhibitors may contribute to low ALP. RA patients are less likely to develop low ALP.

P1-143

Clinical efficacy of denosumab for severe or refractory osteoporosis in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] The purpose of this study is to clarify the efficacy of denosumab (DNS) for severe or refractory osteoporosis in patients with rheumatoid arthritis. [Materials and methods] Twenty four RA patients with severe osteoporosis (T score ≦-2.5) or without response to bisphosphonate treatment were includes in this study. All patients were treated by DNS 60mg every 6 month and were observed more than 1 year after DNS treatment. Mean age of these patients was 73.2 years old, and mean disease duration was 11.8 years. The rate of glucocorticoid use was 41.0% and mean dose of glucocorticoid was 2.67mg/day. Mean DAS28-CRP at baseline was 2.51. Mean T score of femoral neck, proximal femur and lumber spine at baseline were -2.92, -2.60 and -1.80, respectively. [Results] At 12 months of DNS treatment, mean DAS28-CRP was 2.09. There was no difference between DAS28-CRP at baseline and 12 months. On the other hand, Mean T score of femoral neck at 12 months of DNS treatment increased to -2.70 from -2.92. Similarly, mean T score of proximal femur at 12 months increased to -2.40 from -2.60. There was no fracture of spine and extremities during observation period. [Conclusion] DNS treatment might be effective for severe or refractory osteoporosis in patients with rheumatoid arthritis.

P1-144

Denosumab increase the bone mineral density irrespective of the biological disease-modifying antirheumatic drugs and pretreatment of osteoporosis in patients with rheumatoid arthritis with osteoporosis

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Conflict of interest: None

[Objective] We assessed the effect of the bDMARDs use, pretreatment of OP on BMD change in patients with RA treated denosumab. [Methods] This study included 140 RA patients treated with denosumab. BMD at the lumbar spine and proximal femoral were evaluated by DXA at baseline and 1 year after treatment. We evaluated the influence of bDMARDs use and pretreatment of OP for BMD change. [Results] BMD change at the lumbar spine, proximal femoral and femoral neck were 5.9% (p<0.01), 4.0% (p<0.01), 1.2% (p=0.36). There were no differences in BMD change at the lumbar spine, proximal femoral and femoral neck between 45 patients (TNF: 23, TCZ: 13, ABT: 7, TOF: 2) with bDMARDs and 93 patients without bDMARDs (6.0 vs 5.8%: p=0.31, 4.3 vs 4.1%: p=0.57, -0.2 vs 1.8%: p=0.18), and among TNF, TCZ, ABT (TNF vs TCZ: p=0.83, 0.98, 0.81, TNF vs ABT: p=0.83, 0.41, 0.97, TCZ vs ABT: p=0.98, 0.43, 0.9). There were no differences in BMD change between 74 patients (BP: 58, PTH: 16) with pretreatment of OP and 66 patients without pretreatment of OP (6.9 vs 5.4%: p=0.41, 0.9 vs 4.0%: p=0.22, 2.0 vs 1.2%: p=0.68), and between BP and PTH (6.2 vs 6.9%: p=0.49, 4.8 vs 0.9%: p=0.35, 0.9 vs 2.0%: p=0.49). [Conclusions] Denosumab improved BMD in patients with RA independently regardless of the type of bDMARDs, pretreatment of OP.

P1-145

Effects and problems of denosumab 3-year treatment for bone vulnerability in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Denosumab has been reported safety and therapeutic effects. The pharmacological mechanism of denosumab is expected to be useful in preventing and improving bone fragility in patients with rheumatoid arthritis. The purpose of study is to compare the effects of primary osteoporosis patients and rheumatic patients on osteoporosis and to examine their problems and effects. [Methods] The subjects were 15 patients with primary osteoporosis (PO group), 15 patients with rheumatoid arthritis (RA group), and the average age of 30 patients was 75.5 years old. The bone mineral density (BMD) was investigated in the lumbar spine and femur using the DXA. Bone metabolism markers were examined the serum concentration of TRAcp5 and TBS was examined from lumbar BMD. [Results] In both groups, the lumbar BMD and area of femoral trochanter were increased significantly after 3 years treatment, and TRAPc5b was suppressed about 30% compared to the pretreatment value. On the other hand, the area of femoral neck did not increase significantly in the RA group. TBS showed a significant increase in the PO group as well as changes in lumbar BMD, but there was no significant difference in the RA group. [Conclusions] Long-term treatment observation is required for the RA group when compared to the PO group.

P1-146

The clinical changes of patients with glucocorticoid-induced osteoporosis by the interventional examination from pharmacist for one year

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Conflict of interest: None

[Objective] To investigate 1-year clinical outcome of interventional examination by pharmacist for patients with glucocorticoid-induced osteoporosis (GIO) in our hospital. [Methods] Patients who visited the department of rheumatology in our hospital from June to August 2018 and took prednisolone (PSL) more than 3 months at the time were resisterd. The pharmacist got hearing and the treatment regimen with patients and the chief physician. We checked the GIO risk factor and serologic bone metabolism markers (P1NP, BAP, TRACP5-b, a change of sNTX). Medical record was used to got clinical information and retrospective analysis. [Results] 38 patients could be catched up for next one year (average age 74.9, 71% female, average dose of PSL 4.3 ± 2.8mg/day). The GIO risk factor score decreased in 8 cases and increased in 12 cases. The medication for GIO was changed in 20 cases. The serum levels of sNTX was decreased in the group of patients changed the therapeutic drug compared with the group of not (p=0.045). One patient had a new bone fracture.

[Conclusions] The number of patients could be checked and changed their madication for GIO by the examination of pharmacist.

P1-147

Prevalence and treatment rate of osteoporosis in patients with rheumatoid arthritis at first appearance to specialty section

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Conflict of interest: Yes

[Objective] RA is frequently concomitant with osteoporosis (OP). The aim of this retrospective study is to know prevalence and treatment rate of OP in patients with RA at first appearance. [Methods] Toyohashi RA Database was used. 95 patients had visited our hospital and was diagnosed as RA. BMD was measured in lumbar spine (LS), total hip (TH) and femoral neck (FN). Patients were categorized as two groups: N-RA (patients who were diagnosed as RA at first) and A-RA (patients who had been already diagnosed as RA in other hospitals or clinics). Prevalence of OP was evaluated using only BMD (%YAM was 70% or less). Prevalence of treatment of OP was also investigated. [Results] Case (mean age): Female N-RA 38 (63.6), Male N-RA 21 (66.4), Female A-RA 30 (67.2) and Male A-RA 6 (69.0). Prevalence of OP (%) in LS, TH and FN was as follows. Female N-RA: 10.5, 10.5, 28.9. Male N-RA: 0, 4.8, 9.5. Female: A-RA 0, 23.3, 36.7. Male A-RA: 0, 0, 0. Prevalence of treatment of OP in N-RA was 5.1% at first appearance and 39.0% after our evaluation. Prevalence of treatment of OP in A-RA was 47.2% at first appearance and 58.3% after our evaluation. [Conclusions] New-coming RA patients was frequently concomitant with OP in which treatment was needed. FN was the important part to diagnose OP in RA patients.

P1-148

The treatment status of glucocorticoid induced osteoporosis (GIO) and attempt to GIO in AORA registry

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Conflict of interest: None

[Objective] Glucocorticoid induced osteoporosis (GIO) is one of the bone metabolism disorder caused by glucocorticoid (GC). In order to prevent GIO, we have stated “Use GC with shorter term and lower dose” . The purpose of this study was to investigate the GIO treatment status and the changes of GC use in Akita orthopedic group on rheumatoid arthritis (AORA) registry 2017 and 2018. [Methods] 652 patients (2017 group) and 684 patients (2018 group) who were treated target in the guidelines on the Management and Treatment of GIO of the Japanese Society for Bone and Mineral Research in 2014 were included. [Results] Altough there was no significant difference in GIO treatment rates (67.2% vs 65.5%), men in both groups had significantly lower treatment intervention rates than women (34.8% vs 70.2%, 42% vs 71.4%, p <0.01). The GC dose was significantly lower in the 2018 group (3.9 ± 1.9 vs 3.7 ± 1.9, p = 0.01). Although the GC dose decreased, disease activity was significantly lower in the 2018 group for both DAS-28CRP and DAS28-ESR (2.61 vs 2.27, p <0.001, 3.2 vs 2.78, p <0.001). [Conclusions] The current study showed that GC dose decreased in 2018, but there was no deterioration in disease activity, suggesting the possibility of dose reduction according to patient condition.

P1-149

Hydroxychloroquine use for our SLE patients, with the analysis of efficacy and safety over three years

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Conflict of interest: None

[Objective/Methods] To analyze the efficacy and safety of Hydroxychloroquine to our SLE patients, who kept using it over three years. [Results] 32 cases were prescribed HCQ, average age 41.3 ± 14.3 years old, with the duration less than one year: eight cases, one to two years: six cases, two to three years: ten cases, more than three years: eight cases. One case stopped using it because of severe diarrhea, but no other cases had any adverse events. Among the patients with the duration of more than three years use, one case become nephrotic and was added immune suppressive therapy, but the others experienced no intensification of the treatment. During the three years, the average value of markers which shows disease activity changed as follow; dsDNAIgG 82.0 ± 84.9 to 16.5 ± 7.8 IU/mL, C3 65.6 ± 16.6 to 78.8 ± 14.3 mg/dL, CH50 24.3 ± 9.9 to 30.0 ± 9.1 U/mL, and the average dose of glucocorticoid decreased from PSL 4.4 ± 3.5 to 1.2 ± 2.1 mg/day (p=0.047, five cases of GC free). No cases of Hydroxychloroquine Retinopathy were found. [Conclusions] Our date showed that Hydroxychloroquine is effective and safe to our SLE patients.

P1-150

Clinical features and curative effects of patients with systemic lupus erythematosus treated with belimumab combination 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 21 SLE patients who had passed 12 months after the administration of BEL at our hospital and Yodogawa Christian Hospital, patient background, treatment course after 3, 6 and 12 months and adverse events were examined retrospectively. [Results] Age was 46.2 ± 14.1 years, 19 women and disease duration was 13.4 ± 11 years. At the time of BEL administration, MMF 7 cases, TAC 13 cases, HCQ 9 cases and multiple target therapy 9 cases were combined use. Before administration, C3 81.3 ± 20.4 mg / dl, anti-ds-DNA antibody titer 33.0 ± 47.7 IU / ml, SELENA-SLEDAI 4.4 ± 3.2, and PSL level was 11.2 ± 6.1 mg / day. Significantly increased from 3 months after BEL add on, serum C3 level increased (P = 0.03), anti-ds-DNA antibody titer decreased (P = 0.002), SELENA-SLEDAI improved (P = 0.03), PSL could be reduced (P = 0.001), and these effects persisted even at 12 months (P = 0.013 / 0.0005 / 0.007 / <0.0001). During the course, herpes zoster and cytomegalovirus infection were occurred by one case, but both improved. [Conclusion] Disease activity improves after BEL introduction and steroid dose reduction is possible, but we should pay attention to infectious diseases.

P1-152

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. [Method] Fourteen patients receiving the maintenance therapy of SLE were enrolled in this study. Dose of prednisolone (PSL), titer of anti-DNA antibody, WBC count, serum complement and SLE disease activity index (SLEDAI) were examined retrospectively at 0 and 12 months after administration of BEL. [Results] The mean dose of PSL was significantly reduced (mean±S. E) (baseline: 6.1±1.1 mg/day, 12 months after administration of BEL: 3.0±0.6 mg/day, *p=0.013*, respectively). There was no statistical signifi-

cant between before treatment by BEL and after treatment in SLEDAI, the titer of anti-DNA antibody, WBC count and serum complement. In this observation period, no one could achieve the cessation of PSL. However, there were patients almost completely suspend PSL. As for adverse event, bacterial pneumonia (n=1) and pulmonary cryptococcosis (n=1) was revealed. [Conclusion] Our study is suggested that co-treatment with BEL on standard SLE therapy could be enable to prevent the flare of SLE and to reduce the dose of PSL with statistical significance among the patients under the maintenance treatment of SLE.

P1-153

The prediction for improvement of immunological index in systemic lupus erythematosus with Belimumab

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Conflict of interest: None

[Objective] The effectiveness and safety of Belimumab (BLM) have been announced, but it is still insufficient. It is not clear to whom it is particularly effective. This study aims to explore the predictive factors that improve immunological index in patients treated with BLM. [Methods] This retrospective study comprised 20 patients with SLE who has treated with BLM in Shinonoi General Hospital and Kitasato Medical Center between May 2018 to October 2019. We examined predictive factors of improve anti-DNA antibody after starting BLM. [Results] We recruited 20 patients with a mean age of 35.9 years, mean diseases duration 13.0 years. The organ involvement includes 16 lupus nephritis, 5 neurological involvement, 5 hematocytopenia, 15 rash on the skin, and 9 arthritis. After starting BLM, anti-DNA antibody titer decreased significantly ($p = 0.0143$) and the dose of steroid decreased ($p = 0.0061$). Anti-DNA antibody titers did not decrease in patients who had received steroid pulse therapy or who had used calcineurin inhibitors ($p=0.3262$, $p=0.5027$, respectively), but decreased in patients who had received IVCY of MMF ($p=0.0607$). [Conclusions] There was a difference in autoantibody titer depending on the treatment method. The accumulation of future cases was considered necessary.

P1-154

The utility of monocyte CD64 (Fc gamma RI) as activity maker for neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

[Objective] Interferons (IFN)-α is known to play a pivotal role for the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE). The monocyte CD64 (mCD64) enhances expression by IFNs. We have reported a tight correlation between mCD64 expression levels and SLE disease activity index (SLEDAI) and shown that mCD64 expression is a simple and useful biomarker for evaluating disease activity in SLE patients. Although neuropsychiatric manifestations are critical to the management of SLE, there have been no precise and convenient biomarkers assessing the activity of NPSLE. We investigated the utility of mCD64 expression as a biomarker for NPSLE. Methods] The mCD64 levels were assessed quantitatively in 5 patients with NPSLE by using flow cytometry. The mCD64 levels were compared with SLEDAI, cerebrospinal fluid (CSF) IL-6, and so on. Results] The mCD64 were significantly enhanced at the median of 38,541 molecules/cell in active phase. The mCD64 levels were significantly decreased at the inactive phase of the NPSLE after treatment ($p=0.03$). The mCD64 levels correlated with SLEDAI ($r=0.72$, $p=0.02$) and CSF IL-6 levels ($r=0.66$, $p=0.02$). Conclusions] mCD64 expression may be a potential biomarker for evaluating not only the disease activity but also the response of treatment in NPSLE.

P1-155

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 systemic lupus erythematosus (SLE) patients treated with belimumab (BLM) and its efficacy. [Methods] This study included 18 cases treated with BLM in University of Tsukuba hospital. We retrospectively evaluated 1) baseline characteristics, 2) purpose of BLM therapy, 3) clinical course in 12 cases treated with BLM for 24 weeks, and 4) adverse events (AE). [Results] 1) Mean age was 35.4±10.7 years old. Mean disease activity index (SLEDAI) and anti-DNA antibody titer were 7.0±3.8 and 46.6±57.6 IU/mL, respectively. Mean prednisolone (PSL) dose was 16.7±9.2mg/day. BLM was administrated by subcutaneously in 13 cases and by intravenously in 5 cases. 2) BLM was used for remission induction in 3 cases, to control disease activity in 6 cases refractory to previous therapy, for maintenance therapy in 1 case, and to reduce PSL dose in 8 cases. 3) Dose of PSL and SLEDAI score was significantly reduced at 24 weeks after BLM initiation. The anti-DNA antibody titer was improved, but which was not statistically significant. 4) Six cases experienced AE. Although severe AE were not reported, BLM was discontinued in 3 cases due to AE. [Conclusions] BLM might be effective for the improvement of disease activity and the reduction of PSL dose in patients with SLE.

P1-156

Immunological adverse event in three patients medicated with belimumab

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Conflict of interest: None

Background: Belimumab for systemic lupus erythematosus (SLE) exhibits efficacy and relatively few side effects. We report 3 cases of adverse events during the administration of belimumab. Case1 was a 57-year-old woman who suffered SLE from 1999. Although her treatment, it has been difficult to decrease steroids, and the administration of belimumab (BLM) started. However, arthritis was worsening and methotrexate relieved her symptoms. Case2 was a 35-years-old woman, she diagnosed SLE in 2013. Administration of BLM improved her immunologically data and decreasing PSL, but skin ulceration of her foot happened. Antibiotics were not effective and increased PSL was needed. Case3 was a 44-years-old man, he developed SLE with dermatomyositis in 2017. Administration of BLM improve his symptoms and PSL gradually decrease. But nephrotic syndrome developed and minimal change nephrotic syndrome was diagnosed by renal biopsy. Increasing steroids were needed. Conclusion: In all cases, indicators of disease activity showed improvement, but developed a pathological condition requiring increased steroids or additional immunosuppressive agents. During the administration of belimumab, it was considered necessary to pay attention to conditions other than systemic lupus erythematosus.

P1-157

A case of systemic lupus erythematosus in which intractable verruca vulgaris markedly improved after initiation of belimumab

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Conflict of interest: None

[Case] 19-year-old girl [HPI] She developed SLE at age 9 and was

complicated by lupus nephritis (class V) and APS. While treatment, lupus enteritis and decreased complement were observed, and the disease control was poor, so multi-target therapy of PSL, MMF, and Tac was required. The verruca vulgaris that had been observed in the left footpad since the age of 9 was resistant to dermatological treatment and continued to spread widely in the toes and fingers. When HCQ was added from the age of 17, the disease became stable. At the age of 19, Tac was discontinued after the dose of PSL was reduced to 6 mg. Belimumab was added 2 months later to reduce the amount of steroid in the future. [Progress] Since the beginning of belimumab, verruca that had not improved in treatment so far have rapidly shrunk and disappeared, and after 3 months it has almost disappeared, leaving no scar or pigmentation. [Summary] The improvement of verruca in this case may be related to the normalization of cellular immunity due to the withdrawal of Tac two months ago. However, from the time course of belimumab initiation and the improvement of verruca, it was possible that the correction of excessive autoimmune pathology with belimumab had some effect on the improvement of verruca.

P1-158

The effect of hydroxychloroquine on complement status in patients with systemic lupus erythematosus; Analysis of Japanese real-world patients with SLE in a large single center over twelve-month period

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Conflict of interest: None

[Objective] Complement is a biomarker known to be correlate with disease activity of systemic lupus erythematosus (SLE). However, it is not well-known how complement level changes after starting hydroxychloroquine (HCQ) in patients with SLE. The aim of this study is to investigate the effect of HCQ on complement levels over a 12-month period in a large single center cohort of SLE. [Methods] We retrospectively collected the data of all the 244 lupus patients treated with HCQ from the electrical medical recordat St Luke's International Hospital. We extracted the following parameters during the period between April 2008 and March 2018; baseline characteristics, complements levels (C3 and C4) at baseline1 month, 3 months, 6 months, 9 months, and 12 months after starting HCQ. [Results] Total 244 patients on HCQ were included. The mean age of these 114 patients was 40.2 years and 108 patients (94.7%) were female. The level of C4 (mg/dL) increased significantly ($p < 0.001$) after starting HCQ. Especially, the level increased more dramatically from month 1 to month 3 compared to the other periods, after initiating HCQ. [Conclusions] The level of complements increases after initiating HCQ therapy in real-world patients with SLE in Japan. The effect tends to emerge 3 months after starting HCQ.

P1-159

A case of steroid resistant systemic lupus erythematosus on dialysis treated with belimumab

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Conflict of interest: None

[Case] 48-year-old female [Present illness] SLE was diagnosed at the age of 17 based on fever, butterfly rash, arthritis, hypocomplementemia, ANA and anti-ds-DNA antibody positivity. Complicated alveolar hemorrhage led to treatment with high dose corticosteroids (CS) and intravenous cyclophosphamide (IVCY). Type five lupus nephritis was diagnosed at the age of 25 and steroid pulse therapy followed with high dose CS and IVCY. Maintenance dialysis was initiated from age of 41. Persistent arthritis with sustained high level of anti-ds-DNA antibody have led to consecutive 4 mg/day dexamethasone (DEX). She was admitted due to catheter infection. [Clinical course] Infection resolved with antibiotics. However, DEX was increased up to 8 mg/day due to prominent arthritis with hypocomplementemia and high anti-ds-DNA antibody titer (1280 IU/ml). Arthritis were improved soon. Mycophenolate mofetil (MMF) was added but discontinued because of leukopenia. Following belimumab (BEL) initiation, serological parameters were remarkably improved with significant decrease of anti-ds-DNA to 33IU/ml after 23 weeks. [Clinical significance] BEL can be a valuable treatment choice for SLE patients resistant to consecutive high dose CS in whom hydroxychloroquine was unusable because of dialysis.

P1-160

Initial therapy including two immunosuppressants and belimumab for severe and refractory systemic lupus erythematosus

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Conflict of interest: None

A 20-year-old woman developed thrombocytopenia, butterfly rash and positive tests for antinuclear antibody/anti-DNA antibody/anti-phospholipid antibody. With the diagnosis as systemic lupus erythematosus (SLE) diagnosed, she was treated with hydroxychloroquine (HCQ) 200 mg/day without organ damage. In January of year X, bilateral leg edema, appearance of proteinuria (up to 10.7 g/gCr) and exacerbation of thrombocytopenia were observed. Pulse steroid therapy, followed by prednisolone (PSL) 50 mg/day and mycophenolate mofetil (MMF) 1000 mg/day, was given immediately. Although thrombocytopenia improved, she developed abrupt chest pain and the enhanced chest computed tomography showed pulmonary thromboembolism, for which anticoagulation therapy was introduced. Another cycle of pulse steroid therapy, intravenous belimumab 520 mg and tacrolimus (TAC) 3 mg/day were added further for refractory lupus nephritis before the discharge at day 36. Renal biopsy revealed lupus nephritis IV-G (A). During the following 7 months, proteinuria gradually decreased and finally disappeared with PSL 3 mg/day and multi-combination therapy. Thus, this patient with severe and refractory lupus nephritis has been successfully treated with HCQ, PSL, MMF, TAC and belimumab without any obvious adverse events.

P1-161

The risk of irreversible renal failure in patents with systemic lupus erythematosus

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Conflict of interest: None

Aims: In Japan, the use of HCQ in SLE was approved only in 2015. As HCQ is generally introduced from the initial phase of treatment outside Japan, there are few cases in which HCQ is introduced in the maintenance phase after the initial treatment is completed, and there is little evidence regarding such use of HCQ. Therefore, we aimed to elucidate the effects and significance of adding HCQ to the treatment and continuing it for ≧ 104 weeks in SLE patients in the maintenance phase. **Methods:** We analyzed 30 patients with SLE in the maintenance phase undergoing outpatient treatment and who were administered HCQ for ≧ 104 weeks. We assessed the SLEDAI scores, anti-DNA antibody titer, CH50 value, and corticosteroids (CS) maintenance dose (PSL equivalent dose) at the baseline and 12, 24, 52, and 104 weeks after the initiation of HCQ therapy. **Results:** At week 104, a significant improvement was observed as compared to the baseline in the SLEDAI scores, anti-DNA antibody titer, CH50, and PSL maintenance dose. **Conclusion:** Treatment with HCQ for two additional years in patients undergoing maintenance therapy for SLE was demonstrated to be effective in terms of reduction in the SLEDAI score and anti-DNA antibody titer, improvement in CH50, and reduction in the PSL dose.

P1-162

The therapeutic effect of hydroxychloroquine impacting on the factors related to metabolic syndrome in systemic lupus erythematosus

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Conflict of interest: None

[Objective] We investigated the therapeutic effect of hydroxychloroquine (HCQ) for the factors associated with metabolic syndrome (MetS) in systemic lupus erythematosus (SLE). [Methods] Patients with SLE, who have been consecutively treated in our department, were classified into those with and without HCQ administration. Blood pressure levels, serum levels of LDL-C, HDL-C, triglyceride (TG), and CRP, which were measured during 3-month study period, were compared between two groups (60 patients in HCQ group and 88 in non-HCQ group). [Results] The mean period since the diagnosis of SLE was 11 years in HCQ group, whilst being 9 years in non-HCQ group. The mean administration period of HCQ was 14 months. Serum levels of LDL-C and CRP were lower in HCQ group than those in non-HCQ group (99.5±23.9 vs.120.5±30.9mg/dl, 0.08±0.15 vs.0.35±0.91mg/dl, respectively). There were no significant differences in other factors. SLEDAI, dosage of corticosteroid, and the administration frequency of hyperlipidemic drugs; meanwhile tacrolimus was more frequently administered in HCQ group. [Conclusions] Our result, in which low serum levels of LDL-C and CRP were maintained in HCQ group, suggested that improved factors related to MetS may be implicated in the therapeutic efficacy of HCQ in patients with SLE.

P1-163

Relationship between steroid dose reducing effect of hydroxychloroquine HCQ and daily dose, actual body weight and renal function of SLE patients

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Conflict of interest: None

Objective: HCQ is used as a standard treatment for SLE, but due to concerns about retinal toxicity, the 2019 EULAR Guidelines recommend not exceeding 5 mg/kg per actual body weight per day. In this study, we investigated the relationship between HCQ dose and subsequent prednisolone (PSL) dose, actual body weight and renal function of SLE patients in our rheumatic division. Method: SLE patients (73 cases) who have continued HCQ for more than 1 year from January to June 2019 are recruited. We investigated their age, sex, HCQ dose, PSL dose at the start and 1 year after HCQ, renal function retrospectively from the medical record. Result: The median age was 47.5 years, median daily HCQ dose was 4.5 (2.0-7.2) mg/kg. The PSL dose was 5.5 (2.5-50) mg/day at the start of HCQ, 4.5 (0-11) mg/day 1 year after the start of HCQ. PSL dose reduction was achieved 61% of HCQ <4.9mg/ kg patients and 82% of >5.0mg/kg (p=0.066), 70% of eGFR<59, 67% of eGFR>60 patients (p=0.028). Conclusion: In this study, PSL could be reduced at daily doses of HCQ>5 mg/kg patients, and was significantly reduced in patients with eGFR<59. Although an increase in blood concentration of HCQ can be expected to reduce PSL, there is concern over toxicity due to an increase of cumulative dose.

P1-164

Cartilage thickness of finger joints in patients with systemic lupus erythematosus evaluated by ultrasonography

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Conflict of interest: None

[Objective] We have reported that patients with SLE and joint manifestations showed tendon lesions at least comparable to those with RA. Further, we evaluated finger joint cartilage of healthy controls and RA patients by US and demonstrated cartilage injury in RA. In this study, we examined the cartilage thickness of finger joints in SLE patients with joint manifestations by US. [Methods] We evaluated cartilage thickness (2-5 MCP joints and PIP joints, bilaterally) of 25 patients with SLE with the joints placed in ~90 degrees flexion. Cartilage thickness was measured from the base of the cartilage to the interface artefact at the cartilage surface. Those results were compared with 42 healthy controls matched for sex, age, height and body weight using a propensity score. [Results] The cartilage thickness of MCP joints in SLE patients was 0.3-0.8mm (median 0.5mm), and 0.2-0.6mm (median 0.4mm) for PIP joints. Median total thickness of MCP joints was 4.1 mm in SLE and 4.5mm in healthy controls (p=0.098) and it was 3.0 mm and 2.9mm, respectively, for PIP joints. Cartilage thickness in SLE patients did not show any significant correlation with age, height, body weight or disease duration. [Conclusions] In general, cartilage injury of finger joints in SLE patients is not so severe.

P1-165

Factors that distinguish neuropsychiatric systemic lupus erythematosus with diffuse manifestations from corticosteroid-induced psychiatric disorders

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Conflict of interest: None

[Objective] An increased cerebrospinal fluid (CSF) IL-6 level is reportedly useful for distinguishing neuropsychiatric systemic lupus erythematosus (NPSLE) with diffuse manifestations from corticosteroid-induced psychiatric disorders (CIPDs); however, the CSF IL-6 assay is very time-consuming. Also, a rise in the albumin quotient (Qalb) and hypocomplementemia may be risk factors for CIPD development. We sought a simple risk marker replacing the CSF IL-6 level. [Methods] We compared data obtained from blood and CSF samples, obtained at the onsets of SLE patients, with diffuse manifestations among 33 episodes; we used the Mann-Whitney U-test to this end. Blood and CSF data (including serum C3 values and CSF Qalb concentrations) were analyzed in NPSLE and CIPD patients. [Results] The CSF IL-6 level tended to be higher in those with more CSF cells, as did the Qalb and anti-dsDNA antibody titers in the diffuse NPSLE group. However, none of the Qalb or dsDNA antibody titer, nor the serum C3 value, differed significantly between the diffuse NPSLE and CIPD groups. [Conclusions] An elevated CSF cell number might be useful to differentiate diffuse NPSLE from CIPD but, in this work, the difference did not attain statistical significance. Further work is required.

P1-166

Comparison on Systemic Lupus Erythematosus (SLE) Disease Activity Score (SLE-DAS) and SLE Disease Activity Index 2000 (SLEDAI-2K): A Cross-sectional Study

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Conflict of interest: None

[Objective] The SLE-DAS has been developed as a new continuous global score to assess disease activity in SLE with improved sensitivity to change as compared with the SLEDAI-2K. We aimed to compare the SLE-DAS to SLEDAI-2K cross-sectionally and investigate its validity. [Methods] Newly diagnosed consecutive SLE patients who were admitted to our hospital from April 2010 to December 2018 were eligible. Scores of the SLE-DAS and SLEDAI-2K and other clinical features were compared cross-sectionally. [Results] A total of 63 patients with mean age 37 were included; 58 cases were women, and 25 cases were diagnosed as lupus nephritis by renal biopsy. Median scores of SLE-DAS and SLEDAI-2K were 14 and 13, respectively. A moderate correlation was observed between SLEDAI-2K and SLE-DAS ($\rho = 0.52$). The correlation with SLE-DAI-2K was not observed in the patients with high SLE-DAS scores ($\geqq 14$, $\rho = -0.03$), whereas it was evident in those with low scores (<14, $\rho = 0.52$). The renal components of SLEDAI-2K and SLE-DAS were correlated with the urinary protein levels ($\rho = 0.67$ and 0.75, respectively). [Conclusions] SLE-DAS and SLEDAI-2K were moderately correlated but seemed to perform differently. The difference between the 2 indices tended to be bigger in cases with high disease activities.

P1-168

Real-world validation of the 2019 SLE EULAR/ACR classification criteria

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Conflict of interest: None

Objectives: We evaluated the new 2019 EULAR/ACR classification criteria in real-world practice. **Methods**: We retrospectively reviewed patients aged ≧ 15 years who visited our hospital in 10 years. Three criteria, 1997 revised ACR criteria, 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria, and 2019 EULAR/ACR criteria were applied to our patients who had been diagnosed with SLE. **Results**: The study consisted of 93 patients, including six male patients. The mean age was 43.8 (ranged from 16-82) years. The sensitivity was 100% for the 1997 reviewed ACR criteria, 95.7% for the 2012 SLICC criteria, and 93.5% for the 2019 EULAR/ACR criteria. The mean scores of the 2019 EULAR/ACR criteria were 21 (ranged from 8-45). Six patients were not classified as having SLE according to the 2019 EULAR/ACR criteria. Among these six patients, five had a low antinuclear antibody titer (<1:80). The remaining patient had only eight points on the new criteria and was also not classified as having SLE based on the 2012 SLICC criteria. **Conclusions**: The 2019 EULAR/ACR criteria have sensitivity similar to that of previous criteria. We need to take into consideration previous SLE criteria to diagnose patients who have a low antinuclear antibody titer.

P1-169

Validation of the 2019 EULAR/ACR classification criteria for systemic lupus erythematosus: the significance of anti-nuclear antibody

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Conflict of interest: None

[Objective] The 2019 EULAR/ACR classification criteria for systemic lupus erythematosus (SLE) specify anti-nuclear antibody (ANA) ≧ 1:80 as an entry criterion. This study was performed to determine the characteristics of SLE with low ANA titer. [Methods] This was a retrospective analysis of 124 consecutive patients diagnosed with SLE at our hospital from 1999 to 2019. Clinical parameters, such as organ involvement, specific antibodies, and disease activity, were compared between patients with ANA ≧ 1:80 and < 1:80. [Results] All patients fulfilled either of the former criteria. Eleven patients (8.9%) showed ANA < 1:80. One of these patients had mild symptoms at initial diagnosis followed by the development of other symptoms and specific antibodies, and another showed severe thrombotic thrombocytopenic purpura and required plasma exchange. There were no significant differences between patients with ANA ≧ 1:80 and < 1:80, except that the latter tended to show thrombocytopenia (15% vs. 46%, respectively; $p = 0.016$). [Results] The new classification criteria exclude SLE patients with low ANA titer, and they were not in a biased group. However, low platelet count may be helpful in cases with low ANA titers that are difficult to diagnose.

P1-170

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] 6 cases with anti-DNA antibody elevation just before surgery and 2 cases with decreased complement value. 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. [Conclusions] The possibility of the onset of immune complex deposition in muscle tissue may be the cause of heart disease in SLE patients.

P1-171

The Effects of Anti-glutamate Receptor Subunit GluN2 Antibody on Disease Activity due to Systemic Lupus Erythematosus without Neuropsychiatric Involvement

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Conflict of interest: None

[Objective] Autoantibody against N-methyl-D-aspartate receptor subunit GluN2 (anti-GluN2) are known to be related with diffuse psychiatric/neuropsychological syndromes in NPSLE. The aim of this study is to clarify the association of damages due to SLE activity other than NPSLE and serum anti-GluN2. [Methods] Sera were collected from SLE patients with active disease (N=127), anti-GluN2 were measured in ELISA and clinical information was collected from the past medical history, retrospectively. [Results] Patients were subdivided into those with NPSLE (n=37) and those without NPSLE (non-NPSLE) (n=95). SLEDAI was significantly higher in patients positive for anti-GluN2 (p=0.006) in non-NPSLE, but not in NPSLE (p=0.705). Among autoantibodies, anti-GluN2 positivity was a significant risk for higher SLEDAI in non-NPSLE (p=0.007). In univariate analysis with components of SLEDAI, anti-GluN2 positivity was a significant risk for pleuritis, arthritis, fever, hypocomplementemia, leukocytopenia or anti-DNA positivity in non-NPSLE. Multivariate analysis resulted with high odds ratio, 3.60 for arthritis (95% confidence interval 1.19-11.65, p=0.007). [Conclusions] Anti-GluN2 existing in serum can be pathogenic, causing damages related to lupus activity even in SLE patients without complicating NPSLE.

P1-172

Characteristics of the overlap syndrome of systemic lupus erythematosus and rheumatoid arthritis

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Conflict of interest: None

[Objective] Overlap of systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) is known to be a rare syndrome as Rhupus. The aim of this study is to clarify the characteristics of Rhupus. [Methods] We identified patients who had been diagnosed with overlap syndrome of systemic lupus erythematosus and rheumatoid arthritis in our university in October 2019. Clinical charcteristics, laboratory data, and treatment were investigated. [Results] Twenty eight patients with Rhupus were identified and enrolled in the analysis. The mean age was 55.5 years old and 97% were female. The timing of diagnosis was simultaneous in 2 patients (7%) and RA precedent in 5 patients (17%). The age of diagnosis was 41 years old for RA and 39 years old for SLE. The positivity of autoantibodies were 64% for rheumatoid factor, 50% for anti-CCP, ANA for 89%. anti-DNA in 32%, anti-Sm in 7%, and anti-SSA in 56%. In X-rays, 79% had typical erosions with ankyloses in 79%. In contrary, as for organ involvement of SLE, only 11% had renal involvement and 4% had neuropsychiatric in-

volvement. For RA, 50% were treated with biologic agents or JAK inhibitors. For SLE, the main treatment was low dose glucocorticoids and hydroxyl chroloquine. [Conclusions] Characteristics of overlap syndrome of SLE and RA were reported.

P1-173

The potential for monotherapy with hydroxychloroquine in patients with SLE

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) is reported as effective in combination with other therapies, but its efficacy of monotherapy has not been reported. Thus, we examined the efficacy of HCQ for naïve SLE patients. [Methods] We conducted retrospective study in 8 SLE cases treated with >6 months of HCQ monotherapy at our institution from July 2016 to October 2019. [Results] Of 8 patients with SLE, all were females with average age (41.8) with mean disease duration of 27.5 months. Mean body weight, dose of HCQ, SLEDAI scores were 54.5kg, 225.0mg, and 9.0, respectively. 1 and 7 patients were classified as BILAG A and B, respectively. Seven of 8 patients showed improvement of BILAG after 6 months of HCQ treatment which accompanied with significant decrease in HCQ and SLEDAI (2.5) as well (P <0.01). Improvement of mucocutaneous, musculoskeletal, and nephropathy was seen by HCQ treatment while serological activities remained. Relapse occurred in 3 of 8 patients, and the cumulative remission rate was 87.5% at 2 months and 57.1% at 24 months/36 months. [Conclusions] Monotherapy with HCQ seems to be a candidate for the treatment for patients without severe organ involvement while potential to mild lupus nephritis remains such as class II/Class V in category B (BILAG).

P1-174

Clinical characteristics of disease flare in systemic lupus erythematosus/mixed connective tissue disease associated pulmonary hypertension

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Conflict of interest: None

[Objective] To investigate clinical characteristics of disease flare in systemic lupus erythematosus/mixed connective tissue disease (SLE/MCTD) associated pulmonary hypertension (PH). [Methods] We examined SLE/MCTD patients diagnosed with PH by right heart catheter in our hospital from 2000 to 2018. We divided them into 3 groups according to disease status after achieving remission; PH flare, non-PH flare and sustained remission and compared baseline clinical characteristics and right heart catheter findings. [Results] Eighteen patients were enrolled. Mean age was 47.8±13.9years. Two patients (11.1%) experienced PH flare, 7 (38.9%) non-PH flare and 9 (50.0%) sustained remission. Significant higher SLEDAI at baseline and poor reduction of mean pulmonary pressure (mPAP) after the treatment were observed in PH-flare than non-PH flare and sustained remission (p=0.05, p=0.01). Patients with non-PH flare also had poor reduction of mPAP comparing with patients with sustained remission (p=0.51). Further analysis revealed a significant correlation between change of mPAP from baseline and SLEDAI at flare (r=0.9, p<0.01). [Conclusions] Degree of mPAP change after treatment may give some information to predict future PH or non-PH flare in SLE/MCTD associated PH.

P1-175

The effects of antiphospholipid antibodies by detailed analyses of APTT waveform

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Conflict of interest: None

[Objective] To investigate the characteristics of detailed analyses of APTT waveform based on the number of antiphospholipid antibodies (aPL) in patients with connective tissue diseases (CTD) and other conditions. [Methods] The aPL and the detailed waveform of APTT including 1st derivative curve (DC) height, 2nd DC peak1 time and height were measured by depicting 1st and 2nd DC and analyzed based on the number of aPLs. [Results] Among 61 patients, scleroderma were in 19, systemic lupus erythematosus in 12, other CTD in 9, antiphospholipid syndrome in 11, and aPLs positives in 10. There were 27, 19, 4 and 11 patients who had aPLs in 0, 1, 2, or 3. APTT, 1st DC peak1 height, 2nd DC peak1 time, 2nd DC peak1 height were different among the number of aPLs ($\rho<0.0001$, respectively). APTT were 28.9 [26.8, 31.4], 30.9 [29.1, 38.2], 31.1 [27.3, 54.2], and 60.7 [45.9, 73.7] seconds, and 2nd DC peak height were 839.9 [666.1, 962.2], 669.6 [346.4, 946], 608.4 [137.8, 956.7], and 119.3 [30.6, 196] mabs/s^2 according to the number of aPLs. Half of patients with APTT over 37 seconds and 68.8% with 2nd DC peak 1 height under 310 mabs/s? had 3 aPLs. [Conclusion] The detailed analyses of APTT waveform demonstrated that those were influenced by the number of aPLs.

P1-176

Serum immune abnormalities in systemic lupus erythematosus-associated hemophagocytic syndrome

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Conflict of interest: None

[Objective] To clarify the relationship between hemophagocytic syndrome (HPS) associated with systemic lupus erythematosus (SLE) and serum immune abnormalities at the onset of HPS. [Methods] We examined the features of clinical findings and serum immune abnormalities at the onset of HPS in SLE patients with HPS from 2004 to 2019. [Results] Of 232 SLE cases, 8 cases (3.4%) developed HPS. Three cases (one case twice) suffered recurrence of HPS and a total of 12 episodes were evaluated. Three of patients developed HPS at the diagnosis of SLE. Serum anti-dsDNA antibody levels were 475.2 ± 726.0 IU / ml, and below the reference value in 9 episodes (66.7%). Serum C3 levels were 50.0 ± 23.7 mg/dl and below 60 mg/dl in only 50% of episodes. Serum CRP levels were 1.0 ± 0.9 mg/dl, and ferritin levels were 5686.4 ± 7112.1 mg/dl. Other clinical manifestations were skin abnormalities (91.7%), lupus nephritis (58.3%), joint pain (50.0%), and central nerve abnormalities (16.7%). All patients were treated with steroids, combined with tacrolimus in 41.7% and cyclosporine in 25.0%. One patient died of disseminated varicella, but the others recovered with improvement of immune abnormalities. [Conclusions] Serum immune abnormalities are not always accompanied with SLE-associated HPS.

P1-177

Etiology and treatment of systemic lupus erythematosus in Kushiro Red Cross Hospital

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Conflict of interest: None

[Objective] Our purpose is to investigate etiology and treatment of systemic lupus erythematosus (SLE) in Kushiro Red Cross Hospital. [Methods] We respectively identify 247 outpatients registered as SLE from 2013 to 2019. After excluding patients who has diagnosed as another disease and moved from other hospitals, we extract data on etiology and

treatment in 105 patients (female 98). Furthermore, in 89 patients we can access to official format of Japan Intractable Diseases Information Center, we extract clinical information. [Results] Patients has diagnosed at the age of 14-83 (mean 39.1). Common symptoms are arthritis (63.7%) and skin symptoms (45.5%). In 55 patients (50.9%) with renal disease, 27 patients received renal biopsy. 5 patients (4.8%) has been followed with no treatment. Except for 52 patients (49.5%) who has received glucocorticoid (GC) therapy and 3 patients (2.9%) who has received hydroxychloroquine, 50 patients (55%) has received both GC and other immunosuppressants. We cannot recognize outcomes of 27 patients, but 7 patients (6.7%) died and 3 patients (2.9%) moved to long term hospitals. [Conclusions] Etiology and clinical symptoms of our study are consistent with previous studies. We recognize GC remains key drug, but immunosuppressants is also essential.

P1-178

Clinical characteristics of systemic sclerosis cases with improved lung function after high-dose cyclophosphamide intravenous infusion

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Conflict of interest: None

[Objective] To study differences between good and poor responders to IVCY in lung function with SSc patients. [Methods] SSc patients treated with IVCY were selected from inpatient registry of our hospital. They were classified into good and poor responders by %FVC changes between before and one year after IVCY, and assessed each clinical data before IVCY. [Results] Thirty-one cases were included, and 24 cases in which pulmonary function was followed were assessed; 16 good responders and 8 poor responders. The mean age was 52.7±13.1 years in the good response group and 63.0±13.2 years in the poor response group, with 13 (81.3%) and 7 (87.9%) women, respectively. The diffuse cutaneous SSc was 6 cases (37.5%) in the response group and 6 cases (75%) in the poor response group (p value 0.08). Anti-RNP antibody was positive for 6 cases (37.5%) in the good response group and 0 cases in the poor response group (p value 0.07). RDW was assessed in 10 patients in the response group and 6 patients in the poor response group, and 13.7±0.7 in good responders and 14.98±1.1 in poor responders (p value 0.04). [Conclusions] Our study showed good respond to IVCY in the low RDW group, and poor response in the diffuse cutaneous SSc and anti-RNP antibody-negative group.

P1-179

Characteristics of effective cases of combination therapy with prednisolone and oral tacrolimus or azathioprine for progressive interstitial pneumonia with systemic sclerosis

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Conflict of interest: None

Objectives: We retrospectively investigated characteristics of effective cases of combination therapy with prednisolone (PSL) and tacrolimus (TAC) or azathioprine (AZA) for progressive interstitial pneumonitis with systemic sclerosis (SSc-PIP). *Methods:* Eighteen patients were TAC and 19 were AZA treated groups. *Results:* In TAC treated group,17 patients were women with the median age being 65 (range 38-81) years. In response to treatment 1 year after, IP improved in 6 patients, stable in 12 patients, and the improved group tended to be older and the anti-U1-RNP antibody tended to be positive compared to the stable group. Presently, IP improved in 6, stable in 5 patients. In AZA treated group,13 patients were women with the median age being 69 (range 56-77) years. In response to treatment 1 year after, IP improved in 5 patients, stable in 11 patients, and the improvement group tended to have more men than the stable group. Presently, IP improved in 5, stable in 11 patients, and the improved group tended to be more positive for the anti-U1-RNP antibody than the stable group. *Conclusions:* The combination therapy of PSL and TAC or AZA for SSc-PIP is effective in elderly patients and anti-U1-RNP antibody positive in TAC treated group, and male and anti-U1-RNP positive in AZA treated group.

P1-180

The predictive factors of poor prognosis in Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD): a retrospective observational study

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Conflict of interest: None

[Objective] The purpose of this study is to investigate the predictive factors of progressive ILD for early intervention with Nintedanib in patients with SSc. [Methods] 59 cases with SSc with an onset of the first non-Raynaud's symptom within 7 years admitted in our hospital from April 2012 to October 2019 were enrolled. We assessed the baseline clinical characteristics and prognosis. Risk factors of SSc-ILD progression have been reported as follows: 1) Diffuse cutaneous SSc (dc-SSc), 2) Anti-topoisomerase antibody, 3) Respiratory symptoms, 4) Low baseline FVC (<65%), 5) Low baseline DLco (<55%), 6) KL-6 >500 U/mL, and 7) SP-D >110 ng/mL. We evaluated that how many number among these 7 items exist in patients with SSc-ILD who showed poor prognosis during observation period of this study. [Results] 26 cases were diagnosed with dc-SSc. Among 13 patients with dc-SSc followed for over 1 years, patients of death or progressive ILD had more than 3 items of 2) - 7) above. If the risk of progressive ILD in cases with dc-SSc is defined as those with 3 or more items, 15 cases met the definition. [Conclusions] Patients with dc-SSc who were met the above definition may have a poor prognosis. This definition may be helpful for early intevention with Nintedanib to improve the prognosis of SSc-ILD.

P1-181

Clinical characteristics of systemic sclerosis (SSc) related heart involvement (SSc-HI)

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Conflict of interest: None

[Objective] The aim of this study is to investigate clinical characteristics of SSc-HI based on a new definition (WSF/ESC, 2019). [Method] We enrolled 249 SSc patients fulfilling ACR/EULAR 2013 classification criteria in our clinic between 2014 and 2019. Based on ultrasonic echocardiography (UCG), patients with left ventricle asynergy or pericardial effusions but without ischemic heart disease or valvular diseases were classified into SSc-HI. We compared clinical characteristics between SSc-HI and the control without significant findings on UCG. [Result] Out of 208 SSc patients in whom UCG data were available, 51% had 1> findings. LV asynergy was in 20%, diastolic dysfunction in 73%, pulmonary hypertension in 24%, and pericardial effusion in 8%. Twenty five were classified into SSc-HI, of which 68% were women, mean age was 65±11 years old, mean disease duration was 8.7±9.2 years, and diffuse cutaneous SSc was 36%. Older age (p=0.001), male (p=0.036), and lack of arthropathy (p=0.029) were relevant to SSc-HI in univariate analysis. Multivariate analysis revealed older age (p=0.004) and male (p=0.038) were related factors for SSc-HI. Four patients with SSc-HI died, whereas no one in the

controls. [Conclusion] This study suggests that older age and male are related factors for SSc-HI.

P1-182

A clinical study to explore the effect and safety of disposable warmer for the Raynaud's phenomenon observed in systemic sclerosis

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Conflict of interest: Yes

[Objective] Raynaud's phenomenon (RP) is a circulation disorder observed in systemic sclerosis (SSc). The oral vasodilators are ineffective or can cause unnecessary vasodilation. One measure that SSc patients can take on a daily basis is warming with disposable warmers. We conducted a clinical study to find out its effect for RP and where the appropriate warming site was. [Methods] The subjects were 14 SSc patients. Eight were diffuse cutaneous and 6 were limited cutaneous SSc. After obtaining the consent, the neck, elbows, and wrists were warmed with disposable warmers in the order instructed for 1 week for each site. There was 1 week interval between each site. The self-scoring for RP was recorded daily with visual analog scale (VAS). At the next day of finishing each site, the thermography (TG) was taken after the adaptation at 24 °C. [Results] Compared to the VAS during the interval period, a decrease was observed during the neck or elbow warming. No significant change observed in TG. There were 3 burns cases during neck periods. [Conclusions] Disposable warmer may be effective for RP, and it may be differ depending on the site. While neck was expected, there were concerns about safety issues. The objective method such as TG should be improved, since the weather effects were large.

P1-183

Clinical Usefulness of High Resolution Manometry for the Upper Gastrointestinal (GI) Involvement in Patients with Systemic Sclerosis (SSc)

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Conflict of interest: None

[Purpose] Upper GI tract is most commonly affected in SSc. Our aim is to show the usefulness of high-resolution manometric test (HRM) to detect upper GI lesion at earlier phase in SSc. [Methods] SSc patients who visited our clinic between April and October 2019 and fulfilled 2013 ACR/EULAR classification criteria were involved. Patients examined HRM were further extracted. Esophageal status was evaluated by upper GI endoscopy (ES) and HRCT. Esophageal motility disorders (EMDs) and lower esophageal sphincter (LES) pressure were evaluated by HRM. Some were assessed by the questionnaires for GERD (GerdQ) and swallowing functional evaluation (EAT-10). [Results] Three patients (2 dcSSc, 1 overlap) were included. Mean age at onset and disease duration were 53 and 8 years, respectively. Two was on PPI. All had esophageal dilatation by HRCT. GERD classified into the Los Angeles Classification stage A was found in 2 by ES. All had EMDs (2 ineffective esophageal motility and 1 absent contractility) and low LES pressure. Questionnaires were examined in 2 early dcSSc. No typical sign of GERD was detected by GerdQ. One was suspected to have dysphagia by EAT-10. Even though, both had EMDs and low LES pressure by HRM. [Conclusion] HRM might help to detect GI involvement at earlier phase in SSc.

P1-184

Classification of patients with diffuse cutaneous SSc based on timing of peak of skin thickness

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Conflict of interest: None

[Objective] To examine the association of the disease duration from onset to peak of modified Rodnan total skin thickness score (mRSS) with prognosis in early diffuse cutaneous systemic sclerosis (dcSSc). [Methods] This study enrolled early dcSSc patients with disease duration less than 5 years, who were registered in the SSc database on Nippon Medical School Hospital. mRSS change over time and the associations between time of peak mRSS and major organ events were investigated. [Results] Of 45 patients included in this study, 76% were female, the mean age of onset was 51 years. Total four patients died. Chronological change of mRSS showed a bimodal pattern. The patients were divided into two groups, 28 in early peak group and 17 in late peak group by the cut-off value of the disease duration from onset to peak of mRSS at 21 months. Early peak group was significantly associated with anti-RNA polymerase III antibody and short duration between onset to 1st visit ($p = 0.02$, $p < 0.0001$, respectively). Major events occurred when mRSS increased. There was no difference in the cumulative survival rate between the two groups. [Conclusions] Early dcSSc may classified into two groups based on timing of peak of skin thickness, and cumulative incidence of major organ events was higher in late group.

P1-185

Changes in sensitivity by the revision of classification criteria for systemic autoimmune rheumatic diseases

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Conflict of interest: None

[Objective] To elucidate the changes in sensitivity by the revision of classification criteria for systemic autoimmune rheumatic diseases and their overlap syndrome. [Methods] A total of 952 patients with systemic autoimmune rheumatic diseases 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, 1987 revised ACR criteria and 2011 ACR/EULAR criteria for RA, 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, 297 (old) and 389 (new) patients met RA criteria, and 12 (PM) /7 (DM) and 11 (PM)/12 (DM) patients met old and new criteria. Twenty-three and 27 patients were identified as overlap syndrome by the old and the new criteria sets, and the number reduced to 7 (old; 5 SLE-SSc and 2 SLE-PM) and 6 (new; 5 SLE-SSc and 1 SLE-PM) when patients with RA-overlap were excluded. [Conclusions] The revised classification criteria showed an improved sensitivity, and SLE-SSc overlap syndrome has been still predominant except for RA-overlap.

P1-186

Clinical and serological features of anti-centromere antibody positive limited cutaneous systemic scleroderma

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Conflict of interest: None

[Objective] Anti-centromere antibody positive limited cutaneous systemic scleroderma (lcSSc) tends to be neglected because of the mild range and degree of skin symptoms compared to diffuse cutaneous type. Howev-

er, it progresses chronically and complicates severe organ dysfunction and merges many other autoimmune diseases. Clinical features of centromere antibody positive lcSSc are examined. [Methods] 100 patients who had hospitalized in our outpatient clinic from 2012 to 2019 were enrolled. All patients met the American College of Rheumatology classification criteria for lcSSc. We assess their clinical characteristics and data. [Results] Clinical characteristics; Incidence of Raynaud phenomenon and sclerodactylia were 76 and 88%. Organ damages; interstitial pneumonia, pulmonary hypertension, PBC, Sjogren syndrome, Hashimoto's disease, SLE were 29%, 26%, 48%, 58%, 46% and 18%, respectively. Incidence of antibodies; anti-SS-A Ab was 41%, anti-TPOAb/anti-TG Ab was 46%, M2 Ab was 33%, anti-dsDNA Ab was 10%, anti-RNPAb was 8% and anti-Sm Ab was 2%. [Conclusions] Anti-centromere antibody positive lcSSc complicates interstitial pneumonia, pulmonary hypertension, primary biliary cirrhosis, Sjogren's syndrome, Hashimoto's disease and SLE at extremely high rates.

P1-187

A retrospective analysis of 20 patients with localized scleroderma

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Conflict of interest: None

[Objective] Localized scleroderma (LS) is an autoimmune disease characterized by the sclerosis of skin and its underlying tissue. The disease may cause functional impairment and disfigurement especially in pediatric cases. Early diagnosis and treatment are important to prevent disease development. In this study, we investigate the clinical features of LS in our hospital. [Methods] Retrospective chart reviews were performed of 20 patients with LS at Yokohama City University Hospital from 2006 to 2019. [Results] The mean age at onset was 22.3 years. 9 patients had pediatric-onset LS. The male: female ratio was 7:13. The mean time between symptoms onset and diagnosis was 2.5 years. The subtype was plaque subtype in 9, linear scleroderma in 3, and generalized morphea in 8. In analysis for autoantibodies, antinuclear antibody was positive in 10 while ssDNA was positive in 3. 9 patients, included 7 pediatric patients, required systemic therapy. Of the 8 patients were treated with combination therapy with prednisolone (PSL) plus methotrexate (MTX). All patients had a complete or partial response. No recurrence was observed. [Conclusions] In our analysis pediatric patients had more severe LS than adult. Combination therapy with PSL plus MTX is beneficial for severe pediatric cases in active phase.

P1-188

The case of anti-MDA5 antibody positive dermatomyositis (DM) during making thorough examination to left gingivitis and left eyelid swelling

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Conflict of interest: None

[Case] 45 years old, men. From the end of June, he had swelling of left gum. At the beginning of August, he attacked over 38°C of fever and had left eyelid swelling with redness. He was admitted to our department on 5th, cause of left eyelid swelling. There was no evidence by brain MRI. He treated with antibiotics, but from 16th, he was re-attacked high fever and appeared erythema at right back. From 20th, we stopped antibiotics. We also examined skin biopsy. At that time, the new erythema appeared at both palmers and he had slightly myalgia on both femoral muscles. We examined specific antibodies (Ab) and femoral MRI. The result of skin biopsy was superficial perivascular dermatitis with vascular degeneration and MRI had a finding of myositis on medial grate muscle. The serological examination was no positive but anti-MDA5-Ab (anti-MDA5). We diagnosed anti-MDA5 positive DM and treated with steroid (1mg/kg). We added the immunosuppression therapy because of increasing ferritin, KL-6, and appearance of ILD after steroid. [Conclusion] We experienced the case of anti-MDA5 positive DM that was difficult to reach in a diagnosis. It was suggested that steroid and combinations of immunosuppressive therapies were needed to control disease activity and prevent progression from early stage.

P1-189

The relationship between antibodies and clinical symptoms in inflammatory myopathy in our hospital

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Conflict of interest: None

MSA and MAA are frequently observed in IIMs, and their association with clinical manifestation is known. [Objective] To clarify the positive rate of MSA and MAA in our hospital, and the relationship between autoantibodies and clinical manifestation. [Methods] At our hospital, 78 patients with IIMs were included. MSA and MAA were measured by ELISA and line blot, and the relationship between these autoantibodies and clinical symptoms was examined. [Results] 69 of 78 cases were positive for MSA or MAA. Interstitial lung lesion (ILD) complication rates were MDA-5 (100%), ARS (94%), Ku (71%), PM-Scl (64%), SRP (50%), TIF1γ (20 %). In particular, rapidly progressive ILD (RPILD) was observed in 8.8% and 33% of ARS and MDA-5 positive cases, respectively. In addition, joint symptoms were observed in 50% or more of ARS, Ku, and PM-Scl positive cases. In TIF1γ positive cases, 80% had a history of malignancy or complications. No clinical symptoms specific to antibody-negative cases were observed. On the other hand, in 8 patients with multiple MSA or MAA, RPILD was observed in 25%. [Conclusions] We clarified the positive rate of MSA or MAA in our hospital and the association with clinical features. It was suggested that multiple MSA or MAA positive cases may have serious clinical symptoms.

P1-190

The outcome in patients with anti-TIF-gamma-positive dermatomyositis having malignancies who preceded treatment of cancers

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Conflict of interest: None

[Background] There has been no sufficient report on the outcomes in patients with anti-TIF1γ-positive dermatomyositis (DM) who have previously been treated for tumors. We studied 4 patients with anti-TIF1γ-positive DM treated as such. [CASE 1] 67 year-old female diagnosed as DM with cecum cancer resulted in improvement of both rash and muscle weakness by surgical operation. [CASE 2] 76 year-old male diagnosed as DM with lung cancer. Skin rash was improved by chemotherapy. [CASE 3] 71 year-old male diagnosed as DM with lung cancer. Dysphagia developed and intravenous immunoglobulin (IVIG) was initiated and rash was improved. Chemotherapy and radiation therapy was introduced for cancer. Since dysphagia remained, a gastrostomy was constructed. [CASE 4] 44 year-old female. Breast cancer was pointed out and remission was achieved by chemotherapy. Recurrence of breast cancer developed, which accompanied DM. In spite of the chemotherapy started, dysphagia developed, and steroid with IVIG was started, which resulted in improvement of rash and dysphagia. [Conclusion] In patients with anti-TIF1γ-positive DM,

preceding treatment with cancers may be associated with favorable outcomes of DM. Dysphagia may remain or appear. Treatment strategies should be established in this patient population.

P1-191

A case of anti-PL-7 antibody positive necrotizing myopathy

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Conflict of interest: None

A 77-year-old woman was admitted to our hospital due to a 2-year history of dyspnea on exertion (DOE) and a 1-year history of bilateral proximal muscle weakness. After 1 month of systemic evaluation, however, the patient's muscle weakness worsened. The patient was transferred to our department. On admission, serum creatine kinase (CK) levels increased to 226 U/L, and anti-PL7 antibody was positive. A muscle biopsy from biceps was performed, and necrotizing myopathy (NM) with necrotic and regenerated myofibers were observed. A phrenic motor nerve conduction study showed the presence of diaphragm weakness. Based on these findings, the patient was diagnosed with anti-PL7 antibody positive NM. She was treated with prednisolone (PSL) at a dose of 40 mg/day and intravenous immunoglobulin therapy. Despite tapering of PSL, the muscle weakness and DOE gradually improved, and the levels of serum CK was lower limit of normal. Finally, the patient was discharged at our hospital 3 months after admission. We report a rare case of anti-PL7 antibody positive NM, which showed sufficient response to immunosuppressive therapy. It is necessary to evaluate muscle biopsy specimens immunologically and measure anti-ARS antibodies such as anti-PL7 antibody for prognostic prediction.

P1-192

Five cases of interstitial pneumonia with anti-MDA5 antibody-positive dermatomyositis: Retrospective analysis on clinical parameters to predict the prognosis of the disease

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Conflict of interest: None

[Objective] Clinical characteristics suggesting the prognosis of interstitial pneumonia (IP) associated with anti-MDA5 antibody-positive (aMDA5Ab$^+$) dermatomyositis (DM) remain largely unknown. [Methods] Five cases of IP with aMDA5Ab$^+$ DM admitted to our institution between January 2012 and April 2019 were retrospectively analyzed. [Results] Three cases survived and two cases died during hospitalization for IP with aMDA5Ab$^+$ DM. Mean age of patients who survived (Group A) and died (Group B) were 39.3 and 69.0 years, respectively. Muscle weakness was seen in one case in Group A, in which the serum CPK level was 1,282 U/l (Mean CPK levels were 74.75 U/l). Mean values of various laboratory tests were **as** follows*:* Anti-MDA5 antibody, 1875 in Group A and 4200 in Group B; LDH (IU/l) 507.3 in Group A and 301.5 in Group B; KL-6 (U/ml), 550.0 in Group A and 643.5 in Group B; SP-D (ng/ml) 193.1 in Group A and 32.35 in Group B; CRP (mg/dL) 3.767 in Group A and 0.5800 in Group B; and ferritin (ng/mL) 1008 in Group A and 489 in Group B. Mean duration between hospitalization and occurrence of related symptoms (days) was 58.33 in Group A and 52.50 in Group B. [Conclusions] Surviving cases were younger and showed higher levels of LDH, SP-D, CRP and ferritin and lower levels of anti-MDA5 antibody and KL-6.

P1-193

Summary of previous reports of therapeutic apheresis with PM/DM-IP

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Conflict of interest: None

[Objective] The prognosis of PM/DM-IP is improving with multidisciplinary treatment. Especially, many successful cases of endotoxin adsorption therapy (PMX) and simple plasma exchange (PE) are reported in Japan, but it was not covered by insurance. To improve this situation, we considered through previous reports. [Subjects] 32 reports among 494 cases searched in Japan medical abstracts society in October 2019. [Methods] 494 cases were searched. About these reports, those subjects are detected; age, gender, autoantibodies, PM / DM / CADM, complications, clinical indicators, immunosuppressants, modality of therapeutic apheresis, and outcomes. [Results] There were 2 case series and 30 case reports. The average age is 65.4 years and the M/f is 16/24. CADM / PM / DM is 34/5/1 cases and 27/40 patients survived. In almost all cases, three immunosuppressants were used in combination. 10 PE and 20 PMX were performed. Respiratory failure and KL-6 levels had a relatively rapid improvement and tended to survive if re-exacerbation could be prevented. [Conclusions] The effects of PMX and PE in PM/DM-IP were the accumulation of case reports. In order to therapeutic apheresis in the future, it was considered necessary to immediately collect data and each case report.

P1-194

Anti-MDA5 antibody-positive dermatomyositis with two pulmonary opacity following different courses

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Conflict of interest: None

A 32 year-old woman presented with fever, joint pain, rash and cough. Two months later, she was admitted to our hospital. CT revealed consolidation of adjacent to the pleura at lower lobe and we diagnosed her as organizing pneumonia. A blood test revealed positive anti-MDA5 antibody (3,650U), we diagnosed her as dermatomyositis with organizing pneumonia. She received intravenous methylprednisolone pulse therapy (1,000mg for 3days), following oral prednisone (50mg/day) and tacrolimus. Her symptoms and pulmonary opacity had improved, we could taper prednisolone gradually. After 8weeks of the initial treatment, CT showed random GGA at upper lobe. As an exacerbation of interstitial pneumonia, 6 courses of intravenous cyclophosphamide pulse (500mg/m2 every 2weeks) were administered. With these treatments, random GGA remained to some extent without progression of interstitial pneumonia. When prednisone dosage was reduced to 15mg/day, her consolidation of adjacent to the pleura at lower lobe appeared. After TBLB she was diagnosed with relapse of organizing pneumonia. We continued the treatment without progression of interstitial pneumonia. Interestingly, we experienced a rare case of positive anti-MDA5 antibody dermatomyositis with two different types of pulmonary opacity.

P1-195

Clinical investigation of dermatomyositis patients with malignancy

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Conflict of interest: None

[Objective] To investigate the clinical significance of dermatomyositis (DM) patients with malignancy. [Methods] In patients with DM diagnosed at our hospital between January 2016 and October 2019, we retrospectively investigated clinical features stratified by the presence of malignancy within 2 years before and after diagnosis of DM. [Results] Subjects were 57 cases. The average observation period is 22.1 ± 30.3 months. The mean age at onset was 58.3 ± 14.2 years, and 24 cases (42.1%) were male. Nine cases (15.7%) had malignancy. There were 3 gastric cancers, 2 breast cancers, 1 prostate cancer, 1 oropharyngeal cancer, 1 myelodysplastic syndrome, and 1 cancer of unknown primary. The group with malignancy was

older (70.3 ± 12.2 years old VS 56.0 ± 13.6 years old, P = 0.0084). The group with malignancy tended to have more dysphagia (P = 0.0536). There was no difference between the two groups in sex, muscle weakness, serum CK, serum aldolase, serum LDH, serum ferritin, serum CRP, serum KL-6, prevalence of interstitial lung disease, and use of immunosuppressant. In the group with malignancy, 8 out of 9 cases died and the prognosis was poor (P=0.095). [Conclusions] These results suggest that DM patients with malignancy have an elderly onset and dysphagia and a poor prognosis.

P1-196

Ulcerative colitis related myositis characterized with gastrocnemius myalgia syndrome that diagnosed by proximal muscle biopsy

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Conflict of interest: None

49-year-old female has been diagnosed with ulcerative colitis (UC). After 4years, UC worsened and she was difficult to walk due to lower legs pain. Erythema with tenderness in the lower leg and skin biopsy performed. Panniculitis were recognized the fascia and fasciitis was observed. She was not shown muscle weakness. MRI of the extremities deteted that the area around the achilles-tendon was shown high signal intensities. The other biceps muscles also suggested myositis. The electromyography was shown myopathy only in the distal legs. Antinuclear antibody 1:1280, but disease-specific autoantibodies are positive only for anti-RNP antibody 30.5 Index. Brachii muscle biopsy was performed. The muscle cell membrane was positive for anti-HLA-class I antibody, and mononuclear cell infiltration was more increased under the fascia than the muscle bundle, and inflammation spread from the fascia to the muscle fibers. No vasculitis findings and eosinophil infiltration were observed. Prednisolone was started, symptoms improved. Inflammatory bowel disease with myalgia of lower legs is known as gastrocnemius myalgia syndrome. Recently, pathological examinations revealed myositis, but there was no report of myositis in muscle biopsies other than the lower leg.

P1-197

Clinical significance of anti-signal recognition particle antibody (aSRP-Ab) in inflammatory myopathies

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Conflict of interest: None

[Objective] Inflammatory Myopathies are known as muscledisorders due to immunological mechanism. Anti-signal recognition particle antibody (aSRP-Ab) is used as a serological marker of immune-mediated necrotizing myopathy, which is characterized by necrotic and regenerative muscle fibers without inflammatory cell infiltration. To elucidate the clinical features of aSRP-Ab positive myopathy patients. [Methods] Clinical features such as symptoms, laboratory data, radiographic findings, treatment, were analysed in 4 patients with aSRP-Ab positive myopathy. [Results] Primary diagnosis are dermatomyositis (2 cases) or polymyositis (2 cases). All patients had severe neck and limb muscle weakness, dysphagia, and muscle atrophy. Serum creatine kinase (CK) were markedly elevated (8850.0±357.4U/L). Histology showed a predominant muscle fiber necrosis with regeneration in the absence of inflammation. All patients were initially treated with corticosteroids, however, additional immunosuppressive drugs and/or intravenous immunoglobulin were required. CK was improved in most patients, however, muscle weakness was not fully recovered. [Conclusions] aSRP-Ab is associated with severe muscle weakness. Further investigation is required in order to develop a better treatment strategy in aSRP-Ab myopathy.

P1-198

A case of anti-signal recognition particle antibody-positive immune-mediated necrotizing myopathy with treatment-resistant interstitial pneumonia

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Conflict of interest: None

A 68-year-old woman had mild interstitial pneumonia and was followed without treatment. She had dyspnea on exertion, bilateral femoral muscle pain and muscle weakness. CK was elevated (6270 U/L). Her CT showed consolidation in the bilateral lower lungs. Histopathological findings in muscle biopsy revealed necrosis and regeneration of muscle fibers, with no or little lymphocyte infiltration. She was diagnosed as having inflammatory myopathy with interstitial pneumonia (IP), and oral prednisolone, intravenous cyclophosphamide, tacrolimus were initiated. CK decreased to the normal level. Her chest radiological findings were improved. Positive anti-signal recognition particle (anti-SRP) antibody was confirmed. Her prednisolone dose was gradually tapered. Two years later she had a flare of IP. Her prednisolone dose was increased to 40 mg/day and tacrolimus was changed to azathioprine. Some cases of anti-SRP antibody-positive immune-mediated necrotizing myopathy associated IP were resistant to treatment. the Early treatment with corticosteroid and immunosuppressants may improve the clinical outcomes of myopathy.

P1-199

A case of successful treatment with intravascular immunoglobulin without high-dose steroids for dermatomyositis associated with lung cancer

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Conflict of interest: None

[Case] 70s male [History of present illness] 8 months before, he was diagnosed with small cell lung cancer, and chemotherapy was started. Then, he was referred to our department because of generalized muscle pain, swelling of the face, erythema and dysarthria. [Findings on Admission] Eyelids and cheeks were swollen, and erythema was observed from the scalp, chest and abdomen. There was muscle grasping pain. Examination showed CK elevation and anti-TIF1γantibody positive. [Clinical Course] We diagnosed dermatomyositis associated with small cell lung cancer, and treated with Intravascular immunoglobulin (IVIG) without high-dose steroids. After treatment begins, the condition of dermatomyositis was controlled and the next chemotherapy was administered. [Discussion] Currently, for dermatomyositis associated with malignant tumors, immunosuppressive therapy is often performed in parallel with chemotherapy. However, immunosuppressive therapy is a concern for the development of malignant tumors and the risk of infection. We experienced a case of dermatomyositis associated with lung cancer successfully treated with IVIG without high-dose steroids. IVIG does not cause immunosuppression, so it may be an effective and safe treatment option for dermatomyositis associated with malignant tumors.

P1-200

Inclusion body myositis after 20 year-history of polyarthritis and muscle weakness

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Conflict of interest: None

[Chief complaint] muscle weakness [History of present illness] A 76-year-old man was referred to us for slowly progressive muscle weakness. At age 50, rheumatoid arthritis was diagnosed and methotrexate con-

trolled the joint pain. After age 60, the patient gradually developed reduced grip strength, and proximal muscle weakness with difficulty in lifting his arms and extending his knees. Statin was discontinued for elevated serum creatinine phosphokinase level, although muscle weakness progressed with normalized CPK. [Clinical course] The physical examination showed atrophy in medial thigh, and weakness in finger flexor and quadriceps. On laboratory test, antinuclear antibody, rheumatoid factor, anti-CCP antibody, and anti-SSA antibody were positive. The MRI showed a high signal in the right biceps muscle on DWI. The muscle biopsy was notable for rimmed vacuoles. He was diagnosed as inclusion body myositis. [Clinical significance] Arthritis followed by slowly progressive muscle weakness was challenging in reaching a diagnosis, but distal muscle weakness and rimmed vacuoles in muscle biopsy were the hallmarks of the inclusion body myositis. Autoimmune conditions including Sjogren syndrome and rheumatoid arthritis have been reported to be associated with inclusion body myositis.

P1-203

Successful treatment with tocilizumab for a refractory patient with Takayasu arteritis who had recurrent pseudoaneurysms after aortic graft replacement

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Conflict of interest: Yes

A male in his 30s was diagnosed as aortic regurgitation and ascending aortic aneurysm with a maximum minor diameter of 59 mm after the workplace health check in 2011. He underwent Bentall operation and hemiarch replacement, and he was also diagnosed as Takayasu arteritis (TAK) (Numano's classification IIb) pathologically. Prednisolone (PSL) was started at 30mg dose per day postoperatively, but because of lack of inflammation, it was tapered rapidly and was temporarily discontinued. However, in 2013, a pseudoaneurysm was detected and he underwent total arch replacement. Furthermore, in 2016, he suffered from another pseudoaneurysm under PSL treatment and he was forced to undergo stent graft replacement (TEVAR). Due to the recurrent pseudoaneurysms under PSL treatment, tocilizumab (TCZ) was started in addition to PSL in 2017. After starting TCZ, there have been no worsening vascular lesions including pseudoaneurysms on imaging test. In addition, the dosage of PSL could be reduced to 6mg/day, and both his obesity and liver dysfunction were normalized. This case indicates that inflammation should be strictly controlled in the patients with TAK during the perioperative period. TCZ might be effective for refractory patients with TAK who needs surgical replacement therapy.

P1-204

Long-term usefulness of tocilizumab for patients with Takayasu's arteritis

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Conflict of interest: None

[Objective] To investigate efficacy and safety of tocilizumab (TCZ) for patients with Takayasu's arteritis (TAK). [Methods] We examined 1) background, 2) concomitant drugs, 3) CRP, 4) prednisolone (PSL) dose, 5) relapse and adverse events (AE), in patients with TAK who started TCZ between Aug 2017 and Sep 2019 in our hospital, retrospectively. [Results] 1) 9 patients (female 8/male 1, 24.8±7.8 years old, 5.2±4.5 years of disease duration, 5 cases of type IIa and 4 of type V) were investigated. TCZ was used for the first induction therapy (Tx) in 2 cases and the maintenance Tx in 7 cases. 2) In 2 cases of induction Tx, 1.0 and 0.52 mg/kg/d of PSL was concomitantly used. In 7 cases of maintenance Tx, 0.21±0.09 mg/kg/d of PSL was used, and all 7 cases received concomitant immunosuppressants (MTX in 4 cases, AZA 4, CsA 2, and MMF 1). 3) CRP (1.8±2.3 mg/dl at 0W) significantly decreased after 4W. 4) In 2 cases of induction Tx, PSL doses were tapered to 0.27 (56W) and 0.09 (104W) mg/kg/d, respectively. In 7 cases of maintenance Tx, PSL doses were significantly decreased after 16W (0.16±0.05 mg/kg/d). 5) Although 2 relapses and 2 AE occurred during 63.6±31.8W of observation period, the retention rate was 100%. [Conclusions] TCZ had a steroid-sparing effect and high retention rate in Tx for TAK.

P1-206

A case of giant cell arteritis presented with sixth nerve palsy

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Conflict of interest: None

[Presentation of case] A 76-year-old woman was referred to neurosurgery department of our hospital because of diplopia, malaise, and headache for 2 weeks. Her headache spontaneously improved in several days from onset, but diplopia continued. Magnetic resonance imaging of the head showed no abnormal findings. Because C-reactive protein elevated up to 6.65mg/dL, she was referred to our department. [Course] Physical examination revealed an enlarged left temporal artery (TA) and isolated left abducens nerve palsy. Since ultrasonography for TA showed "halo sign", strongly suspected for giant cell arteritis (GCA). After TA biopsy, prednisolone (PSL) 50mg/day was initiated. Histopathologic findings consist with GCA, and tocilizumab (TCZ) 162mg/every week was initiated concomitantly. After 3 days of initiation of PSL, diplopia disappeared. PSL could be tapered without relapse after treatments initiation. [Clinical significance] Optic nerve involvement is common feature of GCA and other cranial nerve palsy were also reported as symptom of GCA. Isolated abducens nerve palsy is reportedly rare but should be considered as a feature of GCA.

P1-207

A case of HLA-B52 positive aortitis that appeared after the onset of pneumococcus pneumonia and improved spontaneously

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Conflict of interest: None

[Case] 68 years old man had fever, dyspnea and chest pain after improvement of pneumococcus pneumonia. CT and MRI scans showed thickening of the blood vessel wall and fat around the blood vessel from the aortic arch to abdominal aorta. His fever and radiographic aortitis were improved spontaneously. Subsequent examination revealed HLA-B52 positive, but SNP of IL-12p40 was a non-risk allele. [Discussion] The development of Takayasu arteritis reported to be associated with HLA-B52 positivity, IL-12p40 production and NK cells. NK cells have been reported to be important that the immune response to pneumococcus pneumonia and IL-12 production. So they might have contributed to the development of Takayasu arteritis. The background, and environment factors are considered to be related, and it was a very interesting case in considering its pathogenesis.

P1-208

A patient with drug-associated large vessel vasculitis

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Conflict of interest: None

A 68-year-old female with uterine cancer was treated with TC regimen (PAC+CBDCA) after surgery. In addition, she was administered with pegfilgrastim for preventing chemotherapy-induced febrile neutropenia. She had fever, liver dysfunction, and proteinuria on day 14 during the third course of TC. Contrast-enhanced computed tomography revealed inflammation of large vessel, from the aortic arch to the brachiocephalic and left subclavian artery. She was negative for autoantibodies, including anti-neutrophil cytoplasmic antibodies. After discontinuation of pegfilgrastim, her symptoms and abnormal findings in imaging tests had spontaneously subsided. These clinical course suggested that she had pegfilgrastim-associated vasculitis. Some previous studies reported the occurrence of pegfilgrastim-associated vasculitis; it could occur not only after the first adminiatration, but also after the second or third administration; and the onset could be on day 3 through day 15. Pegfilgrastim-associated vasculitis usually involves small vessels, such as cutaneous vasculitis, and large vessel vasculitis is rare. If idiopathic fever is observed after administration of pegfilgrastim, comprehensive examinations should be performed considering the possibility of drug-associated vasculitis.

P1-209

A case of aortitis suspected to be related to G-CSF

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Conflict of interest: None

<Case>69 year-old female<Present history>The patient was diagnosed with sphenoid sinus chondrosostoma, and started chemotherapy (doxorubicin) at our cancer center. Two weeks after administration, neutropenia appeared requiring administration of a G-CSF preparation (pegfilstigram). Two weeks after the first administration of pegfilstigram, a blood test showed a high CRP value of 33.5 mg/dL, and it was normalized without any intervention. Chemotherapy was continued, and the same dose of pegfilstigram was administered for neutropenia. Two weeks after the second dose, CRP increased to 21.8 mg/dL, and thoracoabdominal computed tomography (CT) revealed thickening of the thoracic to abdominal aortic wall, and he was admitted to our department. <Progress after hospitalization>Blood culture was negative, and no findings suggesting infectious aortitis or giant cell arteritis were obvious. On the 16th day of admission, CRP was 0.2 mg/dL, and an improvement in aortic wall thickness was observed on thoracoabdominal CT. Finally, we diagnosed this case with aortitis induced by pegfilstigram. <Discussion>G-CSF preparations are widely used for neutropenia due to chemotherapy, but complications of aortitis are known as a rare side effect. It is necessary to pay attention to the complication.

P1-211

Clinical study of tocilizumab treatment for Takayasu arteritis in our department

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Conflict of interest: None

We investigated the clinical manifestation of four patients with Takayasu arteritis (TA) resistant to treatment with steroids and immunosuppressants in our hospital. All cases were female. The patient's median ages were 43 years old, average disease duration 7.25 years, median durations from diagnosis to tocilizumab (TCZ) administration was 45months. There were 2 cases of type IIa, 1 case of type I, and 1 case of type III, and no coronary or pulmonary artery lesion. HLA B52 was positive in 1 case and B39 in 1 case. In the initial treatment, steroids were administered to all patients. They relapsed with steroid tapering, and combined with immunosuppressants (2 methotrexate, 2 azathioprine, 2 cyclosporine). The effect was insufficient with the immunosuppressants, and TCZ (sc 2 cases, iv 2 cases) was started in all cases. One of them was a switch case from infliximab. Symptoms improved after the initiation of TCZ, steroid and immunosuppressant doses could be reduced. In one case, TCZ reduced disease activity and resulted in safe pregnancy and childbirth. In a Japanese clinical phase 3 study, the no recurrence rate of TA at 24 weeks after the first administration of TCZ was reported to be 50.6%, and TCZ was considered to be effective for relapsed intractable TA.

P1-212

A case of aortitis associated with PEGylated granulocyte-colony stimulating factor

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Conflict of interest: None

[Case] A 58-year-old female with breast cancer with Stage III received 4 courses of adjuvant chemotherapy that included dose-dense Adriamycin and Carboplatin. After that, she got the initial chemotherapy including dose-dense Paclitaxel. The next day, she was administered G-CSF and left our hospital. She developed back pain, epigastric pain and fever at home. When she admitted to our hospital for the second chemotherapy, her laboratory results showed elevated C-reactive protein (CRP). Her blood cultures were negative and autoantibodies were negative. Contrast-enhanced computed tomography (CE-CT) revealed concentric thickening of the thoracic descending aorta. Infection and autoimmune disease were unlikely, so she was diagnosed with aortitis. To treat the aortitis, she was started on 30mg of oral prednisolone 6days after the administration. Her symptoms disappeared rapidly and CRP became negative within two weeks. A repeat CE-CT scan showed no signs of aortitis 38days after the administration. [Clinical Significance] G-CSF associated aortitis is a rare disease. When a patient who administered G-CSF treatment develops fever, elevated inflammatory reaction and back pain, we should suspect drug-induced aortitis. CE-CT is suitable for detecting aortitis.

P1-213

A case of Takayasu arteritis in which remission was achieved with tocilizumab combined with low dose methotrexate

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Conflict of interest: None

The case was a 49-year-old woman. A medical checkup pointed out an increase in CRP and she visited our hospital. Takayasu arteritis was diagnosed from abdominal bruit in the upper umbilical region and aortic wall thickening in the ascending, abdominal aorta and aortic arch on contrast-enhanced CT. Prednisolone 30mg was started, CRP decreased, and the wall thickening was improved by imaging, but CRP increased again with prednisolone reduction. Although methotrexate and azathioprine were added, they could not be continued due to ineffectiveness or side effects respectively. After tocilizumab weekly subcutaneous injection was started, CRP became negative. Follow-up contrast-enhanced CT revealed thickening of the arterial wall at the bifurcation of the common iliac artery, so ^{18}F-FDG PET/CT was performed. Because focal ^{18}F-FDG uptakes were observed in the common iliac bifurcation, methotrexate 6mg/week was added again, but the dose was reduced to 4mg/week due to liver damage. After eight months, ^{18}F-FDG PET/CT was examined again, ^{18}F-FDG uptakes observed near the common iliac bifurcation disappeared, and remission was achieved on the PET-CT. It was suggested that evenif remission was not achieved even by tocilizumab, remission could be achieved by adding low dose immunosuppressant.

P1-215

A case of Takayasu arteritis associated with MPO-ANCA positive Hypertrophic pachymeningitis

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Conflict of interest: None

A 63-year old man was referred to our hospital with general fatigue in March, 2019. He had a difference of right and left upper limb blood pressure. Laboratory examinations revealed a CRP level of 3.33 mg/dl and an ESR of 100 mm/hr. The patient was positive for RF and MPO-ANCA and negative for ACPA, ANA and PR3-ANCA. PET/CT revealed the accumulation of FDG in the ascending aorta, aortic arch, descending aorta, brachiocephalic trunk and left subclavian artery. Stenosis and wall hyperplasia of the pulmonary artery was observed on contrast CT. Endocranial hyperplasia at the Th level 2-8 was observed on spine MRI. The patient was diagnosed with Takayasu arteritis associated with MPO-ANCA positive hypertrophic pachymeningitis. Neither RA nor ANCA-related angiitis was diagnosed. The patient was treated with PSL from July 2019 and his CRP level and ESR normalized gradually. Wall hyperplasia of ascending aorta, aortic arch, descending aorta, and pulmonary artery showed improvement on contrast CT. Endocranial hyperplasia was reduced on in spine MRI. Takayasu arteritis is a disorder that affects large vessels. There are reports of GPA complicated by MPO-ANCA positive hypertrophic pachymeningitis. This case is rare and we present this case with a discussion of the relevant literatures.

P1-216

FDG-PET/CT for the disease activity assessment of Takayasu's arteritis treated with tocilizumab: Two cases report

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Conflict of interest: None

[Objective] We report two cases that evaluated the effectiveness of FDG-PET/CT for the disease activity assessment of Takayasu's arteritis (TAK) treated with tocilizumab (TCZ). [Case 1] A 29-year-old woman with neck pain. Ultrasonography (US) detected wall thickening and stenosis of carotid artery. CT showed wall thickening involving the ascending to abdominal aorta. She received prednisolone (PSL), and added methotrexate (MTX) due to relapse of neck pain. And TCZ was initiated, due to worsening carotid artery stenosis. Five years later, she had transient chest pain without serum CRP elevation. There was no significantly uptake in PET scan. We determined no relapse. [Case 2] A 26-year-old woman with neck pain. US detected wall thickening and stenosis of carotid artery. CT showed wall thickening involving the aorta and branch arteries. PSL was started and cyclosporine (CyA) was added due to relapse. And, CyA was changed to TCZ sc. She had chest pain without serum CRP elevation. There was uptake in the descending aorta. Despite MTX addition improved her symptom, we considered the disease activity continued from re-examination of PET scan. [Discussion] We need to comprehensive evaluate clinical symptoms and imaging studies for assessment of the disease activity of TAK with TCZ therapy.

P1-217

A case of large-vessel vasculitis with pulmonary hypertension caused by complete occlusion of the left pulmonary artery

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Conflict of interest: None

A 74-year-old man visited our hospital due to exertional dyspnea. Blood test showed elevated serum CRP level, and echocardiography showed TRPG of 66.7 mmHg. Contrast-enhanced CT showed wall thickness of the ascending aorta and pulmonary arteries, complete occlusion of the left pulmonary artery and stenosis of the origin of the right pulmonary artery. Pulmonary ventilation/perfusion scintigraphy showed a defect in the entire left lung. Brain MRA and temporal artery biopsy showed no abnormalities. PET-CT showed FDG accumulation in the ascending aorta and left pulmonary artery. HLA-B52 positive was also found. Based on these findings, the patient was diagnosed with large-vessel vasculitis complicated by pulmonary hypertension (PH), and treatment with prednisolone (PSL) and tocilizumab was started. The elevated CRP level and PET-CT findings improved, and PSL was tapered. The present case was suspected to have Takayasu arteritis (TAK) rather than giant cell arteritis because he was HLA-B52 positive and had pulmonary artery lesions. It is reported that the prognosis of TAK complicated with PH is poor. In this case, in addition to immunosuppressive treatment, multimodality therapy including pulmonary vasodilators and catheter/surgical treatment should be considered.

P1-218

Two cases of young female Takayasu's arteritis using tocilizumab in the earliest term

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Conflict of interest: None

Clinical significance: TAK occurred in young females. we treated them with immunosuppressants considering the affection of patients' fertility. TCZ is useful for the patients. Here, we expressed 2 cases of young females with TAK using TCZ for the earliest term. Case 1: A 23-year-old female was diagnosed TAK with her 10 years' general fatigue, 1 year's fatigue of both her upper limbs, 3 months' her syncope, her decreased both upper limbs blood pressure (BP), elevated serum CRP level (1.3 mg/ dL), and stenosis at the beginning of the 3 branches of her aortic arch. Thus, she was referred to our division. Case 2: A 26-year-old female was diagnosed TAK with her 6 yeas' chest discomfort, elevated serum CRP level (8.6), her decreased both upper limbs BP, AR, aortic root enlargement, ascending aorta aneurysm, and stenosis at the beginning of the 3 branches of her aortic arch. Consulting a practitioner with her chest abnormal shadow, she was referred to our cardiovascular surgery division for the aim of operation. In the both, we decided to consider surgery after prior medical treatment and treated them with PSL 1 mg/kg/day. Their bilateral upper limbs' BP and their CRP were improved; thereafter, we added TCZ-SC considering their fertility, and tapered the PSL's dose.

P1-219

Takayasu arteritis with systemic lupus erythematosus and antiphospholipid antibody syndrome -a Case Report

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Conflict of interest: None

[Case Report] A 53-year old female with history of systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome (APS), who have been treated with predonisolone (PSL) 9 mg/day and cyclosporine (CyA) 75 mg/day, hydroxychloroquine (HCQ) 200 mg/day, came in for consultation due to epigastoric pain and back pain. Epigastric pain and back pain developed from September X. The symptoms continued to worsen, and she was admitted to our hospital for the purpose of close examination and treatment. Increased inflammatory response, increased red sedimentation, increased hepatobiliary enzymes, and contrast CT showed wall thickening around the thoracoabdominal aorta at the level near the diaphragm. Blood culture, β-D glucan, and T-SPOT were negative and the antibacterial drug was not effective. Therefore, the infection was negative, and Takayasu arteritis was diagnosed. HLA-B52 was also positive. Treatment was started by increasing the dose to 40 mg of PSL, and pain and inflammatory responses improved rapidly. Two weeks after the start of treatment, contrast CT showed improvement in aortic wall thickening. [Conclusions] We experienced a case of Takayasu arteritis in an SLE patient with antiphospholipid syndrome. There are few reports on the combi-

nation of Takayasu arteritis.

P1-220

FDG-PET/CT findings in patients with Takayasu arteritis and giant cell arteritis

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Conflict of interest: None

[Objective] To analysis the FDG-PET/CT (PET/CT) findings in patients with Takayasu arteritis (TKA) and giant cell arteritis (GCA). [Methods] We clarified the radiographical and clinical characteristics in patients with TKA and GCA. We evaluated seven patients with TA and compared them with six patients with GCA. PET/ CT was performed for all patients before treatment from April 2016 to October 2019. [Results] FDG accumulation in the internal carotid artery and ascending or descending aorta was highly observed in both TKA and GCA patients up to 80%. An up-take of FDG in abdominal aorta was observed in six patients (86%) of GCA patients whereas that was not observed in TAK patients. In addition, temporal, lilac and thigh arteries were affected in GCA patients, suggesting more extensive distribution of arteritis compared to that of TAK group. PET/CT also revealed enthesitis in five GCA patients (71%). [Conclusions] Distribution of FDG uptake in the large vessels was different between TAK and GCA. The affected large vessel walls were more extensive in patients with GCA than that of TAK patients.

P1-221

Correlation between FDG-PET / CT or temporal artery ultrasound and temporal artery biopsy in diagnosis of giant cell arteritis

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Conflict of interest: None

[Objective] GCA is diagnosed by diagnostic imaging such as ultrasonography, MRA, and PET-CT and pathological examination of the temporal artery. In this study, we investigated the correlation between imaging tests and biopsy results for patients who were diagnosed with GCA. [Methods] For 17 patients who met 3/5 or more of the 1990 ACR classification criteria in our hospital from April 2014 to October 2019, we evaluated temporal artery ultrasound or FDG- PET / CT and temporal artery biopsy at the time of diagnosis. And we analyzed the results. [Results] The patient background was an average age of 78.4 ± 7.9 years, 9 males (52.9%), and the mean ESR and CRP before treatment were 92.1 ± 32.8 mm / 1h and 15.5± 10.2 mg / dl, respectively. In temporal artery biopsy, 15 out of 17 cases (88.2%) were comparable to GCA. Five cases (62.5%) showed large vessel vasculitis on FDG-PET / CT, and all of them corresponded to GCA in pathological results. On the other hand, three cases with no findings on FDG-PET / CT showed wall thickening on temporal artery ultrasound. All of them showed GCA findings in the pathology. [Conclusions] Both FDG-PET / CT and temporal artery ultrasound are effective examination tools for GCA. Combining both tests may improve the accuracy of GCA diagnosis.

P1-223

Clinicopathological study on temporal artery biopsy

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Conflict of interest: None

[Objective] To clarify the pathological characers of temporal arteritis [Methods] 13 cases, 58-79 years-old, including 6 males and 7 female, had been invesgated histologically. [Results] Thickening of the intima and the adventitia of the arteries were both observed in all cases. Inflammation was observed in the intima of 12cases, in the media of 10 cases and in the adventitia of only 6 cases. Lymphocytes and plasma cells were often observed. Neutrophils were seen in 7 cases and eosinophils in only 3 cases. Multinuleated giant cells were seen in only 7 cases. [Conclusions] More active inflammation was observed in the adventitia than in the intima in this study, though the intima was said to be mainly damaged histologically in temporal artery patients. Giant cells also could not be observed in some cases. These observation could suggest that temporal arteritis might be similar disease to Takayasu arteritis.

P1-224

Two cases of giant cell arteritis diagnosed after longstanding polymyalgia rheumatica

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Conflict of interest: None

Case 1: An 88-year-old woman complained of scalp pain, a mild decline in vision, and appetite loss. She was diagnosed with polymyalgia rheumatica (PMR) 5 years ago and had been treated with prednisolone (PSL) until 3 months before. PET/CT showed abnormal uptake of FDG in bilateral temporal arteries and ultrasound displayed a concentric arterial wall thickening. Diagnosis of giant cell arteritis (GCA) was made. She was treated with PSL again, in a dose of 20 mg/day. Her symptoms improved rapidly. Case 2: A 78-year-old woman was seen in our rheumatology clinic because of abnormal uptake of FDG in right temporal artery in PET/CT performed two weeks before. She had a partial glossectomy at 69 years old. PET/CT has been performed every year to detect relapse. She experienced bilateral girdle pain associated with elevated serum CRP 13 months before. A biopsy of the right temporal artery revealed granulomatous inflammation with giant cells. She was treated with PSL 25 mg/day. Her symptoms improved rapidly. Conclusion: It was reported that patients who develop GCA after the onset of PMR were associated with a significant risk for ischemic blindness. When patients with PMR complain of new head ache, they should be evaluated for GCA and aggressively treated without delay.

P1-225

A case of giant cell arteritis with tongue ulcers

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Conflict of interest: None

A 78-year-old female started to have discomfort in the tongue and temporal pain on mid-June, 20XX. The swelling and pain of the tongue gradually deteriorated, and tongue ulcers and necrosis occurred in early July. The blood tests showed increased white blood cells and high CRP, and she was admitted to our hospital. Ultrasonography showed uniform IMT thickening of the bilateral internal carotid artery, and a CT scan revealed thickening of the arterial wall from the aortic arch to the descending aorta. We diagnosed the patient as having giant cell arteritis (GCA). Oral prednisolone 1 mg/kg/day was started. A temporal artery biopsy, performed 7 days after the treatment, showed inflammatory cell infiltration in the adventitia and proliferation of small blood vessels. Although symptoms tended to improve, CRP positivity persisted, and a new lingual infarction was observed 9 days after the treatment. Steroid pulse therapy was performed, which resulted in the improvement of the tongue ulcers and the thickening of the arterial wall. Tocilizumab was initiated and PSL was tapered. GCA tends to be more common in white people from North America and less in Asians. Cases of tongue ulcers due to GCA have been reported overseas, but not yet in Japan.

P1-226

Comparison of treatments for two different types of giant cell arteritis (GCA)

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Conflict of interest: None

[Objective] To compare the differences between treatments of cranial GCA (C-GCA) and large vessel GCA (LV-GCA). [Methods] Patients diagnosed as GCA from 2011 to 2018 were divided in two different groups, C-GCA which was proven by the superficial temporal arteries biopsy (STAB) and LV-GCA which was diagnosed by cntrast CT and/or PET-CT and/or MRI. Their treatments at initial time and in a year were analyzed retrospectively. [Results] 10 patients were classified as C-GCA and 13 patients were classified as LV-GCA which included 3 STAB positive patients. The average age was 74.3±9.0 in C-GCA group and 71.3±7.0 in LV-GCA group. The initial dose of Prednisolone (PSL) was 37.5±11.2mg/day,36.9±8.0mg/day. After 1 year treatments, PSL dose was declined by 7.2±3.6mg/day vs 5.7±2.8mg/day. While PSL dose was less in LV-GCA group, most of patients in LV-GCA group were treated by additional immunosuppressive drug such as Methotrexate or Azatioprine. [Conclusions] Patients in LV-GCA group were treated by less dose of PSL with more additional immunosuppressive drug. One reason would be explained by difficulties in distinguishing GCA from Takayasu arteritis which needed more intensive treatment.

P1-227

Progressive interval prolongation and withdrawal of Tocilizumab in relapsed giant cell arteritis

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Conflict of interest: None

[Objective] To investigate its effectiveness of progressive interval prolongation and withdrawal of Tocilizumab (TCZ) therapy for relapsed cases of giant cell arteritis (GCA) in spite of standard therapy. [Methods] We retrospectively reviewed GCA cases treated with TCZ which was in remission at least 6 months. Three cranial GCA and one large vessel GCA were included. Their age, gender, disease duration, number of steroid withdrawals, number of interval prolongation or withdrawal of TCZ, and number of relapses. [Results] All subjects were female, and its average age was 73 years old. Disease duration until TCZ started was 18.8 weeks. There were 4 cases of successful steroid withdrawal, 4 case of interval prolongation of TCZ, and 2 case of withdrawal of TCZ. there was one case of relapse, which had symptoms of PMR. [Conclusions] It was suggested that the use of TCZ for relapsed case of giant cell arteritis may contribute to progressive interval prolongation or withdrawal of TCZ.

P1-228

A case of hemophagocytic syndrome in giant cell arteritis with tocilizumab therapy

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Conflict of interest: None

A 67-year-old female was admitted to our hospital with fever in July 2018. She was diagnosed with myelodysplastic syndrome (MDS) by bone marrow examination. The risk of MDS was low and she had no medication for MDS, but fever wasn't improved, so prednisolone (PSL) therapy (40 mg/day) was started. Fever was improved, but she relapsed many times with tapering of PSL. She presented headache in December 2018, and temporal artery biopsy revealed inflammatory cells infiltration around blood vessels, so we diagnosed her as giant cell arteritis (GCA). PSL was up to 50mg/day and weekly subcutaneous tocilizumab (TCZ) was initiated in January 2019. Fever and headache were rapidly improved, and the dose of PSL were tapered. She had fever again 8 weeks after initiation of TCZ therapy. Laboratory tests showed hyperferritinemia (15103ng/ml) and thrombocytopenia (62000/μl). She was hospitalized with a diagnosis as hemophagocytic syndrome (HPS), and PSL was up to 50mg/day, plasma exchange were performed for 5 days, and cyclosporine A was started. She was improved, and PSL was tapered. There have been reported some cases of HPS in autoimmune disease after TCZ therapy. This is the first report of HPS in GCA with TCZ therapy. TCZ was effective for GCA, but we should be care of the complication.

P1-229

A case of thoracic aortic aneurysm detected during the long-term course of polymyalgia rheumatica

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Conflict of interest: None

[Case] A 73-year-old man was diagnosed with polymyalgia rheumatica (PMR) 16 years ago. Started with prednisolone 10 mg, the dose was reduced to 2 mg, but relapsed. Increased again to 10 mg, his symptom was tribial shoulder pain, without fever, headache, claudication and visual field impairment. However, his CRP did not become negative, and steroids were adjusted in the range of 3-6 mg. As an abnormal lung shadow was found on his chest X-ray in year X, chest CT was performed. Ascending aortic aneurysm about 60mm in diameter was found accidentally. Ascending aortic replacement was performed. Giant cell arthritis (GCA) was diagnosed because of worm-eating necrosis and disappearance of elastic fibers in the media and some multinucleated giant cells appearing around the necrotic tissue in almost all of the excised aortic specimens. [Discussion] A part of PMR is known to association with GCA, and the presence of large vascular lesions is associated with poor prognosis. The unstable CRP in this case seems to reflect arteritis. It is important to suspect and evaluate the existence of GCA from an early stage when the inflammatory response of PMR is unstable and steroids cannot be paused for a long period of time without its typical symptoms.

P1-230

A Rare Case of Giant Cell Arteritis Presenting Ptosis and Diplopia

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Conflict of interest: Yes

We hereby report a rare case of giant cell arteritis (GCA) who developed diplopia and ptosis as early symptoms. A 78-year-old male presented with fever, right temporal headache, ptosis of the right eyelid, and diplopia 2 weeks before admission. Physical examination showed adduction palsy of the right eye, impaired upward and downward deviation, and ptosis of the right eyelid without abductive palsy and vision loss. CRP and ESR were elevated. Contrast-enhanced computerized tomography (CT) revealed enhancement of walls of bilateral temporal and vertebral arteries, and thickening of walls of left subclavian artery and the aortic arch. FDG-PET-CT showed FDG uptake in right temporal artery and the aorta, especially the aortic arch. Diagnosis was confirmed by the biopsy of the right temporal artery, which revealed a narrowing lumen and granulomas with giant cells. He was immediately treated with steroid pulse therapy, followed by high-dose prednisolone (1mg/kg weight). CRP and ESR normalized, and headache and fever were resolved 2 days after administration. Ptosis and diplopia were improved 3 weeks after initiation (5 weeks after onset). In conclusion, we need to recognize ptosis and diplopia as an eye symptom of GCA and early treatment is important to avoid vision loss.

P1-231

A case of IgG4-related rhinosinusitis

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Conflict of interest: None

A 86-year-old woman presented with proptosis of both eyes. Seven years prior to this presentation, mandibular lymphadenopathy became gradually enlarged, so resection was performed and the tissue showed no malignancy. A month prior to this presentation, she was referred to ophthalmology department at our hospital. MRI revealed intraorbital masses on both sides, and IgG4-related disease was suspected with IgG 3002 mg/dl and IgG4 897 mg/dl. Specimen of lymph node biopsy performed seven years prior to this presentation was reevaluated, many IgG4-positive plasma cells were found, and IgG4 / IgG was 50%, so IgG4-related disease was diagnosed. Computed tomography (CT) scan was performed, soft tissue was observed inside the right maxillary sinus. There are no other mass lesions. She referred to otolaryngology department, chronic right maxillary sinusitis was diagnosed. After diagnosis of IgG4-related disease, prednisolone at 25mg/day was started. Proptosis of both eyes quickly improved. Twenty seven days after the start of steroid therapy, CT scan was performed to determine the therapeutic effect. Intraorbital masses remained, but it was reduced, and the soft tissue in the right maxillary sinus disappeared. There were few reports of IgG4-related rhinosinusitis, therefore we reported.

P1-232

Hepatic inflammation pusedo-tumor post operation of pancreatic malignant lymphoma accompanied with autoimmune pancreatitis

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Conflict of interest: None

[case] 55 years old, female [chef complaint] not applicable [history] When she was 40 years old, she was sufferd from pancreatitis. When she was 50 years old, laboratory date showed her hepatic injure, Serum IgG4 838 mg/dl, CT revealed the pancreatic head tumor and MRI revealed narrowing of extrahepatic bile duct. we started to treat with PSL 30mg for suspected of autoimmune pancreatitis (AIP) and IgG4-related sclerosisng cholangitis. After that, her hepatic injure and pancreatic head tumor had improved. When she was 55 years old, following CT revealed pancreatic tail tumor. We performed distal pancreatectomy and splenectomy. By the pathology of the specimen, the tumor was diffuse large B-cell lymphoma with 10/ HPF IgG4 positive cells. Therefore she didn't wish to treat with adjuvant chemotherapy, we restarted PSL 2mg treatment 4 months. 10 months later after PSL treatment, PET-CT revealed a hepatic tumor. We diagnosed that the tumor reoccurred a malignant lymphoma (ML), we perfomed hepatic lateral segmentectomy. The tumor contained over 100/ HPF IgG4 positive cells and was diagnosed hepatic inflammation pusedo-tumor. [Conclusion] Here, we report AIP complicated with pancreatic ML secondary to hepatic inflammatory pusedo-tumor with literature.

P1-234

A case of severe visual loss associated with the onset of IgG4-related disease

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Conflict of interest: None

The case is a 74-year-old woman. From 74 years of age, swelling of the right sternocleidomastoid muscle, right parotid adenoma, and bilateral lacrimal adenoma were observed. IgG4-related eye disease was suspected and ophthalmology was introduced, severe vision loss (0.02) in the left eye and a mass shadow in contact with the left optic nerve were pointed out. Early treatment intervention was considered appropriate due to the fact that severe visual loss was observed and that findings consistent with IgG4-related disease were obtained from the results of cervical lymph node and skin biopsy. Therefore, steroid pulse was performed and PSL 0.5 mg/kg/day was started. 9 days after the start of treatment, the visual acuity improved to 0.6. The PSL dose has been reduced to 5 mg/day. the mass shadow touching the optic nerve has disappeared and no relapse has been observed. [Clinical significance] This is a case of severe visual loss associated with the onset of IgG4-related disease. In this case, steroid was successful. However, the patient did not complain of decreased visual acuity, so it took more than a month to start treatment. For early treatment interventions, physicians also need to be aware that with the onset of IgG4-related disease one eye, not both eyes, may develop visual loss.

P1-235

A case of IgG4 related disease with glossopharyngeal and vagus nerve disorders

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Conflict of interest: None

We report a rare case of IgG4 related disease with glossopharyngeal and vagus nerve disorders. A 77-year-old man visited our hospital complaining of hoarse voice and dysphagia from five months ago, these symptoms are considered to be due to glossopharyngeal and vagal disorders. Contrast-enhanced brain MRI did not reveal any special findings, while chest CT showed multiple lymphadenopathy in both axillary, hilar and mediastinal areas, and serological findings showed elevated sIL-2R to 1193U/ml. PET-CT showed not only enlargement of multiple lymph nodes with abnormal accumulation in the right supraclavicular fossa, both axilla, mediastinum, and both external iliac regions, but also autoimmune pancreatitis and retroperitoneal fibrosis. A biopsy was performed from the right axillary lymph node, showing IgG4/IgG positive plasma cell ratio was more than 40%, leading to diagnosis of IgG4-related disease. With 40 mg of prednisolone, right vocal cord paralysis and curtain signs as well as swollen lymph node improved, suggesting that the cranial neuropathy related to IgG4 related disease. Cranial nerve disorders are rare among IgG4-RD, and no lower cranial neuropathy has been reported in the past.

P1-236

A case of IgG4-related sclerosing cholangitis during abatacept administration for rheumatoid arthritis

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Conflict of interest: None

[Case] An 84-year-old male developed bilateral lower jaw swelling in October of year X-10. In February of year X-8, he developed rheumatoid arthritis (RA). In May of the same year, he was administered MTX. At this time, bilateral lower jaw swelling was reduced, and his serum IgG4 level was 102 mg/dl. RA was in remission thereafter, but intravenous abatacept (ABT) was started in February of year X-4 after RA relapse. In October of year X-2, MTX was discontinued due to RA remission, and ABT was continued. In July of year X, serum hepatobiliary enzyme levels increased. Abdominal CT and ERCP revealed wall thickening of the hilar bile duct. In September of the same year, left hepatectomy and biliary reconstruction were performed. The resected specimen exhibited cholangitis with fibrosis, lymphocytes, and plasma cell infiltration. Obstructive phlebitis was also observed in several areas. The IgG4 / IgG ratio of infiltrating plasma cells was 33/76, 43.4%. The serum IgG4 level was 123 mg/dl. The patient was diagnosed with IgG4-related sclerosing cholangitis. [Discussion] Although the usefulness of rituximab as a biologic for IgG4-related diseases has been reported, ABT is also a promising drug. This is the first report of IgG4-related disease developing during ABT administration.

P1-237

A case of lung adenocarcinoma shrank after steroid therapy, complicated by suspected IgG4-RD

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Conflict of interest: None

[Case] The patient was a 66-year-old male. He presented backache and visited our hospital. CT showed a retroperitoneal tumor, an irregular shaped 10 mm nodule in the right middle lobe, and mediastinal lymphadenopathy. Biochemistry results indicated a high serum immunoglobulin G4 (IgG4) concentration at 201 mg/dL. For the purpose of diagnosis and treatment, we initiated prednisolone (PSL) at 0.6 mg/kg/day and tapered to 5 mg/day. All the lesions shrank, therefore, we diagnosed as IgG4-related disease (IgG4-RD) clinically. Fourteen months after we initiated PSL, serum IgG4 levels increased and CT showed enlargement of the nodule. A video assisted thoracoscopic lung biopsy was performed. Intraoperative frozen section showed the mass was adenocarcinoma, and therefore, he underwent the right middle lobectomy and mediastinal lymph node dissection. A pathological examination showed IgG4-positive cells infiltration in cancer stroma and mediastinal lymph node metastasis. After he was discharged, serum IgG4 levels decreased. [Discussion] In this case, we speculated the nodule had shrunk due to steroid therapy because IgG4-RD and lung cancer co-existed. Response to steroid therapy and serum IgG4 levels may be helpful to diagnosis, however, a pathological examination is the most important.

P1-238

Two cases of IgG4-related disease mimicking malignancy or infection

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Conflict of interest: None

The diagnostic utility of serumu IgG4 concentrations is already know, but we have to consider that serum IgG4 titer increase in malignancy or infection, too. A 68-year-old man presented with painless mass in multiple organs, and took biopsy of the lung, immunohistochemical analysis lead us to a diagnosis of IgG4-related disease. High-dose corticosteroid treatment resulted in prompt resolution of the serological, and imaging abnormalities, but he still have hydronephrosis and mass at urinary left tract which highly suspicious for malignancy. Transurethral biopsy was showed urothelial carcinoma. A 65-year-old woman presented with hematuria. Transurethral biopsy was revealed an increased IgG4/IgG ratio with IgG4-positive plasma cells over 10 per high-power field. The serum IgG4 concentration was elevated at 143 mg/dL. Urinary bacterial and mycobacterium cultures were negative. These results lead us to a diagnosis of IgG4-related disease. She was treated with low-dose corticosteroid, but anemia progressed gradually. We cultured urine repeatedly and mycobacterium tuberculosis was detected. We started anti-tuberculous drug. These cases suggest that we have to consider the possibility of comorbid disorder like malignancy or infection after a diagnosis of IgG4-related disease.

P1-239

Indication of Treatment for IgG4-Related Disease

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Conflict of interest: None

[Objective] IgG4-related disease (IgG4-RD) is successfully treated with corticosteroids. On the other hand, there are some reports of spontaneous remission of IgG4-RD. In this study, we examined the IgG4-RD patients who don't need treatment. [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 the treatment response were analyzed from their medical records retrospectively. [Results] Twenty patients were successfully treated (intervention group), and 14 patients were followed up without treatment (non-intervention group). In the non-intervention group, serum albumin was significantly higher (intervention group vs non-intervention group: 3.58±0.75 vs 4.11±0.56 mg/dl), and serum IgG was lower (2993±1687 vs 1901±1030 mg/dl mg/dl) than the intervention group. The number of organ involvements was significantly lower in the non-intervention group (3.80±1.61 vs 2.36±1.15). None of the non-intervention group required new intervention during follow-up. [Conclusions] This study suggest the possibility of follow-up without intervention in the patients with a small number of organ involvements, high serum albumin and low serum IgG.

P1-240

Successful treatment of refractory Behçet's disease with Apremilast

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Conflict of interest: None

[Case] A 44-year-old male with relapsing genital ulcers, oral ulcers, and pustular skin lesion was transferred to our hospital with seizure. Head MRI showed scattered high-intensity lesions on FLAIR images in bilateral temporal lobe medial, cerebral cortex. Cerebrospinal fluid analysis showed elevated protein of 65 mg/dL and cell count of 34/?L. Therefore, he was diagnosed with encephalitis due to acute neuro-Behçet's disease (BD). Encephalitis and mucocutaneous lesions were ameliorated by administration of 60 mg/day prednisolone (PSL) with colchicine (COL), and adalimumab. However, by reducing the dose to 35 mg or less of PSL, the patient developed mucocutaneous lesions, suggesting relapse of BD. Although adalimumab was switched to other TNF inhibitors, infliximab was not effective as well as golimumab. Consequently, he was treated with, COL, methotrexate, azathioprine, and certolizumab pegol in addition to PSL 35 mg. Nevertheless, steroid-sparing effect was not obtained. Concomitant use of apremilast (APR) ameliorated mucocutaneous lesions, and PSL was able to reduce to 5 mg. [Discussion] There is limited data with position of APR among those treatment. We report a BD patient complicated with refractory mucocutaneous manifestation dramatically improved with APR.

P1-241

Two cases of ileocecal ulcer similar to intestinal Behcet's disease with trisomy 8

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Conflict of interest: None

[Case 1] A 82-year-old female had a fever, abdominal pain and oral ulcers during four months. Colonoscopy revealed ileocecal multiple ulcers similar to Behcet's disease (BD). She was admitted to our hospital because of unsuccessful treatment with colchicine, salazosulfapyridine, prednisolone and adalimumab. The diagnostic criteria for BD were not fulfilled. Bone marrow examination showed trisomy 8. High-dose prednisolone and infliximab was administered. However, perforation of the ulcer was complicated, and resected by surgery. A month later, relapse of intestinal ulcer occurred with melena. She was treated with cyclosporine, which was effective in this case. [Case 2] A 47-year-old female had a fever and abdominal pain refractory to antibiotics. There were multiple ulcers in broad area of colon, particularly ileocecal region, and vagina. The diagnostic criteria for BD were not fulfilled. Bone marrow examination showed trisomy 8. Moderate-dose prednisolone and adalimumab improved the disease activity. [Clinical significance] We experienced rare two cases of ileocecal ulcer similar to BD with trisomy 8. Accumulation of information in this disease is necessary in order to consider the mechanism between chromosomal aberration and inflammation.

P1-242

A Case of Chronic Myelomonocyte Leukemia with Trisomy 8 Complicated with Atypical Behcet's Disease

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Conflict of interest: None

[Case] A woman in her 60s had been suffered from oral ulcers and erythema nodosa for 12 and 10 years, respectively. She was treated with predonisolone (PSL) as Behcet's disease (BD). The dosage of PSL was tapered. However, due to the recurrence of high fever, joint pain and multiple oral ulcers after discontinuation of PSL, PSL was re-started, and methotrexate and colchicine were added. A colonoscopy revealed multiple small erosions at the terminal ileum, which resembled intestinal BD. Although these manifestations were once resolved, she had been frequently hospitalized since then due to her fever, abdominal pain, and diarrhea. For 9 months before the last admission, she had had palpitation and dyspnea, and her lab examinations revealed progressive macrocytic anemia (Hb 5.5 g/dL), and thrombocytopenia (90,000/μL). Her bone marrow examination indicated a chronic myelomonocytic leukemia with trisomy 8. [Clinical Significance] BD patients had higher risk of myelodysplastic syndrome (MDS). Gastrointestinal ulcerations are common in patienst with BD-MDS. The prevalence of trisomy 8 is 80% in BD-MDS patients, in contrast to the 10% in general MDS patients. Trisomy 8 should be considered in atypical BD patients with intestinal involvements and BD patients with hematological disorders.

P1-243

A case of multirefractory intestinal Behçet's disease treated with golimumab effectively

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Conflict of interest: None

A 38-year-old female was diagnosed as having Behçet's disease by oral and genital ulceration, erythema nodosum, intestinal involvement. Prednisolone 30mg/day was started. Because ileocecal ulceration persisted, we administered mesalazine. However, she complained abdominal pain and diarrhea. So, we administered adalimumab. Due to secondary failure to it, we switched it to infliximab. Then, we administered cyclosporine. Due to infusion reaction, we switched infliximab to certolizumab pegol. Due to secondary failure to it and complaints of digestive symptom, we switched it to golimumab 50mg per month. Because it was insufficient, we increased doses of it (100mg per month) and it was substantially effective and continued. Although reports are rare, golimumab is a option for multirefractory intestinelBehçet's disease.

P1-244

A Case of Behcet's Disease (BD) Difficult to Diagnose with Crohn's Disease (CD)

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Conflict of interest: None

30-year-old female, temporomandibular joint pain, and vulvar ulcer also appeared in March. Later, left ankle pain and fever appeared. She felt misty vision on her left eye and was diagnosed with left iritis in ophthalmology. On April 3, she had a vulva ulcer and visited a general hospital for gynecology. Although the ulcer lesion was shallow, and two aphthous stomatitis appeared on the lip mucosa on the same day. We could not rule out BD. Recurrent aphthous ulcer of the oral mucosa, vulva ulcer, and iridocyclitis were positive for three main symptoms and diagnosed as Incomplete BD. Lower gastrointestinal endoscopy was performed, and small erosions were found around the cecum. Histopathological examination revealed granuloma lesions consisting of crypt abscesses, multinucleated giant cells, and epithelioid cells. These findings required differentiation between Crohn's disease and Behcet's disease. Behcet's disease with epithelioid granuloma is sporadic and difficult to differentiate from Crohn's disease. Therefore, it is essential to make a comprehensive diagnosis based on clinical findings.

P1-245

A case of refractory intestinal Behcet's disease (BD) with ileocecal resection

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Conflict of interest: None

[Case] 53 years old female [Chief complaint] melena, abdominal pain [Present illness] At age 47, the patient was diagnosed as BD (incomplete) due to oral ulcers, skin lesions, vulvar ulcers, arthritis. At age 50, she was diagnosed with intestinal BD because of melena and ileocecal ulcer. Administration of PSL 20 mg/day improved symptoms and under the combined use of colchicine and IFX. However, it was difficult to reduce the dose of PSL 12.5 mg/day or less after repeated minor relapse. At age 53, attempts to change IFX to ADA was failed and multiple aphthous ulcers occurred on upward colon in addition to known lesions. Increased dose of PSL 30-60 mg/day showed poor improvement. After laparoscopic ileocecal resection and colostomy were performed, abdominal pain and inflammatory response were improved quickly then we were able to reduce dose of PSL and resume ADA. [Discussion] Since intestinal BD had a high recurrence rate after surgical treatment, it seemed there were many difficulties in making judgments on the course of conservative treatment. The accumulation of surgical treatment cases is expected today as biologics become available. We evaluate the effectiveness of ileocecal resection or appendectomy from the viewpoint of IBD (inflammatory bowel disease) in a broad sense.

P1-247

A case in which oral ulcer was negative when diagnosed as incomplete Behcet's disease, but became positive after diagnosis

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Conflict of interest: None

[Clinical significance] For Behcet's disease, oral ulcer is an essential classification standard in the international standard. This case had acute onset fever, joint pain, uveitis, and epididymis. He was diagnosed as incomplete Behcet's disease although oral ulcer was negative, but oral ulcer developed after diagnosis. The course of this case is considered to be rare and highly suggestive, and I would like to report this case based on literature considerations. [Case] A 24-year-old male had multiple arthritis and fever 3 months before the visit, and visited our emergency department for worsening joint pain. At that time, folliculitis and conjunctival hyperemia were observed. During follow-up, uveitis and epididymis were observed, and he had HLA-B51 locus as an auxiliary diagnostic item. For this reason, incomplete Behcet's disease was diagnosed althought oral ulcers did not appear at this point. However, an oral ulcer appeared during follow-up, the diagnosis of incomplete Behcet's disease became more reliable.

P1-249

Vascular Behcet's disease preceded by deep vein thrombosis; A case report

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Conflict of interest: None

[Case report] A 34-year-old woman was referred for further examination and treatment of painful and swollen leg. Her blood test revealed a high CRP level and contrast CT showed deep vein thrombus. Therefore she started apixaban. Deep vein thrombosis was slightly reduced but swelling and pain in the right lower limb persisted, and CRP remained high. Because of idiopathic thrombosis without coagulopathy and stomatitis, she was suspected of having vascular Behcet's disease. After 60mg of prednisolone was given at 18 day, swelling and pain in the right lower limb was rapidly improved, and CRP level became normal at day 30. After that, deep vein thrombosis also disappeared and then gradual reduce the amount of prednisolone. At 10 months after discharge, the dose of prednisolone was reduced to 3 mg, It wasn't until then that she got common symptoms of Behcet's disease including stomatitis, genital ulcer, and erythema nodosum. Finally, she was diagnosed as incomplete type of Behcet's disease. [Discussion] In this case, early symptom of Bechet's disease was only stomatitis. Therefore we cannot diagnose as Behcet's disease. When deep vein thrombosis was coexisted with signs of Behcet's disease, it is important to keep vascular Behcet's disease in mind.

P1-250

A Case of Vascular Behçet's Disease with Chronic Inferior Vena Carval Sternosis but without Budd-Chiari syndrome

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Conflict of interest: None

[Objective] We reported a patient with vascular Behcet's disease having chronic vena caval stenosis without Budd-Chiari syndrome. [Methods] A 58 year-old man was admitted to our hospital because of request his clinical care from C hospital. Since 26 year of age, he showed recurrent oral and genital ulceration, and thrombophlevitis, and at 31 year of age, he was was diagnosed as Behcet's disease at A hospital. After then, he showed two episode of hemoptysis because of a shunt between pulmonary artery and bronchial artery and stenosis of inferior vena cava (IVC). At 46 year of age, he was pointed having amnesia of unknown origin after further examination by MRI and MMSE. [Results] Physical Ex: General Condition was well but amnesita was present. Varicoses on upper abdominal wall, edema and skin scar of lower legs. Loaboratory: WBC 4700 Hb 11.2 PL-C 22.5 CRP 0.2 d-dimer 0.6 T-bil 0.3 AST 20 RF 56. He was confirmed as having vascular Behcet's disease and chronic stenosis of inferior vena cava, although there was no portal hypertension. [Conclusions] Previous reports showed that chronic stenosis of IVC was gradulally continued without symptoms in contrast with acute stenosis of IVC. The patient was treated with 5mg of prednisolone and warfarin for vascular Behcet's disease.

P1-252

2 Cases Report: Macrophage Activation Syndrome Developed Immediately after the Administration of Tocilizumab in Patients with Active Adult-onset Still's Disease

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Conflict of interest: None

[Case 1] A woman in her 30s was diagnosed with adult-onset Still's disease (AOSD) based on fever, arthralgias, rash, sore throat, leukocytosis, and increased serum ferritin. Because her AOSD was refractory to high-dose steroids, tocilizumab (TCZ) was administered. However, macrophage activation syndrome (MAS) developed in 8 days. Readministration of TCZ resulted in MAS recurrence. Eventually, she needed high-dose steroids for several weeks before attaining the remission and tapering the dosage of steroids. [Case 2] A man in his 30s was diagnosed with AOSD based on fever, arthralgias, rash, sore throat, lymphadenopathy, leukocytosis, and increased serum ferritin. Because his AOSD was refractory to high-dose steroids, TCZ was administered. However, MAS developed in 2 days, which was ameliorated by pulse steroids. TCZ was readministered twice along with IV steroids, but TCZ caused drug eruption and was ineffective. Eventually, although his AOSD had improved to some extent with high-dose steroids for 4 more weeks, his polyarthritis persited and serum CRP remained high. Thus, TCZ was readministered along with antihistamine, which seemed effective without inducing MAS or drug eruption. [Clinical significance] Although rare, there were cases with possible TCZ-induced MAS in active AOSD.

P1-253

Clinical features of elderly patients with Adult onset Still's disease

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Conflict of interest: None

[Background] Adult onset Still's disease (AOSD) affects young adults characteristically, whereas many elderly AOSD patients were observed in recent epidemiological studies in Japan. [Objective] To investigate backgrounds and clinical features of elderly patients with AOSD. [Methods] We identified patients who were hospitalized for treatment of AOSD in Kurashiki Central Hospital from 2001 to 2019. We classified them by age at onset, and retrospectively investigated their clinical features. Yamaguchi's criteria (1992) were used for diagnosis. [Results] Of the 45 patients, mean age of onset was 50.0 years and 19 (42.2%) patients were over 65 years old at onset. Anemia ($p=0.0023$), thrombocytopenia ($p=0.046$), and Macrophage activating syndrome (MAS, $p=0.011$) were significantly more in patients over 65 years than in those under 65 years. When we classified patients by age of onset in another way, 16-34 years, 35-54 years, 55-74 years, and over 75 years, the complication of MAS were significantly increased in older age ($p=0.0067$). There were no significant correlations between the recurrence rate and age of onset, complication of MAS, serum ferritin level, each immunosuppressant. [Conclusions] Elderly AOSD patients might be more likely to have severe complications.

P1-254

Intravascular lymphoma mimicking adult-onset Still's disease: A case report

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Conflict of interest: None

We report the case of a 49-year-old man who presented with polyarthritis after a sore throat with negative antinuclear antibody and RF seven months before admission. Polyarthritis was improved with Prednisolone (PSL) and MTX. He developed a high fever, and pancytopenia, high LDH (600 U/L), and high ferritin (3000 ng/ml) emerged one month before admission. A thorough investigation only revealed hemophagocytosis. Bone marrow biopsy and random skin biopsy tests showed no evidence of malignancy. There was increased uptake of ^{18}F-FDG in the long-bone marrow but not in the spine and pelvis. Tibia bone marrow biopsy was not helpful for the diagnosis of malignancy. We diagnosed adult-onset Still's disease and he was treated with high doses of PSL. His fever improved; however, his hematological findings were unchanged. One month after initiation of treatment, bladder and rectal disturbance, truncal ataxia, and leg paralysis developed. Head MRI findings strongly suggested Intravascular lymphoma; however, bone marrow biopsy was still undiagnostic. Soon after, his general condition deteriorated, and atypical cells emerged in his peripheral blood. A hematologist diagnosed intravascular lymphoma clinically, and prompt chemotherapy improved his condition.

P1-255

A case of Subcutaneous panniculitis-like T cell lymphoma diagnosed during the third relapse of panniculitis

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Conflict of interest: None

[Case] A 26-year-old man developed fever and subcutaneous induration of both thighs in 2009 at his 16 years old. Biopsy revealed panniculitis, and diagnosis of lupus panniculitis (LP) was made with positive ANA and anti-dsDNA antibodies. He was treated with prednisolone (PSL) 60 mg/day and cyclosporine A (CyA). LP relapsed twice accompanied with elevated liver transaminases and urinary β2-microglobulin (β2-MG). Increased dose of PSL and CyA were effective twice. In September 2019, right abdominal pain appeared. Retroperitoneal panniculitis was suspected on CT. High fever, spreading erythema with infiltration throughout his body, liver dysfunction, and extremely high urinary β2-MG (117,611 mg/L) gradually appeared after admission. Skin and CT-guided retroperitoneal soft tissue biopsy revealed lymphoma cells rimming around fat cells. The diagnosis of subcutaneous panniculitis-like T-cell lymphoma (SPTCL) was made and he was treated with PSL and CyA again. We considered that he had SPTCL from the beginning of his illness. [Clinical significance] LP and SPTCL are sometimes difficult to differentiate due to similar clinical features and response to PSL and CyA. When LP accompanied with atypical features such as high urinary β2-MG, possibilities for SPTCL should be taken into account.

P1-256

Short-term prognostic factors of polymyalgia rheumatica

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Conflict of interest: None

[Objective] We investigated clinical outcomes in patients with polymyalgia rheumatica (PMR). [Methods] This is a retrospective single-center observational study. We consecutively diagnosed 45 patients with PMR between January 2012 and September 2018 and evaluated their outcomes from medical records from the first year of follow-up. [Results] Although remarkable initial response to prednisolone (PSL) was noted in all patients, 43 (95.6%) were still receiving PSL and 11 (24.4%) showed elevated C-reactive protein (CRP) levels (≧ 0.5 mg/dL) at one year. Multivariate analysis demonstrated that high CRP levels at entry (≧ 10.0 mg/dL) was an independent variable associated with one-year CRP levels (≧ 0.5 mg/dL). Odds ratio was 5.61 (95% CI 1.03, 30.61; $p = 0.047$). Twenty patients (44.4%) were still receiving PSL ≧ 5.0 mg/day, and 13 (28.9%) had PMR symptoms at one year. Multivariate analysis demonstrated that high CRP levels at entry was an independent variable associated with the presence of symptoms at one year. Odds ratio was 17.38 (95% CI 2.80, 107.66; $p < 0.01$). [Conclusions] PMR initially responds well to PSL. However, almost all of the patients were receiving PSL at one year. CRP levels and the presence of symptoms at one year were significantly associated with initial CRP levels.

P1-257

A case of sarcoid arthritis diagnosed by synovium biopsy

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Conflict of interest: None

Sarcoid arthritis is rare and manifests as arthritis involving bilateral small and large joints with multiple organ lesions. It causes synovium thickness, bone erosion and is difficult to distinguish RA. Synovium biopsy is effective for diagnosis, but it is rarely performed. 77 y.o. female was admitted because of suspicion of sarcoidosis with hypercalcemia and mediastinal lymphadenopathy. PET-CT revealed FDG uptake in muscles, bronchial biopsy showed epithelioid granuloma, and ACE levels elevated, therefore we diagnosed sarcoidosis. Arthritis of MCP joints, elbow, and ankles worsened and erythema nodosum developed 4 month later. MRI showed bone invasion, and bone edema in MCP joints. Because of positive RF and negative ACPA, synovium biopsy was performed for differentiation of RA. Synovium is whitish and histopathological findings showed slight lymphocyte-infiltration, but none of synovium cell hyperplasia, neovascularization, and epithelioid granuloma. We diagnosed sarcoidosis totally. After corticosteroids were started, her symptoms were improved. In the initial treatment orientation synovium biopsy is important for differentiation diagnosis, since sarcoid arthritis repeats remission and exacerbation causing functional disorder with bone destruction and joint deformity.

P1-259

A case of chronic eosinophilic pneumonia in which corticosteroid dose could be reduced quickly with mepolizumab

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Conflict of interest: None

An 80-year-old woman with a history of bronchial asthma who had never smoked had fever, cough, dyspnea, eosinophilia, and bilateral diffuse infiltrative shadows on chest X-ray in X-2 year. She was treated with prednisolone (PSL) 30mg (0.5mg/kg)/day for diagnosis of eosinophilic pneumonia at another hospital, and improved. However, due to reducations of steroid, relapses were observed in March X-1 year and January X year. It was thought to be chronic eosinophilic pneumonia, and each time the steroid dose was increased. In June X year, she had fever, increased eosinophil count to 1875/μL, and a new infiltrative shadow, so PSL was increased to 30mg/day. One week later, the infiltrative shadow remained unchanged and the eosinophil count increased to 4594/μL. PSL was increased to 60mg/day, and she was referred to our hospital one weeks later and hospitalized. At that time, the eosinophil count decreased to 130/μL, and the infiltration shadow tended to disappear. However, since she had 3 relapses so far, we have started taking mepolizumab 100mg every 4 weeks for the purpose of suppressing exacerbations and reduce of steroids. After that, PSL could be reduced quickly. We experienced a case of chronic eosinophilic pneumonia in which steroid dose could be reduced quickly with mepolizumab.

P1-261

A case of recurrent rheumatism complicated with sarcoidosis and warm autoimmune hemolytic anemia

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Conflict of interest: None

A 61-year-old male, visited for right shoulder joint pain before X-2 month. One symptom was improved, but other joint pain occurred and repeatedly improved in 2 days. There were no significant collective findings, and X-ray examinations did not point out any results suspicious for rheumatoid arthritis. In Blood tests, CRP elevation was pointed at 0.24 mg/dl. Besides LDH and indirect dominant bilirubin elevation and anemia were shown. Furthermore, serological tests showed RF 29 IU/ml but indicating no disease-specific autoantibodies. Systemic CT showed interstitial pneumonia, longitudinal lymphadenopathy, and splenomegaly. He was diagnosed with recurrent rheumatoid arthritis by his medical history, and was diagnosed with sarcoidosis by lymph node puncture. Regarding pulmonary lesions, VATS was performed, but no diagnosis was made. Anemia was diagnosed as warm autoimmune hemolytic anemia. For recurrent rheumatism, symptomatic treatment with NSAIDs was conducted, and the other diseases were initially followed without treatment. X+12 months later, anemia was grown worth, and medication was started by 1mg/kg of PSL. As a result, anemia and interstitial pneumonia improved. Sarcoidosis is rarely associated with autoimmune hemolytic anemia, and we think this is worth to report.

P1-262

A case of refractory Adult Onset Still's Disease succesfully treated with shortening the duration of intravenous infusion of Tocilizumab

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Conflict of interest: None

[Introduction] We report a cases of refractory Adult Onset Still's Disease succesfully treated with shortening the duration of intravenous infusion of Tocilizumab. [Case presentation] A 55-year-old Japanese woman was diagnosed with Adult Onset Still's Disease based on fever, left cervical adenopathy, neck-chest rash, shoulder arthritis and so on. We started high dose steroid therapy, but it was poor. Cyclosporin and methotrexate were added to high dose steroid therapy. But we changed to Tocilizumab from cyclosporin and methotrexate because of drug eruption and pancytopenia. Steroid could not be tapered by TCZ-IV every 2 weeks, so we changed to TCZ-IV weekly and add tacrolimus few days later. After that, steroid could be effectively tapered and ferritin level improved. [Clinical importance] We suggest the possibility of efficacy of shortening the duration of intravenous infusion of Tocilizumab for refractory Adult Onset Still's Disease.

P1-266

Immunosuppressive drug-associated lymphoproliferative disorder (LPD) of the vertebral column in a patient with rheumatoid arthritis

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Conflict of interest: None

[Case presentation] A 68-year-old woman who was diagnosed with rheumatoid arthritis (RA) at the age of 65. Her clinical remission was maintained with methotrexate (MTX), salazosulfapyridine and bucillamine. One month prior to her admission, she underwent low-back pain, and received a medical examination from the orthopedic department. A X-ray showed that her vertebral had multiple fracture, which was suspected to be due to tumor metastasis. Although image inspections failed to detect the primary source, bone biopsy demonstrated that it was diffuse large B cell lymphoma which was negative for EB virus-encoded RNA (EBER). In order to fix the compression of her spinal cord due to her vertebral tumor, thoracic vertebra rear fixation was performed. MTX was firstly discontinued after diagnosis, but the tumor did not reduce. And then we applied multidrug chemotherapy with rituximab to the patients. The therapy showed good response, and her general condition was improved. [conclusion] We experienced a case of immunosuppressive drug-associated LPD of vertebral column. Although primary bone immunosuppressive drug-associated LPD was rare, we should take the disease into account because it occurs more frequently in tissues other than lymph nodes.

P1-267

Two cases of methotrexate-associated lymphoproliferative disorders (MTX-LPD) accompanied by large multiple pulmonary nodules

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Conflict of interest: None

Case 1: A 70-year-old female was diagnosed with rheumatoid arthritis (RA). She was treated with 12mg/week of methotrexate (MTX), 2mg/day of methylprednisolone, 1000mg/day of salazosulfapyridine, and 50mg/day of iguratimod (IGU). In December 201X, she had severe anemia and multiple pulmonary nodules. She was suspected to have an MTX-LPD, so MTX was discontinued. She was diagnosed with MTX-LPD because of the examination finding that showing infection of EB virus. Then she steadily recovered and multiple pulmonary nodules spontaneously improved. Case 2: A 74-year-old female was diagnosed with RA and she was treated with 6mg/week of MTX, 4mg/day of prednisolone, 0.5mg/day of tacrolimus and 50mg/day of IGU. In 201X August, she had malaise, nausea, left chest pain, back pain, an elevation of hepatic enzyme, multiple pulmonary nodules, and abdominal lymphnodes. She was treated with folinate and stopped taking MTX. There are not lymphnodes which can be had a biopsy, she was clinically diagnosed as MTX-LPD. Then she steadily recovered. Cases of MTX-LPD are often difficult to confirm the diagnosis and sometimes becomes severe. There are some reports of patients with MTX-LPD with multiple pulmonary nodules, and sometimes they recovered by only stopping taking MTX.

P1-268

Methotrexate-associated lymphoproliferative disorder (MTX-LPD) 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-LPDs) 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. [Patients] Six patients who developed MTX-LPD were examined in the period from 2015 to 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 dosage of MTX was 9.2 mg / week. Two of the patients had bDMARDs, infliximab in 1 and tocilizumab in 1. The following LPD subtypes were observed: diffuse large B cell lymphoma (DLBCL) (N=3), Hodgkin lymphoma (N=1) and MALT lymphoma (N=1). All patients discontinued MTX. After withdrawal of MTX, three of these showed spontaneous regression of the tumor while the other patients required chemotherapy. disappeared in three cases. All cases had good clinical courses and are followed. [Conclusion] In the case of patients with RA who are taking MTX, tacrolimus or b DMARDs, MTX-LPD should be noted for early diagnosis.

P1-269

Clinical features and clinical courses in patients with methotrexate associated lymphoproliferative disorders (MTX-LPD)

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Conflict of interest: None

[Objective] To clarify the clinical features and the clinical courses in patients with methotrexate associated lymphoproliferative disorders (MTX-LPD). [Methods] This study included 9 cases with MTX-LPD in Tsuchiura Kyodo General Hospital. We retrospectively evaluated 1) baseline characteristics, 2) clinical course in 9 cases with MTX-LPD after withdrawal of MTX. [Results] 1) The mean age was 70.0±5.6 years old. The mean dose and administration duration of MTX were 7.0±2.6 mg/week and 6.8±5.6 years, respectively.2) LPD regression was observed in 4 cases. The 3 cases had not relapsed after LPD regression, but the other case had shown regrowth and required chemotherapy. In 5 cases, LPD had not regressed and chemotherapy had been given, but 3 patients were dead. Histological types included 5 cases of DLBCL, 3 cases of Hodgkin lymphoma and 1 case of lymphomatoid granulomatosis. EB virus was positive in 5 cases. In regression cases, LPD shrank in 5.8±3.1 weeks and serum sIL2R level was reduced in 4 weeks after withdrawal of MTX. [Conclusions] Aging might be a risk factor of MTX-LPD. Observation of serum sIL2R level for about 4 weeks might be effective for prognosis prediction because LPD and sIL2R level improved in 1 to 2 months after withdrawal of MTX in regression cases.

P1-270

Analysis of iatrogenic immunodeficiency-related lymphoproliferative disorders in our hospital

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Conflict of interest: None

[Objective]. Iatrogenic immunodeficiency-related lymphoproliferative disease (OIIA-LPD) has been recognized during the treatment of rheumatic diseases with immunosuppressants. We analyzed the cases experienced in our institute. [Methods] We analyzed 19 patients who developed LPD during treatment with immunosuppressants. [Results] Age of onset was 69 (median) (63-75) years, female 16, all cases were RA, 2 with systemic lupus erythematosus, 1 with primary biliary cirrhosis, disease duration was 16 (8-28) years. MTX was used in all cases, dose 8 (7-10) mg/w, duration 7 (3-11) years, combined with tacrolimus in 2, infliximab in 2, golimumab in 2, and eternacept in 1. Histology was DLBCL 10, IVLBCL 3, HL 4, PTCL 1, and LPL 1. Improvement was observed following drug withdrawal in 15 out of 19 patients, 7 of which relapsed. Relapse-free survival was 1.5 (0.6-7.25) years. Six cases with relapsed were successfully treated with chemotherapy. Among 4 cases without improvement following drug withdrawal, 2 dies. Overall survival was 2.55 (0.8-5.6) years. [Conclusion] OIIA-LPD has improved in many cases after drug withdrawal, but nearly half relapses. In many cases, chemotherapy is successful after relapse.

P1-271

A case of methotrexate-associated lymphoproliferative disorder (MTX-LPD) complicated with repeated infections and thromboembolism in a rheumatoid arthritis (RA) patient

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Conflict of interest: None

A 75-year-old female was diagnosed with RA in 1996, MTX treatment was initiated in 2009, and arthritis was remitted. Then, abdominal lymphadenopathy was detected in 2014, and MTX was discontinued since MTX-LPD was suspected. Although arthritis was not relapsed by low-dose steroid monotherapy, lymphadenopathy was gradually exacerbated and tumorous lesions were detected in pancreas, liver, and lung. Endoscopic ultrasound-fine needle aspiration was performed in those tissues and the development of MTX-LPD was suspected, while far from conclusive to categorize the type of lymphoma and grade of malignancy. Moreover, pneumocystis pneumonia, cytomegalovirus infections, esophageal candidiasis, scabies, and repeated thromboembolism in deep vein, pulmonary artery, and brain were developed. Such physiological condition interrupted initiation of chemotherapy for MTX-LPD and she was died of liver failure in 2018. Autopsy showed infiltration of large multinucleated atypical lymphocytes (CD3-, CD5-, CD20+) in lymph nodes and liver, and that Epstein-Barr virus-encoded small RNAs were partially detected, indicating MTX-LPD/Hodgkin-like lesion. To our knowledge, this is the first reported case of MTX-LPD/Hodgkin-like lesion complicated with repeated infections and thromboembolism in an RA patient.

P1-272

A Case of iatrogenic immunodeficiency-associated lymphoproliferative disorders that spontaneously regressed after discontinuation of immunosuppressive agents but relapsed with an extranodal lesion

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Conflict of interest: None

A 77-year-old woman was diagnosed with rheumatoid arthritis 16 years ago and had been treated with methotrexate (MTX) and tacrolimus (TAC) for 12 years. CT showed enlargement of left axillary lymph nodes and biopsy revealed diffuse large B-cell lymphoma (EBER positive). Iatrogenic immunodeficiency-associated lymphoproliferative disorders (LPD) was suspected, therefore MTX and TAC were discontinued. The lesions regressed without chemotherapy. One year later, symptoms of arthritis became worse and then TAC was resumed. Three years later, the patient got a fever and elevated CRP. CT showed a 6 cm mass in the liver. Liver biopsy revealed Hodgkin's lymphoma (EBER positive). FDG-PET showed no abnormal uptake other than a hepatic mass. Iatrogenic immunodeficiency-associated LPD has been reported that it often occurs as extranodal lesions even Hodgkin's lymphoma that generally exhibit nodal lesions. Its histopathology present with a variety of phenotypes and it can be composite. We herein describe the case of LPD presented with lymph nodes involvement but recurred with extranodal lesions, which showed different pathology. Iatrogenic immunodeficiency-associated LPD may recur in a different manner even after regression with discontinuation of immunosuppressants.

P1-273

A case of lymphoproliferative disorders with multiple liver masses and hemophagocytic syndrome during immunosuppressive therapy for polymyositis

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Conflict of interest: None

A 68-year-old man was diagnosed with polymyositis (anti-SRP antibody: positive) 7 years before. He was stable with prednisolone (PSL) 5 mg/day, methotrexate (MTX) 20 mg/w, and tacrolimus (TAC) 1.5 mg/day. He complained fever and sore throat. On admission, increased mononuclear cells (24%), atypical lymphocytes, thrombocytopenia (55000/μl), liver damage, and hyperferritinemia (1595 ng/ml) were observed. After admission, positive Epstein-Barr virus (EBV)-PCR (200 copy/μgDNA) and EBV-EA, and hemophagocytosis in bone marrow were revealed. Contrast CT revealed multiple liver masses. Metastatic liver cancer was initially suspected, but upper and lower gastrointestinal endoscopies and PET-CT showed no findings of malignancies other than the liver. Liver biopsy revealed infiltration of CD20-positive large lymphocytes (LMP-1: positive) in the necrotic tissue. He was diagnosed with other iatrogenic immunodeficiency-related lymphoproliferative disorders (OIIA-LPD). Only discontinuation of MTX and TAC improved fever, liver damages and thrombocytopenia, and the liver masses were diminished. There have been few case reports of liver-localized OIIA-LPD. Since this case is suggestive in differential diagnosis, here we report with a review of the literature. Disclosure: none.

P1-274

A late elderly case with severe bradycardia due to cardiac invasion by the methotrexate-related lymphoproliferative diseases (MTX-LPD), that recovered from bed-ridden status with best supportive care to walkable by withdrawal of MTX and introduction of rituximab

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Conflict of interest: None

[Case] An 83-year-old male. Five years ago, rheumatoid arthritis (RA) was diagnosed from polyarthritis, pleurisy, positive RF and ACPA. Disease activity was very low by using a small amount of PSL, methotrexate (MTX), and adalimumab (ADA). But he was aware of pain in the right chest and a subcutaneous mass several weeks ago, contrast-enhanced CT scan showed masses from the right chest to the chest cavity, and some of them were biting into the both atria. Severe bradycardia and decreased

cardiac function occurred. Pathological findings taken from the chest wall showed BV-RNA (EBER) -positive diffuse large B-cell lymphoma, so MTX-related lymphoproliferative disease (MTX-LPD) was diagnosed with the history of MTX administration. Chemotherapy was difficult because of his general condition, so we stopped MTX and ADA and planned palliative care. However, the CT scan 1 month after MTX discontinuation showed a marked reduction in mass. We used rituximab (RTX) as a treatment for MTX-LPD and RA, his ADL was improved. [Discussion] Cardiac infiltration by MTX-LPD is a very rare complication. Positive EBER may have contributed to LPD reduction. RTX may effective for both LPD and RA like this case.

P1-275

Analysis of clinical features of Methotrexate-associated Lymphoproliferative Disorders (MTX-LPD) patients

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Conflict of interest: None

[Objective] To evaluate the clinical features of MTX-LPD with Rheumatoid Arthritis (RA) patients. [Methods] We retrospectively analyzed 32 RA patients who developed LPDs in our hospital from 2006 to 2019. All patients were diagnosed as LPDs by histological examination. [Results] 22 patients were female. The median age at developing MTX-LPD was 73.5 years. The median duration from diagnosis of RA to developing MTX-LPD and MTX treatment were 92.5 months and 50 months, respectively. The median MTX dose at developing MTX-LPD was 10mg/week. 10 patients were EBER-1 positive. The pathologic diagnosis of LPDs were 21 DLBCL, 5 peripheral T-cell lymphoma, and 2 Hodgkin lymphoma. The spontaneous regression by MTX withdrawal (SR group) was observed in 8 patients, and 22 patients required chemotherapy (non-SR group). In SR group, the duration from diagnosis of RA to developing MTX-LPDs and MTX treatment were longer than those of NON-SR group (p=0.008 and 0.016, respectively). The ratio of EBER-1 positive was significantly increased in SR group (p=0.036). In EBER-1 positive patients, the ratio of administration of PSL was increased in comparison to EBER-1 negative patients (P=0.042). [Conclusions] EBER-1 positive and longer treatment with MTX are predictors for the spontaneous regression

P1-276

A patient with methotrexate-asociated lymphoproliferative disorder with at risk for immune reconstitution syndrome due to hepatitis B virus

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Conflict of interest: None

A 67-year-old woman was admitted to this hospital because of pharyngeal masses, nodular/mass shadows in both lungs, mediastinal lymphadenopathy, and sIL-2R 4230 U/L thus suspected of methotrexate-associated lymphoproliferative disorder (MTX-LPD). The patient was diagnosed with rheumatiod arthritis 40 years ago, had been treated with methotrexate (MTX) 8 mg/week for 15 years. 6 months before admission, the patient developed repetitive pharyngitis, also parotid gland pain several days before. On the 1st hospital day, MTX was suspended. Positive for HBs antigen and HBe antibody, negative for HBe antigen, and HBV-DNA quantification 2.3LogIU/ml were revealed. Prednisolone 10mg/day for preventing immune reconstitution syndrome, and entecavir 0.5mg/day for hepatitis B infection were started. The pharyngeal mass and abnormal lung shadows reduced without developing hepatitis. Cervical lymph biopsy revealed no monoclonal lymphocyte proliferation, but numerous atypical lymphocytes and EBER-positive lymphocytes. The final diagnosis was MTX-LPD. When MTX-LPD is suspected, MTX should be suspended immediately, but sudden withdrawal of immunosuppressants in HBV-DNA positive patients could cause immune reconstitution syndrome. This case is notable as these conditions are presented together.

P1-277

Two cases of the rheumatoid arthritis that I got the prompt disappearance of the neoplastic lesion by discontinuation of Mrthotrexate though I had a diagnosis of the frequent occurrence metastasis due to cancer of unknown adrenal tumor, nuclear power plant, and MTX-related lymphoproliferative disease was diagnosed by again

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Conflict of interest: None

[Background, purpose] when accept a mass-related lesion of the frequent occurrence that produced Methotrexate (MTX) during remedy, is a disease given according to a model, but is hard to say with the general disease in the course which is not concerned with rheumatoid arthritis (RA) treatment without receiving lymphoproliferative disease (LPD). It is taken as a frequent occurrence metastasis-related tumor this time in the clinical department except the rheumatic course and reports 2 cases that I discontinue MTX, and got the improvement that is in a state. [case 1] 80 years old, a woman. I took MTX more than RA of the onset, 20 years in X-24 year. After trying enucleation on the suspicion of a right adrenal gland cancer, lymph node metastases at the urology department that after enforcing thorax and the abdomen region CT for fever of the 38 degrees Celsius level, a heat source close inspection purpose in six a year X months, recognized a mass-related lesion derived from adrenal gland to the right retroperitoneum, the adhesion was remarkable and was unresectable, and I performed a biopsy on a tumor, and it was with the end. An intrapulmonary mass-related lesion was judged from chest CT with metastasis and would cancel MTX, and the mass-related lesion disappeared.

P1-278

A case of rheumatoid arthritis with immune reconstitution inflammatory syndrome after discontinuation of methotrexate and etanercept treatment due to myelosuppression and septic shock

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Conflict of interest: None

A 75-year-old woman with rheumatoid arthritis treated with methotrexate (MTX) and etanercept visited our hospital due to diarrhea and disturbed consciousness. Her blood pressure had decreased and laboratory workup showed pancytopenia, renal dysfunction, and elevated C-reactive protein levels with procalcitonin accentuation. She was diagnosed with concurrent Listeria monocytogenes-induced septic shock and MTX-induced bone marrow suppression and was treated with noradrenalin, antibiotics, granulocyte-colony stimulating factor, and folic acid. She recovered promptly from septic shock, renal dysfunction, and bone marrow suppression, but subsequently developed daily high fever. While elucidating the cause of fever, colonoscopy revealed shallow ulcers in the large intestine. The tissue surrounding the ulcers was tested positive on the cytomegalovirus (CMV)-PCR test. Hence, she was diagnosed with CMV colitis and administered ganciclovir for two weeks. The ulcers improved, but the fever persisted. The fever was ascribed to immune reconstitution inflammatory syndrome (IRIS) due to CMV reactivation. Treatment with prednisolone (30 mg/day) resulted in rapid improvement in fever. IRIS was attributed to the rapid recovery of myelosuppression and abrupt withdrawal of immunosuppressive therapy.

P1-279

Clinical course of Autoimmune-associated hemophagocytic syndrome in our hospital: A case series of 18 patients

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Conflict of interest: None

[Objective] We aimed to investigate the clinical course, treatment, and prognosis of Autoimmune-associated hemophagocytic syndrome (AAHS). [Methods] A total of 18 subjects were diagnosed as AAHS in our hospital from April 2009 to September 2019. The diagnosis of AAHS was based on the presence of hemophagocytosis in bone marrow and/ or HLH-2004 diagnostic criteria. [Results] 15 cases were female, and the median age was 44 [27-49] years old. Underlying diseases were systemic lupus erythematosus (SLE) (n=5), mixed connective tissue disease (MCTD) (n=3), and adult-onset Still's disease (AOSD) (n=10). 15 cases showed AAHS as the first manifestation. Prednisolone (PSL) alone or PSL + Cyclosporine (CSA) were used as the first-line treatment. The first-line treatment was effective in 13/18 cases. The second-line treatment was methylPSL pulse + CSA or PSL + intravenous cyclophosphamide for SLE/MCTD, and PSL + methotrexate or PSL + Tocilizumab for AOSD. The second-line treatment was effective in 4/5 cases. Median follow-up period was 765.5 [248.5-1879] days, no one died during the hospitalization due to AAHS. [Conclusions] In our hospital, no patients died due to AAHS or underlying diseases. Further research to anticipate the prognosis, and to determine the appropriate treatment is warranted.

P1-280

Prophylactic effect of sulfasalazine against Pneumocystis pneumonia in patients with rheumatoid arthritis: a self-controlled case series study

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Conflict of interest: None

[Objective] To evaluate the prophylactic effect of sulfasalazine against *Pneumocystis* pneumonia in patients with rheumatoid arthritis. [Methods] A retrospective study was conducted atTokyo Metropolitan Tama Medical Center between 2003 and 2019. Cases of *Pneumocystis* pneumonia diagnosed by polymerase chain reaction of respiratory specimens for *Pneumocystis jirovecii* were enrolled. Incidence of *Pneumocystis* pneumonia was compared between periods with sulfasalazine prescription and those without the prescription in the same case. [Results] We identified 27 cases of *Pneumocystis* pneumonia. While 16 cases received sulfasalazine (eight before and three after the development of *Pneumocystis* pneumonia, and three in both), none of *Pneumocystis* pneumonia developed in the periods with sulfasalazine prescription. [Conclusions] Our study demonstrated that prophylactic effect of sulfasalazine against *Pneumocystis* pneumonia.

P1-281

A Case with Simultaneous Exacerbation of Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) and Progressive Multifocal Leukoencephalopathy (PML)

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Conflict of interest: None

[Case] 54 year-old female [Chief complaint] Right hemiparesis [History of present illness] She was diagnosed as an overlap syndrome of SLE and PM 9 years ago and stably treated with PSL 14mg/day, MMF, and HCQ. However, she was admitted because of the sudden development of right hemiparesis and dysarthria. Brain MRI revealed that T2-high lesions at left coronary cortex and frontal cortex. Combined with finding of serum anti-ribosomal P antibody, SPECT and cerebral spinal fluid (CSF), she was diagnosed as NPSLE and started with steroid pulse followed by PSL 1mg/kg/day, monthly IVCY and plasma exchange (PE). JC virus was detected by PCR in the initial CSF afterwards, and the simultaneous occurrence of PML was suggested. We continued IVCY and PE and reduced PSL quickly to 10mg/day. At 6 months after the treatment, the JC virus was not detected in CSF and no exacerbation was observed. Then she was discharged. [Consideration] SLE itself has immuno-deficient feature and also, immunosuppressive treatment can trigger the onset of PML. Thus we should keep in our mind that immunosuppressants (IS) are discontinued or reduced. In our case, however we continued IS for NPSLE, quick decrease of PSL dose could rescue the patient and result in minimizing the risk of exacerbation of PML and NPSLE.

P1-282

Prospective cohort study for correlation between glucocorticoids dose and infection occurrence in systemic lupus erythematosus patients in LUNA

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Conflict of interest: None

[Objective] In systemic lupus erythematosus (SLE) patients, the amount of the glucocorticoids (GC) which do not increase the infection is unknown. We describe the correlation between current GC dose and infection. [Methods] We conducted a prospective cohort study from database. Induction remission therapy phase patients (Prednisolone (PSL) >15mg) and the patients that we cannot follow-up not less than 1 year were excluded. The most recent daily GC dose is categorized to 4 group, prednisolone (PSL) dose is 0-2.5mg, 2.6-5mg, 5.1-7.5mg, 7.6-15mg. Main outcome was infection requiring hospitalization in 1 year. We analysis the infection occurrence rate in each group, using multiple regression analyses adjusted by sex, age, immunosuppressive agent use. [Results] 290 patients were included. The patients dosing PSL 0-2.5mg occurred 3 in 68, PSL 2.6-5.0 occurred 28 in 111, PSL 5.1-7.5mg occurred 9 in 51, PSL 7.6-15mg occurred 17 in 60. Compared with PSL 0-2.5mg group to the other group, the odds ratio of infection occurrence was 8.00 (95% confidence interval (CI), 2.29-28.0) in PSL 2.6-5.0mg, 5.30 (95% CI, 1.29-21.8) in PSL 5.1-7.5mg, 11.2 (95% CI, 2.92-43.0) in PSL 7.6-15mg. [Conclusions] A small amount of GC may raise infection requiring hospitalization in maintenance phase SLE patients.

P1-283

Clinical characteristics and prognosis of invasive pulmonary aspergillosis in rheumatic diseases

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Conflict of interest: None

[Objective] IPA has been reported not only in neutropenic patients but also in COPD and with immunosuppressive agents. However, there are few reports about IPA in rheumatic diseases. We compared and discussed IPA in rheumatic diseases. [Methods] The subject of the present study are

IPA in rheumatic diseases in Yokohama Municipal Citizen's Hospital and Kitasato University Medical Center, between 2008 and 2019. Diagnosis was defined as acute course, with imaging findings consistent with IPA, positive serologic tests, and culture positives. [Results] 10 cases met the diagnosis of IPA. 7 were RA (mean age 77.8), 2 were SLE (63, 55), and 1 was Behçet disease (67). Respiratory disease was interstitial pneumonia in SLE (1) and RA (2), CPFE in RA (4), and old pulmonary tuberculosis in RA (1). 6 patients with RA were treated with a mean PSL 24 mg (5-50 mg), TAC (2), SASP (2), and BUC (1). SLE patients were treated with PSL (25 mg and 50 mg), MMF (1), and Behcet's disease patient was treated with PSL 30 mg, MTX, and IFX. These patients were treated by VRCZ (4), MCFG (4), CPFG (1), and ITCZ (1). SLE and Behçet disease cases improved, but all 7 cases with RA died. [Conclusions] In our study, IPA in RA with pulmonary disease has a poor prognosis, especially in elderly patients treated with steroids

P1-284

Study of cytomegalovirus reactivation factor in rheumatic diseases

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Conflict of interest: None

[Objective] Reactivation of cytomegalovirus (CMV) results in important opportunistic infections that are frequent during the treatment of rheumatic diseases and are at risk of blindness. In this study, we investigated the factors that affect CMV reactivation. [Methods] 35 patients (10 myositis, 5 SLE, 5 Adult still's disease, 5 Giant cell arteritis, 5 ANCA-related vasculitis, 2 polymyalgia rheumatica, 1 Malignant RA, 1 MCTD and 1 IgG4-related disease) were subjected. When CMV reactivation was clinically suspected, CMV antigenemia was determined by C7-HRP method. They were divided into CMV positive and negative groups. Factors such as age, sex, body weight, initial prednisolone (PSL) dose, PSL dose (mg/kg), cumulative PSL dose, mPSL pulse therapy, WBC/lymphocyte counts, IgG, and albumin were compared between the two groups. Statistical significance was performed by Student's t-test. [Results] The CMV positive group showed significantly greater initial doses of PSL ($p<0.05$), greater numbers of mPSL pulses therapy ($p<0.05$), and greater cumulative doses of PSL ($p<0.01$) compared to the CMV negative group. [Conclusion] These findings suggest that CMV reactivation is more likely to occur in patients that had greater initial doses of PSL, numbers of mPSL pulse therapy or cumulative PSL doses.

P1-285

Experiences in our hospital for sepsis and infectious spondylitis in rheumatoid arthritis

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Conflict of interest: Yes

Objective: In rheumatoid arthritis during immunotherapy, care must be taken to infection. Like septic and infectious spondylitis, infection pneumonia infection, by the use of biologics and aging, the case seemed to be increasing. Cases Biologics were used for all 7 patients. The average age was 76.8 years (62-87) and the duration of the disease was 18.4 years (2-50 years). 5 cases of sepsis, infectious spondylitis (4 iliac muscle abscess, 2 epidural abscess, 3 purulent discitis). x Cases without fever are scattered, the patient himself and surroundings are often difficult to notice, early detection and early treatment is necessary to provide a window for sufficient patient education and casual consultation on physical condition changes. There were cases where the re-biological formulation was also stable. Discussion: In the elderly, the prophylactic use of antibacterial drugs seemed to be important for infection prevention. If coughing and slight fever continue for 10 days, it is necessary to promptly consider the suspected infection and treat the treatment.

P1-286

The value of CMV-IgM antibody for diagnosis of Cytomegalovirus (CMV) infection under immunosuppression with negative C7-HRP

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Conflict of interest: None

[Objective] Early diagnosis is important for CMV reactivation under immunosuppression. So we are screening with CMVpp65 antigen (C7-HRP) usually, but there are negative cases depending on the infected organ. In this study, We have examined the value of CMV-IgM antibody for diagnosis in patients who were suspected of having CMV infection during immunosuppressive treatment but were negative for C7-HRP. [Methods] We examined retrospectively C7-HRP negative 87 patients that measured CMV-IgM antibody suspected of CMV infection between 2017 and 2019 in our department. We diagnosed as CMV infection clinically. We defined that CMV-IgM antibody titer was positive with 1.21 or higher. [Results] CMV-IgM positive group was 21 of 87 patients. CMV infection occurred in 10 of 87 patients and 5 patients were CMV-IgM positive. There was no difference in age, serum IgG / IgM and lymphocytes between positive and negative groups. The sensitivity of CMV-IgM antibody in CMV infection with negative C7-HRP was 50.0%, the specificity was 79.2%. And the negative predictive value was 92.4%. [Conclusions] When CMV infection was suspected under immunosuppression, if C7-HRP and CMV-IgM were both negative, CMV infection could be denied with high probability, and it seemed to be useful as a screening test.

P1-287

Survey of the positive rate change in T-SPOT for 6 years and following up the prognosis of tuberculosis

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Conflict of interest: None

[Objectives] Tuberculosis (Tb) is not still rare infection in Japan. Before immunosuppressive therapy, T-SPOT is usually examined Tb infection including latent infection. Therefore, we investigated the positive rate change in T-SPOT for 6 years and the prognosis of tuberculosis in T-SPOT positive patients. [Methods] We retrospectively collected all T-SPOT data from clinical records of Sagamihara National Hospital from 1 January 2013 to 31 December 2018. The positive patients of T-SPOT were followed up the prognosis in Tb. [Results and Discussion] T-SPOT was examined 6017 samples for 6 years. The positive rate was 5.7%. In 2013, that was 6.9%, and gradually decreased to 4.4% in 2018. The mean age of all patients was 62.0 years old, and that of the T-SPOT positive patients was 68.5 years old. The difference was significant ($p <0.01$). In department of rheumatology, 2927 samples were examined and 5.7% (131 samples) was positive. At the time of examination, there were 7 samples of Tb onset, 23 samples of old Tb, and 85 unknown samples of past Tb infection. Among of positive samples, 71 samples were examined for acid-fast bacilli and 38 samples were initiated prophylactic therapy with isonicotinic acid hydrazide. There were no cases of Tb onset or recurrence of Tb for 6 years.

P1-288

Effects of Treatment Content on The Relationship between Nutritional Status and Infection in Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To clarify the mutual effects among treatments, nutritional status and infections, and these differences between treatments in RA patients. [Methods] The study included 2108 RA patients who were treated in our hospital in April 2016. Clinical findings, treatment contents and prognostic nutritional index (PNI) between patients with infections requiring hospitalization (infection group) and non-infection group during the observation period (2 years). The relationships of PNI and infection were compared between patients with b/tsDMARDs group and Non-Bio, and among bDMARDs types. [Results] Infection group included 74 cases. The infectious risk factors were PNI<45 (OR: 3.20), high DAS28-CRP (OR: 1.60) and non-use of MTX (OR: 2.98). PNI was significantly higher in b/tsDMARDs group (50.5±4.7) than in Non-Bio (48.6±5.1) ($p < 0.05$), but there was no difference in the rate and type of infection between the two groups. Among type of bDMARDs, PNI was higher in the order of IL6i, TNFαi, CTLA4-Ig, but there were no differences in the rate and type of infection. [Conclusions] Malnutrition in RA patients is considered to be infectious risk factor. Although nutritional status varies depending on the presence and type of b/tsDMARDs, may not affect the rate of infections among b/tsDMARDs.

P1-289

Two treatment cases with the maximum-dose antibiotic-impregnated bone cement beads for purulent gonitis with osteomyelitis

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Conflict of interest: None

Introduction: Early treatment is important for purulent gonitis preferably with antimicrobial administration, synovectomy, irrigation, and debridement in a timely manner. We report our experience of 2 cases for purulent gonitis with osteomyelitis treated by bone cement beads containing the maximum dose of vancomycin hydrochloride and amikacin sulfate. **Case1:** A female at the age of 84 received osteosynthesis 9 years ago due to distal femur fracture. She visited our institution for the suspicion of purulent arthritis due to refractory ulceration in knee joint. We reduced the infection by nail extraction of internal fixation material, bone marrow cleansing, and the antibiotic-impregnated bone cement beads. **Case2:** A male at the age of 77 received osteosynthesis and intramedullary nail extraction in distal left femur fracture 60 years ago. He visited our institution for the first time due to a left knee pain with swelling. We alleviated the infection by bone marrow cleansing, and bone cement beads containing of antibacterial agents. **Discussion:** Purulent gonitis may also be associated with osteomyelitis. The maximum-dose antibiotic-impregnated bone cement beads will be effective for osteomyelitis.

P1-290

A case of rheumatoid arthritis and Sjögren's syndrome complicated with liver dysfunction, aseptic meningitis, and muscle weakness of the limbs finally diagnosed as acute hepatitis E

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Conflict of interest: None

[Case] 43-year-old woman of rheumatoid arthritis (RA) and Sjögren's syndrome (SS) was treated with 10mg/week of methotrexate (MTX). She suffered from general fatigue for 3 weeks, headache and neck stiffness for a week, and difficulty in walking for 3 days respectively. She entered our hospital because biochemical test of her blood revealed remarkable elevation of aspartate aminotransferase and alanine aminotransferase. The neurological examination revealed bilateral Kernig's sign, muscle weakness of neck and extremities, disturbance of coordinated movement of upper extremities. The results of nerve conduction study, electromyography, computed tomography of the head, and magnetic resonance image of her spinal cord were normal. The results of cerebrospinal fluid study revealed elevation of mononuclear cells and positive oligoclonal bands and no organisms were observed by culture test. Anti-HEV-IgM, IgA, IgG antibody and HEV-RNA were all positive and genotype was 3b. We diagnosed her as acute hepatitis E and secondary neuromuscular manifestations. Her symptoms and hepatitis were improved spontaneously. [Discussion] It is important to take HEV infection into consideration as a differential diagnosis of hepatitis and neuromuscular symptoms while treating RA and SS patients with MTX.

P1-291

3 case reports of Rheumatoid Arthritis with human T-cell lymphotropic virus type 1 (HTLV1)

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Conflict of interest: None

Case1: A 60-year-old female with rheumatoid arthritis (RA) onset from 2 months ago had 20 swollen joints, 15 tender joints. Rheumatoid factor (RF) 19 IU/mL, anti-CCP antibody (ACPA) 0.7 U/mL. She was treated with MTX 12 mg and PSL 5 mg, however her disease activity was still high (DAS28-CRP 5.53). She had HTLV1Ab and HTLV1-DNA. We treated her with Tocilizumab (TCZ) 162 mg/week. Case2: A 65-year-old female with RA onset from 15 years ago. She was treated with Abatacept 500 mg/4week, Iguratimod 50 mg/day. She had 27 swollen joints, 14 tender joints. RF 38 IU/mL, ACPA 271.0 U/mL. She complained of being HTLV1 carrier, had HTLV1Ab and HTLV1-DNA. Her disease activity was DAS28-CRP 6.02, we treated her by changing to TCZ 162 mg/week. Case3: A 73-year-old female with RA onset from a month ago. She had 27 swollen joints, 19 tender joints. RF 8 IU/mL, ACPA 0.5 U/mL. After she was treated with MTX 10 mg and PSL 10 mg, her disease activity was achieved in remission (DAS28-CRP 1.55). However, She developed adult T-cell leukemia/lymphoma (ATL). It reported that RA patients with HTLV1 have higher levels of IL-6, NF-κB, and less responsivity to treatment than patients without HTLV1, so we need to pay attention to these and the development of ATL when treating RA patients with HTLV1.

P1-292

Efficiency of Musculoskeletal ultrasound for infection in musle, bone, joint, and sofuttissue. (Dianogsis, Teratment, Estimate)

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Conflict of interest: None

[Objective] We discuss the efficency of Musculoskeletal ultrasound (MSUS) for infection in musle, bone, joint, and sofuttissue. And we also used Musculoskeltal ultrasound for dicision the treatment and follow up the cases. [Methods] We estimtimate the focus and activity and the spread of inflammations by using gray scale and power dopplar. We sometimes puncutured the tissue by MSUS guide. We operate the cases with pyogenic arthritis, pyogenic tenosynovitis, absess. And we estimated the treatment respomse with using MSUSa, sometimes changed the therapy and drug. [Results] We could diagnose and rapidly dicide the treatment. And it's useful to serect the operation approach and method of debridement. [Conclusions] It's very useful to use the MSUS for the infection in softtissue.

P1-293

Efficacy of early canakinumab therapy for the sensorineural deafness in cryopyrin-associated periodic syndrome

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Conflict of interest: None

[Background] Cryopyrin-associated periodic syndrome (CAPS) is a rare autoinflammatory disease caused by *NLRP3* gene mutations. The pathophysiology of CAPS accounts for the overproduction of interleukin-1β. We herein report a family of CAPS, and the efficacy of early canakinumab therapy against the sensorineural deafness. [Case] A 5-year-old boy was hospitalized for the investigation of short stature. Elevation of serum C-reactive protein levels, urticaria-like rash, arthritis, bulbar conjunctivitis, and sensorineural hearing loss were observed. We diagnosed him as having CAPS (Muckle-Wells syndrome) with a novel *NLRP3* gene mutation (p. G328E). His mother and maternal grandmother had the similar symptoms and same mutations. All three patients had no periodic fever. The rash, arthritis, and conjunctivitis promptly disappeared after canakinumab therapy in all three patients. On the other hand, with regard to hearing loss, he showed improvement, but his mother and grandmother did not. [Clinical significance] Early canakinumab therapy must be necessary for improvement of hearing ability. This is the novel *NLRP3* gene mutation report (p. G328E), and phenotypic features might include lack of periodic fever. There might be CAPS patients in patients who come to hospital with short stature.

P1-294

Safety of canakinumab for Japanese patients with periodic fever syndromes- from an interim report of post-marketing surveillance

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Conflict of interest: Yes

[Objective] Here we report interim safety data of an ongoing post-marketing all-patient (pt) surveillance of canakinumab (CAN), a human anti-IL-1β monoclonal antibody, in Japanese pts with periodic fever syndromes including colchicine-resistant familial Mediterranean fever (crFMF), TNF receptor-associated periodic syndrome (TRAPS) and hyper IgD syndrome/mevalonate kinase deficiency (HIDS/MKD). [Methods] Data collection was conducted from December 19, 2016 to June 30, 2019. [Results] Among 105 pts registered in this study, 54 pts (39/12/3 pts with crFMF, TRAPS, HIDS/MKD respectively) were assessed as a safety analysis set. The rate of adverse events were 55.6% (30/54 pts). Adverse drug reactions (ADRs) were 25.9%/25.6%/25.0%/33.3% in all pts, crFMF, TRAPS and HIDS/MKD respectively. Common ADRs were upper respiratory tract inflammation (5.6%), rash and osteoarthritis (3.7% each). Serious ADRs were reported in 4 crFMF pts (7.4% of all pts); 2 cases with osteoarthritis and each 1 case with diverticulitis, haemosiderosis, enterovesical fistula, bursitis, bursal fluid accumulation, oedema and pain. Death was observed in a crFMF 41 year-old female, where ADRs were osteroarthritis and pain. [Conclusions] No new safety signal was found compared to previous reports. Further data collection is ongoing.

P1-295

Fever of unknown origin with aseptic peritonitis successfully treated by Tocilizumab. A case report

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Conflict of interest: None

(Case) A 31-year-old female was referred with an unusual history. Three years prior to the referral visit, she developed periodically spontaneous worsening and relieving abdominal pain. Each worsening period was a few days and each relieving one was about a month. Four months later from the first period, she had appendectomy due to the diagnosis of appendicitis. However, the resected one showed intact lumen and neutrophil dominant inflammation in outside of its serosa. Though the findings indicated that the intraperitoneal inflammation extended to subsequently, the origin was unclear. Laparoscopic view also showed broad peritoneum adhesion and clear ascites without evidence of bacterium and malignancy. After the appendectomy, systemic inflammation with fever, peritonitis resulting in enteroparesis and the persisting elevation of serum interleukin-6 level developed. Although the inflammation was refractory to the treatment with prednisolone and colchicine, the trial of Tocilizumab was quite effective. (Clinical Meaning) Though features of her history remind us of auto-inflammatory disease, no mutation of related gene was detected despite of full-screening. We report as a successful treated rare manifestation associated with autoinflammatory without similar reports.

P1-296

Adult-onset chronic recurrent multifocal osteomyelitis (CRMO) in two patients with long-term symptoms successfully controlled with adalimumab

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Conflict of interest: None

[Case 1] A 38-year-old man was admitted to our hospital with an 8-year history of pain in both legs characterized by exacerbations and remissions. He reported difficulty in working without regular NSAIDs use. MRI and bone scintigraphy showed multiple bone marrow changes in the tender areas of the tibial diaphysis and calcaneus. Left calcaneal bone biopsy showed nonspecific bone marrow inflammation; thus, we diagnosed the patient with CRMO. He was administered adalimumab, which improved his symptoms without NSAIDs. [Case 2] A 30-year-old man noticed knee joint pain 13 years before admission. X-ray and MRI showed bone sclerosis around the joints. Bone scintigraphy showed increased uptake in the sternoclavicular joint, sternal angle, xiphoid, femoral trochanter, distal femur, proximal tibia, and lateral epicondyle of the humerus. Steroids, bisphosphonate and methotrexate did not change his condition. Administered adalimumab led to long-term remission. [Discussion] Reports on adult-onset CRMO are few. While skin manifestations and pelvic and thoracic wall lesions are major features of SAPHO syndrome, they are uncommon in CRMO; long-bone lesions are most common. Anti-TNF antibody treatment is reportedly effective. Adalimumab was effective for disease control in the aforementioned cases.

P1-297

The association between clinical features and analysis of mefv gene in 24 patients with Familial Mediterranean Fever (FMF)

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Conflict of interest: None

[Objective] We have analyzed 24 patients (17 female/7 male) with FMF to clarify the association between various clinical features and mutation of *MEFV.* [Methods] Mutated MEFV has been explored. Clinical symptoms and laboratory data were analyzed. [Results] Onset time were 0-53 years-old. Frequencies of clinical symptoms such as periodic fever, headache, arthralgia, abdominal pain, chest pain, myalgia, and cervical lymph nodes swelling were 24/24, 8/24, 9/24, 5/24, 4/24,2/24 and 1/24, respectively. Patients with FMF were divided to 3 groups. Patients with typical compound heterozygous mutations of MEFV (E148Q /M694I in exon 10) were 4 cases (G1). Patients with atypical mutations, except for mutations in exon 10, such as exon 1 (E84K, L110P), 2 (E148Q), 3 (P369S, R408Q), 5 (S503C) and 9 (I591M) were 8 cases (G2). Patients with no mutations were 9 cases (G3). There were no significant differences of age at first visiting hospital, onset age of fever attack, duration of fever attack (D) and frequency of fever attack between G1, G2 and G3, but D in G1 tended to be shorter than group2 and 3. Laboratory examinations were not significantly different between 3 groups. [Conclusions] Two patients in group 1 who received canakinumab treatment because of severe diarrhea and alopecia.

P1-298

An observational Study to determine Factors Associated with Colchicine Efficacy and retention rate in patients with Familial Mediterranean Fever

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Conflict of interest: None

[Background] Familial Mediterranean fever (FMF) is a typical hereditary autoinflammatory disease, in which polymorphisms/mutations in the MEFV gene encoding the pyrin protein, which is important for inflammasome regulation, are implicated in the pathogenesis. Colchicine is the first choice of treatment, and is covered by health insurance in Japan. However, there are few longitudinal reports on the efficacy and continuation rate of colchicine in Japan. [Objencives] To determine the efficacy and continuation rate of colchicine in FMF patients in our hospital, and to identify factors associated with it. [Methods] 38 patients who were diagnosed with FMF in our hospital from 2009 to 2019, were enrolled in the analysis. [Result] Typical cases were 63%, and the E148Q polymorphism of exon2 was recognized in 50%. The colchicine effective cases were 71%, the intolerance cases were 34%, and the overall continuation rate was 89%. The median duration of colchicine ingestion was 867 days, and women were identified as factors associated with colchicine efficacy ($p = 0.047$). No factors related to the continuation rate of colchicine were identified. [Conclusion] To clarify the use of colchicine in patients with FMF in our hospital, and to identify factors associated with its efficacy.

P1-299

Reduction of liver enzymes precede episodic fever in familial Mediterranean fever (FMF): A case report

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Conflict of interest: None

A 47-year-old male was referred to our hospital due to episodic fever complicated with abdominal pain. He had repetitive, acute, self-limited episodes of fever attack complicated with abdominal painfrom 11 year before. The interval of episode was about 2 months. The episodic fever continued about 2 weeks with conservative treatment. Becausefamiliar Mediterranean fever (FMF) was suspected, he started colchicine therapy from 3 years before. The severity of episode was improved partially. At 2 year before, genetic test revealed E148Q heterozygous mutation and he was diagnosed as atypical FMF. Because of incomplete response to colchicine, canakinumab was started. After 3 months, canakinumab cannot improve episode, despite increased doses. Therefore, Canakinumab was terminated. In this case, the reduction in liver enzymes is preceded episode. During episode, the levels of liver enzymes are normal and increase during the interictal phase. Excess liver fat is detected by CT imaging during interval and reduced after episode. [Discussion] In this case, reduction in liver enzymes precedes episodic fever. This suggests that some unknown cause normalizes fatty liver and liver damage prior to episodic fever. This is an interesting case, suggesting pathogenesis of periodicity of FMF.

P1-300

A Case of Familial Mediterranean Fever with MEFV Gene Mutation in Family

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Conflict of interest: None

Familial mediterranean fever (FMF) is an autoinflammatory disease that periodically repeats fever and serosal inflammation. It is said that there are many ethnic groups originating from the Mediterranean coastal area, but in recent years reports have increased in Japan. we introduce an example of a woman who has had gastrointestinal symptoms periodically since the age of 15 and was diagnosed with FMF by genetic analysis and colchicine effect assessment conducted in our department. The case was an 18-year-old woman who had periodic fever and abdominal pain. Endoscopy was performed at the gastroenterology department, but no significant findings were obtained from the biopsy results. Our department suspected her as an auto-inflammatory disease and conducted a genetic test. As a result of genetic testing, exon2: E148Q and exon10: M694I heterozygotes of MEFV gene were detected. She was diagnosed with FMF because she had no symptoms after taking colchicine. Her parents were asymptomatic, but her mother had an E148Q heterozygous mutation and her father had an M694I heterozygous mutation. Based on this, we considered the possibility of family history in the class of isolated cases, Investigated the types of gene mutations in Japan and their association with relatives.

P1-301

A case of atypical familial meditarrenian fever with Sjögren's syndrome

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Conflict of interest: None

[case] A 78-years old woman, with bilateral shoulder and knee joint pain referred to out hospital. Upon examination, the patient had a fever of 38 ° C, and physical findings showed dry eye, dry mouse in addition to joint pain. No skin sclerosis was observed. Blood tests showed increases in CRP and MMP-3, and high anti-SS-A antibody level was revealed, and dry eye met the criteria for Sjogren's syndrome (SjS). And genetic search was performed because the possibility of familial Mediterranean fever (FMF) was considered from the findings such as joint pain with repeated fever sometimes accompanied by abdominal pain, MEFV A heterozygous mutation at S503C in gene exon5 was detected. Based on the above, atypical cases of FMF were considered, and when colchicine was started as a diagnostic treatment, joint symptoms and fever were no longer observed. In SjS, the patient was followed up with symptomatic therapy. As for scleroderma, none of the diagnostic criteria were satisfied. [Clinical significance] We experienced a case of both SjS and atypical type of FMF. For example, even if there is no family history, genetic search may be useful in cases where FMF is suspected based on clinical findings and blood tests.

P1-302

Disappearance of febrile attacks after five years of colchicine treatment in a patient with atypical familial Mediterranean fever

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Conflict of interest: None

[Background] Colchicine (COL) is the mainstay of treatment for familial Mediterranean fever (FMF), effective to 90 percent of them, and diagnostic for atypical cases. I report a atypical FMF (aFMF) patient who was treated with COL for more than 5 years, which led to the disappearance of the febrile attacks (FA). [Case] A 70-year-old woman was referred to our department seven years ago for further evaluation with a 23-year history of fever. Her FA (>38°C) occurred the next day of going out or heavy housework and lasted for one day every two weeks. Since the age of 54, her FA lasted for three days with headache, chest pain, and hip joints pain. Laboratory tests revealed elevated level of CRP (6.58 mg/dl) and ESR (79 mm/h). An *MEFV* analysis showed heterozygous mutation in exon 2 (E148Q/wild-type) and she was suspected of aFMF. COL at a dose of 0.5 mg/day reduced the frequency of high fever, FA after going out, and subjective symptoms. Then she was diagnosed with aFMF. COL therapy was insufficient to eradicate periodic FA, but the higher dose was intolera-

ble due to diarrhea. Finally, complete elimination of FA was achieved after 5 years of therapy and 19 months have passed since her last FA. [Clinical significance] Years of COL treatment may be needed for some aFMF patients.

P1-303

Effectiveness of colchicine for unkown fever identified E148Q/R202Q variants in MEFV gene

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Conflict of interest: None

The MEFV gene is responsible for Familial Mediterranean Fever (FMF). MEFV variants have been identified in not only FMF but also other autoinflammatory diseases. Some reports show that colchicine, which is first choice for FMF, is effective for some autoinflammatory diseases which have MEFV variants. A 29 years old woman developed high fever after influenza vaccine when she was eleven years old. Antibiotics were not effective, and she developed arthralgia and erythema nodosum. She was transferred NHO Mie Hospital. WBC was 4300/ul, CRP was 2.21mg/dl, ANA was 160x, anti ds-DNA antibody was negative, and complement was normal. Accurate diagnosis was not determined, but corticosteroid was effective. However, her symptom recurred after a reduced dose of prednisolone to 9mg. NSAID, MTX, azathioprine, mizoribine, cyclosporine, infliximab, thalidomide (partially effective), cimetidine, etanercept and tacrolimus was not effective. E148Q/R202Q variant in MEFV gene was identified and colchicine was started when she was 26 years old. Now prednisolone can be reduced until 6.5mg and 6md every alternative day and there is no relapse.

P1-304

Whole-genome sequence analysis of Japanese patients with palindromic rheumatism

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Conflict of interest: None

[Objective] Palindromic rheumatism (PR) is a cryptogenic paroxysmal arthritis. Although the pathogenesis is still unknown, it suggests that multiple genes may be involved. Here we searched for disease-related genes by WGS analysis. [Methods] Two cases of mother and child with PR were used for the study. Ten healthy WGS data from a public database were used as controls. Rare variant analysis was performed on detected variants by using SKAT-O, SKAT, and KBAC. The genes significant in SKAT-O and in SKAT or KBAC were defined as significant. On the other hand, we detected shared variants between mother and child. In addition, the Japanese-specific variants and noises were removed. Furthermore, variants with MAF of 5% or more in the 1000 Genomes Project were removed. [Results] 4798618 and 4780461 variants were detected in mother and child, respectively. After removing the polymorphism, 217508 variants were detected. In addition, 1783, 1686 and 1493 genes were significant in SKAT-O, SKAT, and KBAC, respectively (P <0.05). The 493 genes containing 1583 variants found in the Rare variant analysis were significant (P <0.05). [Conclusions] The results suggest that the genes detected in this study may be involved in the pathogenesis of PR.

P1-305

PYCARD/ASC speck formation is increased in the case with the variant lacking exon2 as compared with the wild type

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Conflict of interest: None

[Objective] PYCARD/ASC is an adaptor protein of inflammasomes. We previously reported that PYCARD/ASC lacking exon2 (Δexon2) was dominantly expressed in Japanese patients with palindromic rheumatism. In addition, Δexon2 PYCARD/ASC increased IL-1beta secretion compared with wild-type (WT) (Suganuma *et al*., Asian Pac J Allergy Immunol. 2019). Inflammasome-dependent PYCARD/ASC speck formation is involved in releasing inflammatory cytokines. Here, we analyzed the capacity for PYCARD/ASC speck formation of wild-type or Δexon2. [Methods] HEK293 cells were transfected with expression vectors for WT or Δexon2 PYCARD/ASC-GFP fusion protein and then stimulated by LPS and MSU. Next, we observed cells by using a fluorescence microscope and counted the number of cells that contains specks. [Results] Cells containing single or multiple specks were significantly increased in HEK293 cells expressing Δexon2 compared with WT (58/173 vs 33/155) (P<0.05). We also observed cells containing over three specks only in HEK293 cells expressing Δexon2. [Conclusions] Our results suggest that PYCARD/ASC speck formation is increased in the case with the variant lacking exon 2 as compared with the wild type and it may be involved in inflammasome's function.

P1-306

Two cases of steroid-resistant refractory adult-onset Still's disease with good response to tocilizumab therapy

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Conflict of interest: None

[Introduction] Adult-onset Still's disease (AOSD) generally responds to corticosteroid with good prognosis. But almost half of the patients may repeat flare in their disease course. We present that two cases of refractory AOSD showed good response to tocilizumab (TCZ). [Case 1] A 35-year old woman had spike fever, tender joints, salmon-pink rash, increased white blood cell count, lymphadenopathy, splenomegaly, elevated liver enzyme, and hyperferritinemia (2,243ng/mL). Although she received prednisolone (PSL) 30mg/day, high fever, thrombopenia and hyperferritinemia>20,000pg/mL continued. MPSL pulse therapy twice concomitant with cyclosporin were effective gradually against complication of MAS, however flare occurred after 4 and 7 years of disease onset during corticosteroid tapering. Thus, we started TCZ and she achieved remission. [Case 2] A 31-year old man with fever, tender joints, urticarial rash, sore throat, increased white blood cell count, and hyperferritinemia (823ng/mL). He received PSL 40mg/day concomitant with MTX. After 7 months, AOSD flared. We initiated half mPSL pulse followed by TCZ. He achieved remission. [Conclusion] We report two cases showing that TCZ was effective against AOSD patients experiencing relapse under the conventional immunosuppressive therapy.

P1-308

Bilateral Total Knee Arthroplasty for PAPA syndrome, the first cace report

Akira Izumi, Kenta Kinoshita
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Conflict of interest: None

[Objective] The first case report of bilateral total knee arthroplasty for PAPA syndrome [Methods] 37 years old woman. She received steroid treatment for systemic pyoderma and arthritis at the age of four. After adulthood, she was diagnosed with PAPA syndrome from clinical symptoms. This time she visited our hospital for the treatment of arthritis in both knees. [Results] Since there was no skin infection and no pyogenic arthritis, total knee arthroplasty was performed. The surgical findings were similar to those of normal knee arthropathy, and the pathological findings were nonspecific. However, multiple intra-articular hematomas were repeated for 3 months after surgery. Currently, the postoperative course is good for 1 and a half years after surgery. [Conclusions] Good results have been obtained as a result of total knee arthroplasty for PAPA syndrome in remission.

P2-001

Comparison of estimated glomerular filtration rate measurements in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Estimated GFR based on creatinine in RA patients might overestimate kidney function likely due to low muscle mass. We investigated factors associated with difference of eGFRcr from eGFRcys or modified CKD EPI equations (mCKD-EPI). [Methods] This is a single-center, retrospective study involving 172 outpatients with RA fulfilling ACR/EULAR criteria from Feb. 2019 to Jul. 2019. We used multiple regression to examine whether [eGFRcr-eGFRcys] or [eGFRcr-mCKD-EPI]] as the dependent variables can be associated with routine laboratory tests, therapies and complications as the independent variables. [Results] The mean age was 68.1± 13.5 yrs and disease duration was 2.8 yrs (1.1-8.5 yrs). Mean eGFRcr (69.4± 18.6 mL/min/1.73m^2) was lower than eGFRcys (74.0± 24.6) and mCKD-EPI (75.7±20.0) ($p<0.05$, respectively). Aging, hypoalbuminemia, high hemoglobin levels, elevated erythrocyte sedimentation rate (ESR) were associated with a difference in [eGFRcr - eGFRFcys] ($p<0.05$, respectively). Aging was associated with a difference in [eGFRcr - mCKD-EPI] ($p<0.01$). [Conclusions] eGFRcr were lower than eGFRcys and mCKD-EPI in RA patients. Advanced age, hypoalbuminemia, high hemoglobin levels, and elevated ESR were independently associated with differences in eGFR by Cr and Cys in RA patients.

P2-003

Comparative efficacy of Janus kinase (JAK) inhibitors in the treatment of conventional synthetic disease-modifying antirheumatic drugs (csDMARD)-experienced Japanese patients with moderate-to severe rheumatoid arthritis (RA): A Network Meta-Analysis (NMA)

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Conflict of interest: Yes

Objectives: To compare the efficacy of JAK inhibitors in csDMARD-experienced Japanese patients with moderate-to-severe RA. **Methods:** A targeted literature review was conducted to identify phase 3 randomized controlled trial (RCT) publications of JAK inhibitors that reported results for Japanese populations. Treatments assessed included upadacitinib (UPA) monotherapy as well as UPA, baricitinib (BAR), and tofacitinib (TOF) in combination with csDMARD. Probability of achieving American College of Rheumatology (ACR) scores 20/50/70 at 3 months was estimated using an ordinal Bayesian NMA. **Results:** A total of 4 RCTs were included in the NMA. Estimated median ACR20 responses were 87.8% (95% credible interval: 67.4-97.1%) for UPA 15mg, 82.9% (67.7-92.5%) for UPA 15mg+csDMARD, 78.8% (52.8-93.8%) for UPA 30mg, 78.4% (57.1-92.1%) for TOF 10mg+csDMARD, 77.8% (61.1-89.5%) for UPA 30mg+csDMARD, 73.0% (49.9-89.2%) for TOF 5mg+csDMARD, 71.4% (57.1-82.9%) for BAR 4mg+csDMARD, 68.8% (50.3-83.6%) for UPA 7.5mg+csDMARD, and 36.2% (29.1-43.7%) for csDMARD. Efficacy ranks were consistent for ACR50/70 responses. **Conclusions:** UPA showed good responses among JAK inhibitors in Japanese csDMARD-experienced RA patients. Compared to combination therapy, UPA monotherapy had comparable ACR responses.

P2-004

Advanced therapy and corticosteroid use patterns for rheumatoid arthritis in Japan

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Conflict of interest: Yes

Objective: To describe advanced therapy (AdvTx) and corticosteroid (CS) use for RA in Japan. **Methods**: RA patients 16-74 years old using AdvTx (certolizumab, etanercept, adalimumab, infliximab, golimumab, tocilizumab, abatacept and tofacitinib) were identified in Japanese Medical Data Center claims data during 7/2014-6/2017. **Results**: 700 RA patients started AdvTx: 133 (19%) as monotherapy, 415 (59%) with methotrexate and 152 (22%) with other csDMARDs. The proportion of subjects who switched to (i) concomitant csDMARDs 90, 180, and 365 days after the start of monotherapy was 17% (21/123), 18% (20/110), and 15% (12/80), respectively. (ii) concomitant csDMARDs 90, 180, and 365 days after the start of AdvTx with any csDMARD was 6% (30/486), 8% (36/435), and 10% (35/334), respectively. CS use was 82%, 74% and 68% in the 365, 180 and 90 days prior to AdvTx initiation; and 60%, 68% and 77% in the 90, 180 and 365 days after. Mean total CS dose per patient (standardized to 1mg of prednisone) was 281mg, 440mg and 589mg in the 90, 180 and 365 days prior to AdvTx initiation; it was 212mg, 367mg and 489mg in the 90, 180 and 365 days after. **Conclusion**: Among RA patients in Japan using AdvTx, there was substantial variation in the concomitant use of csDMARDs including MTX, and corticosteroids.

P2-005

A study of collecting information about rheumatoid arthritis in patients with rheumatoid arthritis (The second report) -based on the IORRA cohort

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Conflict of interest: None

[Background] Last year, we reported that RA patients obtained information about RA widely from medical institution and mass media, and information sources were different by age group. [Objective] To examine whether there was a difference in information source about RA according to patients' background. [Methods] The subjects were RA patients participated in IORRA in 2017. Based on patients' self-report, the information sources and patients' VAS with usefulness for information were cross-sectionally evaluated according to patients features; disease duration, DAS28, J-HAQ, and bDMARDs use. [Results] 3470 patients answered. The patient background was as follows; 86.8% female, mean age 62.3 years, DAS28 2.55, J-HAQ 0.58, and bDMARDs user 27.2%. In bDMARDs users, the most frequent information sources were medical institutions (32.2%), television (16.7%), internet (12.3%). The mean VAS of usefulness was highest (72.8) in medical institution. The similar results were obtained non-bDMARDs users. Despite differences in patient background, there was no characteristic change in information sources. In bDMARDs users, the utilization rate of patient support program was 1.8%. [Conclusion] There were no differences in information sources related to RA according to patient background except for age.

P2-006

Retrospective analysis of 89 patients with polymyalgia rheumatica: a single center experience

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Conflict of interest: None

[Methods] We enrolled patients with PMR who visited our hospital

between May 2011 and July 2019. Diagnosis of PMR was based on the Bird's criteria. Of 118 patients who fulfilled the criteria, 29 cases were excluded because of other final diagnoses. Therefore, clinical characteristics of 89 cases were retrospectively reviewed. [Results] The mean age at onset was 71.8 years old, and 39 of the patients were female. Eighteen patients had a history of malignancy. Five-year survival rate was 82.5 % and five-year relapse-free survival rate was 52.3 %. Relapse-free survival rate in patients with young-onset (<72 years at onset) was significantly higher than that in patients with elderly-onset (>72 years at onset). Immunosuppressive agents were more prescribed for patients who relapsed than those who did not. Methotrexate was the most commonly prescribed agent. All patients who once experienced relapse did relapse again within 4 years. None of immunosuppressive agents had protective effects for relapse. [Conclusions] This study results indicate that patients with young-onset PMR have higher relapse rate than patients with elderly-onset PMR.

P2-007

The second report of polymyalgia rheumatica study in our hospital

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Conflict of interest: None

[Back ground and Object] Polymyalgia rheumatica (PMR) is an inflammatory disease of unknown cause and is more common in older people. We examined 65 patients who experienced PMR treatment in our hospital. [Methods] Extract all cases of PMR (including suspicion) from the insurance disease name. The medical record contents and progress were confirmed, PMR, RA, and other diseases were discriminated, and PMR cases were selected and analyzed. [Results] The average age of onset was 74.5 years old, and the oldest onset at our hospital was 90 years old. The annual incidence of PMR in the hospital is increasing. The incidence of PMR and the age of onset at this hospital are correlated, and the onset of older patients increased significantly in recent years (correlation coefficient 0.411). Of the 65 cases, 21 cases were able to perform joint echo at the onset. 66.6% had some kind of active synovitis. When classified into the major joint type, minor joint type, and mixed joint type, the ratios were 28.6%, 14.3%, and 23.8%, respectively. [Conclusions] In patients with PMR diagnosed and treated at our hospital, the onset year and onset age were significantly correlated. Many of the echo findings at the time of onset showed active synovitis in the major joints.

P2-008

The effect of ultrasonographic supplementation on the clinical outcome in the diagnosis of polymyalgia rheumatica

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Conflict of interest: None

[Objective] To clarify whether musculoskeletal ultrasonography (US) findings that are characteristic of PMR contribute to therapeutic effects and outcomes in diagnosed cases of PMR. [Methods] Based on ultrasonograms of patients suspected of having PMR from January 2008 to December 2018, the patient was diagnosed with PMR (US-PMR). We compared the remission rate, methotrexate combined use / amount and amount with PMR group diagnosed without US (nonUS-PMR). We excluded patients who had received steroids and patients whose medical records could not reviewed. [Results] 93% of US-PMR groups remained unchanged (other outcomes under analysis) [Conclusion] The superiority of clinical outcomes was suggested for PMR diagnosis with US.

P2-009

Predictive Factor for Outcome of Corticosteroid Therapy in Patients with Polymyalgia Rheumatica

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Conflict of interest: None

[Objective] To clarify predictive factor for outcome of CS therapy in patients with PMR. [Methods] Retrospective cohort study was performed in patients that was diagnosed as PMR with Bird's criteria and received initial CS therapy at Kitasato university hospital and Kitasato medical center from 2015 until 2019. Event was defined as increase in dose of CS due to exacerbation of PMR following first remission induction therapy, and observation period was from the initial CS therapy. [Results] 79 patients (52 female) with Age 69.9±8.4 years old (mean ± SD), RF 7.4±8.8 IU/ml, CRP 6.9±5.2 mg/dl, PSL 11.98±3.90 mg were included. ACPA was positive only in one patient. There were 19 events, 7 patients were treated with the additional immunosuppressants. 3 were diagnosed as other connective tissue diseases, and 4 were diagnosed as malignant tumor. Event rates at 0.5, 1 and 2 years were 1.4%, 1.9%, and 12.5%, respectively. Cox proportional hazard model demonstrated that normalization of serum CRP in the initial 6 weeks would decrease event. (0.309;95% CI 0.06-0.98, p=0.048). CRP and PSL dose at initial therapy did not contribute to the event. [Conclusions] The results demonstrated that the normalization of serum CRP within 6 weeks was a predictive factor for prevention of relapse in patients with PMR.

P2-010

Ultrasonographic findings and risk factors for RA onset in DMARD naïve patients with arthralgia

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Conflict of interest: None

[Objective] We examined the US findings and risk factors of RA onset in patients with arthralgia. [Methods] DMARD naïve 333 patients with arthralgia was examined (69 patients in the ACPA (+) group, 264 patients in the ACPA (-) group). [Method] All joints of the hand, 10 tendon sheaths of the wrist, and 10 extensor tendons of the fingers were observed by US. GS grade 2 and and/or PD grade 1 or higher had joint synovitis, and PD positive was tenosynovitis and extensor tendinitis. In addition to the 2010 ACR / EULAR classification criteria, RA was diagnosed by evaluating US and HR-pQCT. [Results] US detected 113 cases (34%) of synovitis, 50 cases (15%) of tenosynovitis, and 194 cases (58%) of tendinitis. RA diagnosis at the first visit was 21 cases (6%). RA diagnosis after the first visit was 13 of 312 cases, all 13 cases were in the ACPA (+) group. In RA cases RF titer was significantly higher and age was significantly lower than in non RA group. RF titer at diagnosis significantly increased than at the firsit visit. Synovitis and tendinitis were observed in 23 joints at the same site and synovitis without tendinitis were observed in 4joints (p=0.0002). [Conclusions] In patients with ACPA positive, extensor tendinitis and RF titer were considered to be a risk factor for the onset of RA.

P2-011

the Possibility of Colchicine Therapy in "Palindromic Rheumatism"

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Conflict of interest: None

[Objective] Palindromic rheumatism (PR) is the syndrome characterized by recurrence of redness, swelling and pain around joints within a few weeks. The prognosis is thought to be good. However, PR reportedly progresses to rheumatoid arthritis (RA) in 40-70% within 10 years. [Method] 8 patients were recruited with "PR" symptoms. Clinical course, laboratory results, x-ray and ultrasound (US) findings were assessed retrospectively. [Results] 5 females and 3 males were recruited with age 52.6 years old,

symptom duration 22 months, attack duration 3 days, attack frequency 3/month, swollen joints count 7 and CRP 0.42 mg/dl (median). ACPA and RF were positive in 75% and 63%. X-ray showed osteoarthritis in 2 patients and no RA findings. US was performed in 6 patients. Joint synovial thickening, synovial fluid and power doppler signal was detected in 3, 3 and 4 patients respectively. Periarticular swelling is detected in 3 patients. No crystal was found. NSAIDS relieved symptoms in all, but didn't decrease the frequency. Colchicine (COL) was prescribed in 3 patients. COL ameliorated symptoms and the frequency in all, but 1 patient was diagnosed as RA in 6 months. [Conclusion] COL had some positive effect for "PR" . However, further investigation is needed regarding the efficacy for prevention of RA.

P2-012

The critical role of IL-6 in sustaining joint inflammation in rheumatoid arthritis. The analyses in the cases of tocilizumab re-administration

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Conflict of interest: Yes

[Objective] To clarify the role of interleukin-6 (IL-6) in sustaining the joint inflammatory state in patients with rheumatoid arthritis (RA). [Methods] The role of IL-6 was evaluated by the response to tocilizumab (TCZ) in 307 patients with RA. TCZ treatment was initiated after mean disease duration of 9.2 years, with no less than 168 days of TCZ treatment completed between May 28, 2008, and July 31, 2019. TCZ efficacy was evaluated using the DAS28-ESR, C-reactive protein levels, and EULAR response criteria. [Results] The mean DAS28-ESR decreased from 4.50 at baseline to 2.60, 1.72, and 1.48, respectively, at 1 month, 2 months, and 1 year, respectively, after treatment initiation and was below 1.50 at 10 years. TCZ re-administration to 74 patients with relapsed RA after TCZ withdrawal was also effective. The mean DAS28-ESR decreased from 4.40 at baseline to 2.63, 1.77, and 1.55, respectively, at 1 month, 2 months, and 1 year after retreatment initiation. There were no "no response" cases, based on the EULAR response criteria in both initial TCZ administration and re-administration. [Conclusions] RA was ameliorated by TCZ, regardless of initial administration and re-administration, confirming the essential role of IL-6 in sustaining joint inflammation in RA.

P2-013

Treatment for elderly rheumatoid arthritis (RA) from the viewpoint of inflammatory cytokines

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Conflict of interest: None

[Objective] Inflammatory cytokines are essential for considering pathogenesis of RA, however, there are few reports on its changes caused by aging. We aimed to elucidate what treatments are appropriate for elderly RA from the viewpoint of inflammatory cytokines. [Methods] We measured and compared TNFα and IL6 levels in serum of each 50 patients, elderly (over 65 years; E) and young (under 65 years; Y) RA, and elderly and young control (HC). These cytokine levels were compared for gender, disease duration, mTSS, autoantibodies, treatment, and disease activity (DAS28-CRP). [Results] Serum TNF levels in both groups were higher in E group than in Y group, and RA groups were higher than HC groups (RA; E 1.3 pg/ml, Y 1.0 pg/ml. HC; E 1.1 pg/ml, Y 0.8 pg/ml). On the other hand, serum IL6 levels were not significantly different in aging, but RA group was significantly higher in both age groups than in HC groups (RA; E 5.2 pg/ml, Y 5.4 pg/ml. HC; E 2.4 pg/ml, Y 1.8 pg/ml). [Conclusions] Our data suggested that serum TNFα levels were associated with aging, while serum IL6 levels were associated with developing RA. Therefore, treatment with TNFα or IL6 inhibitor is considerekod to be suitable for elderly RA patients.

P2-014

Relation between pain catastrophizing and non-inflammatory arthralgia. One year follow up

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Conflict of interest: None

[Background] We reported that pain catastrophizing (PC) is involved in Non-inflammatory arthralgia (NIA) of RA patients at the latest conference. [Objective] To investigate relation between PC and pain VAS at 1 year (pVAS) of NIA patients with RA. [Method] 79 patients with RA who referred to our institution, fulfilling following requirements were enrolled; disease duration≧ 6 months, maintaining same b/ts DMARDS and MTX treatment at least 3 months, CRP value <0.5mg/dl, US imaging remission. PC Scale (PCS) containing 3 subscales, magnification, rumination, and helplessness were used to assess PC. Patients were divided into 2 subgroups, PCS≧30 as PC group and PCS<30 as controlled group. To determine confounding factor, univariate regression analysis was used for pVAS. A propensity score -matching (PSM) was generated for age, sex, disease duration, low back pain, HAQ-DI. Multiple linear regression was conducted to determine which subscales of PCS variables were best correlated with pVAS. [Result] The result of PSM showed that pVAS (mm, mean) was 35 in PC group and 20 in controlled group (p value =0.019). In multivariate analyses, helplessness was associated with pVAS. [Conclusion] PC, especially helplessness, had significant impact on the level of pain of NIA-RA.

P2-015

An inflammation mechanism and the treatment of Rheumatoid Arthritis (RA) considered by the relation between Complement (CH50) and antiCCP antibody (aCCPab), rheumatoid factor (RF) (RAPA)

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Conflict of interest: None

[Objective] We examine an inflammation mechanism in the high aCCPab, RF titers in RA statistically and consider the treatment of RA. [Methods] 1545 patients with RA are divided into 3 groups in the negative, low, high level by aCCPab titers and analyzed relations of aCCPab and CH50, MMP-3, CRP,1/serum iron (Fe), Platelet (Plt), immunoglobulinM (IgM) and relations of CH50 and CRP, 1/Fe, IgM next by U test, rank correlation coefficient, multiple regression analysis and as for by RAPA similarly. [Results] MMP-3, a marker of synovitis, was unrelated to aCCPab and RAPA. CRP, 1 / Fe, Plt, IgM were elevated with aCCPab, RAPA titers, but CH50 was constant. As for CH50 and CRP, 1 / Fe had a positive, IgM a negative correlation, and CH50 was associated with IgM more than CRP. CH50 and IgM were elevated with Proinflamatory Cytokine (Cytokine), but CH50 which was activated by IgM decreased, hence, became constant in appearance. [Conclusions] The high titers of aCCPab, RF being considered poor prognosis, not only Cytokine but also IgM-complement system activated by Cytokine occurs the inflammation. We consider that anticytokine therapy is effective because it is elevated Cytokine in the high aCCPab, RF titers and that Steroid combination therapy which inhibits IgM-complement is effective and necessary.

P2-016

Two cases of elderly onset RA

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Conflict of interest: None

<Objective> We report two cases of elderly onset rheumatoid arthritis (EORA). <Methods and results> Case 1. 72-year-old male. he had both knee joint pain from around the age of 61, it was performed left knee joint replacement at the age of 72. Right knee joint pain appeared after two months. Blood test RF40, anti-CCP antibody 304.6, CRP1.81, diagnosed with RA, started Mtx administration, symptoms are reduced. Case 2.

66-year-old male. Since the age of 50, he had a swollen left knee joint pain, and an X-ray examination showed a bone cyst in the left femur and tibia. Left knee pain from the age of 65, edema continues, RA11 in the blood test, anti-CCP antibody 47.3, CRP0.22, diagnosed with RA and started MTX administration. <Conclusions> Elderly onset RA develops over 65 years of age, acute onset is often, high disease activity, there are many cases where the progression of joint destruction is fast. As differential diagnosis, polymyalgia rheumatic, RS3PE syndrome, there is a crystal-related (Pseudo RA) and the like. Currently, the number of elderly patients is increasing, it seems that the number of cases of elderly onset RA is increasing.

P2-017

The role of ADAM12 upregulated proliferation of synovial membrane in rheumatoid arthritis

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Conflict of interest: None

[Introduction] ADAM12 is a member of a disintegrin and metalloproteinase family and has been reported to participate in the development of variety of tumors by degrading ECM and shed precursors, thus promoting cell proliferation, invasion and metastasis. In the current study, we examined the relationship between ADAM12 and the proliferation of synovial cell in rheumatoid arthritis (RA). [Methods] The expression of ADAM12 in RA, osteoarthritis and normal synovium was examined by immunohistochemistry. The cultured synovial fibroblasts obtained from RA patients at the surgery (RASF) were stimulated by TNF-α, TGF-β and PDGF, and the expression of ADAM12 was examined by real-time PCR. After stimulation of TGF-β, the proliferation in RASF was examined by WST-1 assay. The expression of ADAM12 was examined by western blotting, and the proliferation in RASF was examined after siADAM12 transfection. [Results] ADAM12 was highly expressed in RA synovial tissue. Stimulation by TGF-β resulted in upregulation of ADAM12, and the proliferation was enhanced in RASF. Transfection of siADAM12 decreased ADAM12 and proliferation in RASF. [Conclusion] ADAM12 might be involved in proliferation of RASF. It is highly possible to control synovial proliferation by suppressing ADAM12 in vivo.

P2-018

Filgotinib inhibits 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 RA. However, a direct role of filgotinib for osteogenesis has not been demonstrated. Here, we examined filgotinib inhibited proinflammatoly cytokine production in osteoblasts. [Methods] To determine if the JAK-STAT enzyme was expressed in osteoblasts and MG63 (human osteosarcoma cell line), we performed immunohistochemistry. In order to confirm that filgotinib inhibited STAT signaling phosphorylation, IL-6 and IL-6R stimulated MG63 was used for western blotting. To determine whether filgotinib was involved in proinflammatoly cytokine production, cytokines in filgotinib treated MG63 conditioned medium was measured using ELISA. [Results] JAK1, 2 and 3 was expressed in osteoblast and MG63. We found that phosphorylated STAT1 and STAT3 signaling in IL-6 and IL-6R stimulated filgotinib treated MG63 was significantly decreased. MCP-1/CCL2 and CXCL16 in filgotinib treated MG63 conditioned medium was significantly decreased compared with in nontreated MG63 conditioned medium. [Conclusions] These data indicate that filgotinib acts on bone metabolism, suggesting that filgotinib may prevent bone destruction.

P2-019

Effect of adenosine A2A receptor signal on MMP-3 production in RA synovial fibroblasts

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Conflict of interest: None

[Objective] Adenosine (Ado) is the effector molecule of anti-rheumatic effects of methotrexate (MTX). We have previously reported that adenosine inhibits TNFα-induced MMP-3 production via A_{2A} receptor signal using an RA synovial cell line. In this study, we also examined synovial fibroblasts (RA-FLS) from RA patients. [Methods] FLS were isolated from joint surgery specimens from RA patients. After 2nd generation subculture was cultured for 24 hours in the presence or absence of TNFα (1000 pg/ml) with or without the selective A_{2A} AdoR agonist HENECA. MMP-3 concentration of the culture supernatants was then measured using "Panacurea MMP-3 (Sekisui Medical Co. Ltd.). " [Results] MMP-3 production in synovial fibroblasts was increased by TNFα stimulation. This MMP-3 production was inhibited by HENECA, but the inhibition was lower than the decrease in serum MMP-3 level by MTX administration. [Conclusions] MMP-3 production in FLS was inhibited in vitro by the Ado A_{2A} receptor signal, but compared to in vivo Only a slight decrease. This suggests that the anti-rheumatic effect of MTX is not only a direct suppression of MMP-3 production via the Ado A_{2A} receptor signal in synovial cells, but also a synergistic effect with the suppression of inflammatory cytokine production by Ado.

P2-020

Regulation mechanism of Activin A expression and its functional role in rheumatoid arthritis synovial cells

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA), Activin A is widely expressed in the synovium, but its functional role is unknown. The purpose of this study is to clarify the regulatory mechanism of Activin A expression and its function in RA. [Methods] Fresh-RSC; Rheumatoid Synovial Cells from patients with rheumatoid arthritis were stimulated with multiple cytokines, and evaluated gene expression by qPCR. Enzyme-linked immunosorbent assay (ELISA) was used to measure Activin A and CXCL10. The osteoclasts generated from human peripheral monocytes by RANKL stimulation were identified. The expressions of NFATc1 and Cathepsin K were determined by western blotting. [Results] Activin A production in fresh-RSC was markedly enhanced by the synergistic effect of TGF-β1 with inflammatory cytokines including TNFα, IL-1β, and IL-6. Activin A inhibited TNFα-induced CXCL10, but did not affect the expression of inflammatory cytokines and chemokines. In addition, Activin A directly inhibited osteoclast formation in human samples and the expression of NFATc1 and cathepsin K. [Conclusions] TGF-β1 synergistically induces the expression of Activin A in RSC with inflammatory cytokines. Activin A may prevent joint destruction of RA through inhibiting chemotaxis of inflammatory cells and osteoclastgenesis.

P2-021

Continuous decreases in serum titers of rheumatoid factors were related to suppression of joint damage in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To determine whether continuous decreases in serum RF

titers are related to radiographic remisson (RR) in RA patients. [Methods] 130 RA patients were enrolled, who had serum RF titers ≧45 IU/ml, were treated with b/tsDMARDs and were followed up until month 12. RF titers were measured at month 0, 4 and 12 after starting therapy, and a continuous RF decrease was defined as more than a 10% decrease in RF titer during both month 0-4 and 4-12. DAS28-ESRs were calculated at month 0, 4 and 12. Joint damage was assessed by modified total Sharp score (mTSS) at month 0 and 12, and RR was defined as yearly mTSS progression ≦0.5. [Results] Subjects were 102 female and median age 61.7 years with 4.8 years of disease duration, who had median DAS28-ESR 3.92 at month 0. 27, 9, 39 and 55 patients were treated with abatacept, JAK inhibitors, tocilizumab and TNF inhibitors, respectively. 46 cases had continuous RF decreases, and 65 showed RR. The factors related to RR by multivariate logistic regression analysis were disease duration (OR: 0.948 (p=0.042)), a continuous RF decrease (OR: 4.105 (p=0.003)) and time-integrated DAS28-ESR (OR: 0.463 (p=0.002)). [Conclusions] Continuous decreases in serum RF titers were related to radiographic remisson in b/tsDMARD-treated RA patients.

P2-023

What affects the disability of upper limbs in rheumatoid arthritis

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a chronic disease leading to disability of daily life. The purpose of this study is to identify the factors influencing the disability of upper extremities in patients with RA [Methods] We enrolled consecutive RA patients from the Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) cohort who participated in 2014. Clinical data including age, duration of disease, sex, BMI, ACR class, Steinbrocker's stage, HAQ, TJC/SJC 28, and grip strength were collected. The tender or swollen of shoulders, elbows and wrists were collected. We evaluated disease activities using DAS28-CRP/ESR. The disability of upper extremities was evaluated with DASH (disability of the arm, shoulder and hand) score. The effect of baseline characteristics on the DASH scores was assessed. [Results] A total of 317 patients were enrolled in this study. The DASH score was 27.1±22.8 (0-92.5). On multivariate regression models, the explanatory factors of the DASH scores were higher DAS28-ESR, lower grip strength and the tender of elbows. [Conclusions] To reduce disease activity, and examine the patients joints especially elbow and treat the tenders may lead to prevent the disability in the upper extremities in RA.

P2-025

Analysis of predictive factors for continuation in RA patients treated with Adalimumab (ADA) 80mg/2W

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Conflict of interest: None

[Objective] Efficacy of Adalimumab (ADA) has been reported in postmarketing and observational studies regarding its 40 mg / 2W efficacy. However, there are few reports on the efficacy and usefulness of ADA80mg / 2W and its predictors. In this study, we analyzed for predictors of ADA80mg / 2W efficacy. [Methods] From August 2017 to October 2019, 51 out of 81 patients with RA treated with ADA80mg / 2W were observed for 24 weeks. Disease activity like DAS28-CRP and the other parameters, were observed. The endpoint was set at treatment continuation at 24 weeks. The predictive factors contributing to 24 week treatment continuation were analyzed. [Results] Of the 51 patients followed up for 24 weeks, 31 patients (60.8%) could continue ADA treatment. Clinical course of those 31 patients in the continuation group showed significant improvements at 24 weeks. Comparison between the continuation group and the non-continuation group showed significantly lower values of SJC/RF, MMP3 at the time of ADA treatment initiation. [Conclusions] The comparative analysis on the presence or absence of previous biologic use showed no association with treatment continuation, however in the continuation group, biologic treatment immediately before ADA80mg tended to have a higher usage rate of ADA40mg.

P2-026

The efficacy of subcutaneous administration of Tocilizumab every week for rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the efficacy of subcutaneous administration of Tocilizumab (TCZ) every week in Rheumatoid Arthritis patients [Methods] To analysis of Pt's background in our department and affiliated hospital, disease activity score, the effect of treatment compare to every two weeks, the alternation of steroid and methotrexate dosage. [Results] In our fourteen cases, their mean age is 59.3 year-old, stage1/4, 2/4, 3/4, 4/2, Class 1/4,2/8, 3/1, 4,1, three patient's bodyweight was 70-80kg, two patient was above 80kg. Tocilizumab was first biologics in four cases, second biologics in four cases, third biologics in six cases, most previous biologics was etanercept. The mean duration of TCZ every 2 weeks was 17.1 months (1-45months). Rheumatoid factor was positive in all cases. ACPA was positive in 12 cases. Mean Pt VAS was 26.9, Mean DAS-ESR 2.63, Mean CDAI was 8, MTX was prescribed in 7 cases, their average dosage was 6.6mg/week, Predonisolone in 8 cases, 6.6mg/day. All patients in moderate or low disease activity with DAS28-ESR reached to remission after dose escalation of TCZ. The dosage of steroid coudl be tapared as well. One patient had bacterial pneumonia during treatment. [Conclusions] The dose escation of TCZ is useful for achievement of remission in rheumatoid arthritis.

P2-028

Validation of a composite major in healthy people and knee osteoarthritis. Are all healthy people in clinical remission?

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Conflict of interest: None

[Objective] The therapeutic goal of rheumatoid arthritis is clinical remission. The composite major used as a treatment goal had been created for RA patients and has not been validated in healthy people and other diseases. The purpose of this study was to examine the disease activity in healthy people and knee osteoarthritis. [Methods] Nineteen patients who became RF positive at medical check (RF), 25 patients who were diagnosed as non-RA with morning stiffness (MS) and 30 knee osteoarthritis patients hospitalized for TKA (KOA) were included in this study. The disease activity rate of DAS28-ESR, DAS28-CRP, CDAI and SDAI were examined. The HAQ remission rate in each group was also examined. [Results] DAS28-ESR remission were 13 cases (68.4%), 14 cases (56%) and 2 cases (6.7%) respectively for RF, MS and KOA. SDAI remission were 11 cases (57.9%), 7 cases (28%) and 1 cases (3.3%) respectively for RF, MS and KOA. In addition, SDAI moderate disease activity were 1 case, 7 cases and 18 cases respectively for RF, MS and KOA. HAQ remission was observed in 19 cases, 20 cases and 19 cases respectively for RF, MS and

KOA. [Conclusions] It is difficult to fulfill clinical remission in all cases diagnosed to be non-RA, and it is necessary to reconsider the treatment goal and clinical evaluation of RA.

P2-029

Factors predicting DMARDs addition after initial methotrexate monotherapy in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We aimed to determine the factors that could predict the addition of disease modifying antirheumatic drugs (DMARDs) after initial methotrexate (MTX) monotherapy in patients with rheumatoid arthritis (RA). [Methods] This retrospective cohort study included 233 patients with RA treated with initial MTX monotherapy. The primary endpoint was DMARDs addition within 6 months after starting MTX therapy. Factors significantly related to the endpoint were identified using logistic regression analysis. [Results] The median age was 62 (24-90) years, 73% were women, the median swollen joint count (SJC) was 3 (0-28), and the median tender joint count (TJC) was 5 (0-28). DMARDs were added in 66 (28.3%) patients. In the univariate analysis, TJC, SJC, and glucocorticoid intraarticular injection (GCII) history were significantly associated with the endpoint. In the multivariate analysis, by adding age, sex, symptom duration, smoking history, and erythrocyte sedimentation rate to the variables identified in the univariate analysis, SJC (OR: 1.074, 95%CI: 1.103-1.139) and GCII history (OR: 3.423, 95%CI: 1.109-10.563) were independent predictors of the endpoint. [Conclusions] A large SJC and a GCII history may be useful predictors of DMARDs addition within 6 months after starting MTX therapy.

P2-030

Deviation regarding the RA disease activity scores -using NinJa2018 cases

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Conflict of interest: None

[Objective] To examine a deviation of remission rate determined by six RA disease activity measures. [Methods] In 15440 cases registered in *NinJa2018* we compared remission rates by DAS28-CRP, DAS28-ESR, CDAI, SDAI, Boolean remission criteria. 2091 cases are TNF inhibitors, 832 cases T cell co-stimulation inhibitor and 1265 cases IL6 receptor inhibitors. [Results] In all of biologicals administered cases, remission rate was 61.1% in DAS28-CRP followed by 48.1% in DAS28-ESR. SDAI (37.3%), CDAI (34.9%), and Boolean remission was 29.3% (PRACTICE) and 28.4% (TRIAL). Remission rate was lowest in T cell co-stimulation inhibitor (15.0-27.3%). The IL6 receptor inhibitor was large misalignment differences between composite measures (39%), but offset by CRP is small (between SDAI and CDAI was within 5%). Deviation between DAS28-ESR and DAS28-CRP was 6-7% in IL6 receptor inhibitors, but the deviations were about 20% in two other biologicals administered patients. [Conclusions] 1) The remission rate by DAS28-CRP and DAS28-ESR was high. 2) Remission rate was low in T cell co-stimulation inhibitor administered cases. 3) Up to 39% of deviation among the measurement methods was noted in IL6 receptor inhibitors cases, but deviation by the presence or absence of CRP was small.

P2-031

The analysis of relationship between expectancy health life and clinical backgrounds in patients with elderly rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate relationship between drug therapy and health life expectancies we analyzed the clinical courses in elderly patients with rheumatoid arthritis (RA). [Methods] 2014-2018 348 patients with RA. Over 65 years RA patients were mean age 78 ±8.0 M/F 32/133, 68 patients with elderly onset RA mean age 73.4±6.4, disease duration 0.4±0.23 years, followed up during 2 years. End point, loss of health life defined time of long term-care insurance application, Long-term care facility residents, diagnosis of cognitive impairment. We analyzed relationship between RA disease activity HAQ-DI, QOL score SF-36, cognitive examination (MMSE, Moca-J) and loss of health life expectancy. [Results] Loss of expectancy health life was concerned with corticosteroid therapy and comorbidities, not use of b DMARDs, disease activity before therapy. Cognitive impairment patients showed 5% in EORA after therapy, other patients 10%. Loss of expectancy health life related several comorbidities (serious infection, bone fracture, cardiovascular disorders). [Conclusions] The management of elderly RA we should select the safe tool for expectancy health life.

P2-032

The safety of DMARDs in RA patients with interstitial lung disease: systematic review

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Conflict of interest: None

[Objective] To develop 2020 Japanese guideline for the management of RA, we conducted a systematic review for the safety of DMARDs in RA patients with interstitial lung disease (ILD). [Methods] Cochrane Central Register of Controlled Trials, Pubmed, and Ichushi were electrically searched. [Results] We included 7 case series studies (rituximab: 2 studies, abatacept: 2, TNFα inhibitors: 1, tacrolimus 1). Among 62 RA patients treated with rituximab, 94.9% had improvement or no change in forced vital capacity (FVC), 84.2% had improvement or no change in DLCO, and 92.9% had improvement or no change in CT findings. Among 52 patients treated with abatacept, 88.5% had improvement or no change in FVC, 91.3% had improvement or no change in DLCO, and 92.1% had improvement or no change in CT findings. Among 78 patients treated with tocilizumab, 92.3% had improvement or no change in CT findings. Among 46 patients treated with TNFα inhibitors, 69.6% had improvement or no change in CT findings. Among 40 patients treated with tacrolimus, CT score significantly decreased from 1.44±0.77 to 1.42±0.78 (P=0.0039). No studies assessed other safety. All the studies were high risk of bias. [Conclusion] Some DMARDs may be safely used for RA patients with ILD although quality of evidence was very low.

P2-033

Cases of rheumatoid arthritis (RA) with chronic airway lesion that low dose macrolide therapy (LDMT) was effective

Tomoki Katayose
Murayama Medical Center

Conflict of interest: None

Case1: A 75-year-old male has had RA since 4 years ago and was treated with methotrexate (MTX). But the RA activity was severe. CT suggested tuberculosis or non-tuberculosis mycobacterium. Neither the examination of a sputum nor the bronchoscopy showed any particular infection and malignancy. Finally he was diagnosed as rheumatoid bronchiolitis. He was treated with abatacept (ABT). But his RA activity did not improve. After LDMT was added, his RA activity became milder. Case2: A 59-year-old female has had RA since 12 years ago. Although she was treated with infliximab and MTX at another hospital, their effect on her RA gradually decreased, so that infliximab was ceased. When she was transferred to our hospital, her RA activity was intermediate. Although T-SPOT was posi-

tive, her chest CT solely showed inactive lesion. In addition, the sputum culture was negative. Biologic therapy was resumed in combination with isoniazid prophylaxis against tuberculosis. She was treated with ABT. But her RA activity did not improve. After she received LDMT, her RA activity improved significantly. It has been established that LDMT improves chronic airway infection, but the two cases suggest that it can also improve the disease activity of arthritis in RA patients with airway lesions.

P2-034

Examination of the relationship between rheumatoid arthritis and sinus lesions using computed tomography

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Conflict of interest: None

[Objective] To determine the association rate of sinus lesions in rheumatoid arthritis (RA) using computed tomography (CT) and examine the relationship between sinus and lung lesions associated with RA. [Methods] A retrospective analysis was conducted in 96 RA patients who visited the Yamaguchi University Hospital and met the 2010 ACR / EULAR Joint Rheumatoid Arthritis Classification Criteria and underwent analyzable head and neck and chest CT. For the evaluation of sinus lesions, the Lund-Mackay score (LMS) was used, and an LMS ≧ 2 was regarded as having sinus lesions. [Results] The participants included 25 males and 71 females (74.0%), with a mean age of 65.0 years. Multiple logistic regression analysis of the relationship between the presence or absence of sinus lesions and lung CT images showed significantly more tree-in-bud findings, a finding of airway lesions, in the group with sinus lesions. RA patients with sinus lesions were significantly more hospitalized for lower respiratory tract infections after the RA onset. [Conclusions] Examination using CT revealed that sinus lesions were frequently observed in RA. In addition, sinus lesions were significantly associated with RA respiratory tract lesions and hospitalization due to lower respiratory tract infection in RA patients.

P2-035

Glucocorticoid use is risk of sarcopenia and locomotive syndrome in patients with rheumatoid arthritis from the CHIKARA study

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patients have a high frequency of sarcopenia and can be locomotive syndrome due to joint damage and dysfunction. We investigated sarcopenia, locomotive syndrome, and frailty in RA patients. [Methods] The data from a prospective observational study (CHIKARA study) were used. Asian Working Group for Sarcopenia criteria was used for diagnosis of the sarcopenia. The diagnostic criteria was used for locomotive syndrome and frailty. [Results] 83 RA patients were included. Mean age was 66.7 years old, median disease duration was 8.6 years. Mean DAS28-ESR was 2.9. The rate of MTX usage was 82%, biologics usage was 21%, and glucocorticoid (GC) usage was 21.7%. Prevalence of sarcopenia was 43.4%, locomotive syndrome was 36.1%, and frailty was 27.2%. Incidence of new cases sarcopenia was 6.4%, locomotive syndrome was 11.3% and frailty was 9.8%. In the newly developed sarcopenia group, the GC usage rate was significantly higher than that in the non-onset group ($p=0.005$), and in the newly developed group with locomotive syndrome, the GC usage rate was significantly higher than that in the non-onset group ($p=0.025$). [Conclusions] In the new case of sarcopenia and locomotive syndrome had significantly higher rate of GC usage than in the non-onset group.

P2-036

The challenge of improving nutrition of frail patients with rheumatic diseases

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Conflict of interest: None

[Objective] Patients with chronic diseases are prone to develop frailty. Poor nutritional status contributes development of this phenomenon. Practical nutritional management strategy for patients with frail-rheumatic diseases is unknown. [Methods] Elderly (>70y.o.) out-patients at our hospital were screened, and those with either frail or pre-frail were continuously guided by nutritional managers. [Results] 68 % (71/105) patients were classified either with flail or pre-flail. 10 patients with rheumatoid arthritis were intervened. Three patients were underweight. Two patients reported they skip meals. Nine patients habitually take meals that lack protein. In 6 patients, total energy intake was lower than estimated energy requirement. Dietary pattern in 10 patients showed deficient of vegetables. Through the continuous nutritional guidance, improvement of the dietary pattern were seen only in 3cases. [Conclusions] motivating elderly frail-patients with rheumatic diseases to change their dietary pattern is challenging. Nutritional managers should not only to give them specific dietary advice, but also to cooperate with other care staffs in delivering appropriate nutritional support.

P2-037

Examination of the effect of arthritis on the progression of arteriosclerosis by using new model mice ApoE knockout SKG mice

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Conflict of interest: None

Arteriosclerosis is a complication related to the prognosis of RA patients and a problem to be solved. One method for examining the effect of arthritis on the progression of arteriosclerosis is to use an animal model. However, there was no animal model that develops arthritis and arteriosclerosis simultaneously. We mated SKG mice: chronic arthritis model with ApoE knockout mice: arteriosclerosis model to establish model mice that develop arthritis and arteriosclerosis simultaneously (ApoE knockout SKG mice). We used this model to examine the effect of arthritis on the progression of arteriosclerosis. The 14 ApoE knockout SKG mice were divided into two groups, arthritis group and non-arthritis group, and the degree of arteriosclerosis of these groups was compared. The arteriosclerotic area and the arterial stenosis rate at the aortic annulus was significantly increased in the arthritis group compared with the non-arthritis group.

P2-038

A case of rheumatoid arthritis with nephrotic syndrome on tocilizumab therapy

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Conflict of interest: None

65 year-old woman was diagnosed with rheumatoid arthritis (RA) 25 years ago. Various anti RA medicine were ineffective, however tocilizumab (TCZ) treatment started 2 years ago was effective and her arthralgia was relieved. She was hospitalized for nephrotic syndrome 3 months ago. TCZ was suspected to be a nephrotic-inducing medicine and was withdrawn. However, her nephrotic syndrome and RA activity were worsening, and then she transferred to our hospital. After resuming TCZ and increasing PSL, arthralgia and proteinuria improved and she was discharged. Renal biopsy revealed MPGN-like lesion. IF staining revealed full-house pat-

tern. After improvement of arthralgia, TCZ was withdrawn again and her nephrotic syndrome worsens. After second admission, liver damage and hepatic encephalopathy due to unknown origin appeared. TCZ was resumed and PSL increased, but she died on the 48th hospital day. There was a case report of TCZ-induced nephrotic syndrome, whereas TCZ might also contribute to the disease suppression. Considering this dual aspects, it may be desirable not only to discontinue TCZ but also to start other immunosuppressive agent.

P2-039

Clinicopathological findings of CKDG4 and CKDG5D with the MTX-LPD past RA patients

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Conflict of interest: None

[Objective] To clarify the characteristics of CKDG4 and CKDG5D with the MTX-LPD past RA patients. [Methods] Seven RA patients who developed MTX-LPD were investigated in this study. We compared the clinical and laboratory parameters of patients who achieved regression of LPD by MTX withdrawal and evaluated the clinical course of CKDG thereafter. [Results] Four patients achieved regression of LPD by MTX withdrawal. Four patients received biological agents after LPD, and demonstrated an improved disease activity of RA and persistent remission of LPD, whereas two patient experienced renal dysfunction after MTX-cessation, CKDG4 and CKDG5D. [Conclusions] Careful CKD management is needed for the MTX-LPD past RA patients

P2-040

What is the cause of chronic kidney disease in rheumatoid arthritis?

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Conflict of interest: None

[Objective] With the aging of rheumatoid arthritis (RA) patients, the complication of chronic kidney disease (CKD) is increasing. However, it is often not clear what caused CKD. We sought to clarify the cause of CKD in RA patients. [Methods] RA patients with CKD were extracted from patients from April 2018 to June 2019 who regularly visit Nakadoori General Hospital, and the cause of CKD was investigated retrospectively. [Results] Of the 101 RA cases, 30 cases (29.7%) had CKD mergers (eGFR 60 or less). Of these, 10 (9.9%) had CKD G3b or higher (eGFR 45 or lower) that could lead to end-stage renal failure. Causes include 4 cases of ischemic nephropathy due to NSAIDs, 3 cases of cardiovascular disorders, 2 cases of diabetic kidney disease, 2 cases of infection, 1 case of contrast nephropathy, 1 case of chronic glomerulonephritis there were. Some cases had multiple causes. There were 4 cases with acute kidney injury. There were 7 cases of drug-induced nephropathy, accounting for 70% of cases with CKD G3b or higher. [Conclusions] CKD is an important issue for aging RA patients. From this observational study, two issues were identified: acute kidney injury, and drug-induced kidney injury.

P2-041

The safety of DMARDs in RA patients with malignancy: systematic review

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Conflict of interest: None

[Objective] To develop 2020 Japanese guideline for the management of RA, we conducted a systematic review for the safety of DMARDs in RA patients with malignancy. [Methods] Cochrane, Pubmed, and Ichushi were electrically searched. [Results] We included 8 cohort studies (TNFα inhibitors: 6 studies, rituximab: 2, abatacept: 1, MTX: 1). Among RA patients with past medical history (PMH) of breast cancer who were treated with TNFα inhibitors, the relapse rate of breast cancer was not significantly increased (HR: 1.12, 95% confidence interval [CI]: 0.55-1.82). The relapse rate of non-melanoma skin cancer (NMSC) was, however, significantly increased among patients with PMH of NMSC (HR: 1.49, 95% CI: 1.03-2.16). In patients with PMH of any cancer, the relapse rate and incidence rate of secondary cancer was not significantly increased. Among patients with PMH of NMSC treated with rituximab or abatacept, the relapse rate was not significantly increased. Among patients with PMH of breast cancer treated with MTX, the relapse rate was not increased. The relapse rate was significantly increased among patients with PMH of NMSC (HR: 1.60, 95% CI: 1.08-2.37). [Conclusion] Relapse rate and incidence rate of secondary cancer differed by DMARDs and types of cancer although quality of evidence was very low.

P2-042

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 tacrolimus (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 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 monotherapy: 486), in ADA (MTX: 339 TAC: 10 monotherapy: 135), in GLM (MTX: 156 TAC: 14 monotherapy: 61), in TCZ (MTX: 272 TAC: 27 monotherapy: 207), in ABT (MTX: 213 TAC: 49 monotherapy: 178). In ETN, GLM, ABT analysis, the retention rate of TAC group was higher than monotherapy group. [Conclusions] We suspected that in ETN, GLM and ABT therapy, combination therapy with TAC are subsequent options for treatment to RA patient.

P2-043

Usage status of leflunomide in our department

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Conflict of interest: None

[Objective] Leflunomide was expected to have an effect comparable to that of MTX, but in Japan, it is less frequently used and less reported. We examined the therapeutic results of LEF for RA in our department. [Methods] We analyzed 14 cases of 24 patients with rheumatoid arthritis who used LEF from January 2006 to October 2019, excluding cases with collagen disease and cases with insufficient data. [Results] All patients were unable to continue MTX or were ineffective. In all cases, no LEF loading was performed and started with a maintenance dose. There were 2 cases of discontinuation of LEF, the reason for discontinuation was 1 adverse event (cytopenia) and 1 pregnancy request. Patients with a history of interstitial pneumonia were not included, and there was no onset of treatment. The mean DAS28-CRP was 3.74 before administration and 2.84 for 24 weeks after administration. [Conclusions] LEF is considered to be a good indication for patients in whom remission with MTX is difficult and BIO preparations and JAK inhibitors cannot be administered economical-

ly. However, due to the small number of studies, further accumulation of cases is necessary in the future.

P2-044

Maintenance Therapy with Reduced Dose of 25mg Weekly Etanercept in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To evaluate the feasibility of maintenance therapy with reduced dose of 25 mg weekly etanercept (ETN) after achievement of clinical remission. [Methods] We retrospectively reviewed clinical charts of thirty-six biologics naive RA patients (25 women and 11 men, mean age 47.2 years old, mean disease duration 5.8 years, mean DAS28-CRP 4.38) treated with 25mg ETN once a week. Dose reduction was selected for RA patients who maintained clinical remission for more than one year. We investigate the continuation rate of the patients after dose reduction and assessed the dose of ETN during the observation period. [Results] Twenty-nine patients were treated for more than one year with 25mg weekly ETN. Thirteen patients were able to taper the dose of ETN to 25mg once in ten days, then twelve patients (92%) remained of low disease activity / remission. The number of patients with the dose of ETN was two (50mg weekly), thirteen (25mg weekly), six (25mg once in ten days), and four (25mg every other week) respectively. [Conclusions] Dose reduction of 25mg weekly ETN is a possible choice for maintenance therapy in RA patients after achievement of clinical remission.

P2-045

two cases of ra patients, who have achieved long-term remission with golimumab monotherapy

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Conflict of interest: None

(Objectives): We report on two ra patients, who have achieved long-term remission by golimumab (glm) monotherapy. (case1): a 82-years-old woman was suffered from rheumatoid arthritis (ra) for 10 years. we introduced gim50mg at 76-years-old. induction internal medication: methotrexate (mtx) 8mg/week, prednisolone (psl) 5mg/day, bucillamine300mg/day. it became the remission after the glm treatment in 12 weeks. we gained to mtx12mg/week, and glm100mg, too. we discontinued psl in 56weeks. we discontinued all drugs 216 weeks. we maintain remission after glm monotheray for 90weeks. (case2) a 68-years-old woman was suffered from ra for 23years. we introduced infliximab (ifx) at 54-years-old. because second failure, we switched from ifx to glm50mg at 59-years-old. introduction internal medication: mtx6mg/week. because there was not improvement of the disease activity, we increased mtx in quantity to 12mg/week. we gained to glm100mg in 36weeks. it became the remission in 76weeks and discontinued mtx 168weeks. the remission was maintained after glm monotherapy for 122weeks. (discussion) we experienced two cases that achieved long-term remission by glm monotherapy. glm is a drug with less likely to secand failure. glm seemed to be suitable not only for the induction of remmision but also for the maintenance of remission.

P2-046

Elderly rheumatoid arthritis patients' experience with Tocilizumab

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Conflict of interest: None

[Objective] Although the number of elderly rheumatoid arthritis (RA) patients in Japan is increasing, treatment has not been established. [Methods] To analyze the effectiveness, safety and continuation rate of Tocilizumab cases by age in our hospital; to analyze changes in MTX and PSL levels by age, and to assess the efficacy and safety of TCZ.93 patients who had been using TCZ for 2 years, since April 2017, with an average age of 60.1 years, MTX 4.2mg/week, PSL 3.2mg/day, naïve 47%, DAS 28ESR 3.99. [Results] The average observation period of RA patients with TCZ was 12.0 months (6 to 24 months). The mean MTX for all patients was reduced from 4.2 mg/week to 2.2 mg/week, and the average PSL was reduced from 3.2 mg/day to 2.2 mg/day. In particular, in elderly RA patients, the average MTX was reduced from 3.8 mg/week to 1.3 mg/week, and the average PSL was reduced from 4.8 mg/day to 0 mg/day. Disease activity improved from DAS28ESR 3.9 to 2.1 in all patients, and elderly RA patients improved from DAS28ESR 4.3 to 2.0. The 2-year continuation rate for RA patients over 85 years of age was 100%. [Conclusions] For elderly RA patients, treatment with TCZ that suppresses MTX and PSL is considered a safe and efficacious treatment option.

P2-047

Comparison of the efficacy and safety of tocilizumab and sarilmab for RA

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Conflict of interest: None

[Objective] We investigated the efficacy of sarilumab (SAR) compared tocilizumab (TCZ) using clinical endpoints. [Methods] The treatment effect at 12 weeks was retrospectively examined in 31 patients (10 with SAR, 21 with TCZ) started after January 2018. [Results] The patient background of the SAR group at the start of SAR was mean age 66.1 ± 8.54. The sex ratio was 1: 1 and the duration of disease was 18.4 ± 8.6 years. Six cases were combined with methotrexate. Five cases used biologics before using sarilumab. The average DAS-28ESR at the start of SAR was 4.38 ± 1.20, and the average DAS-28ESR at the start of TCZ was 4.43 ± 0.88 (P = 0.93). After the start of SAR, 1 patient was discontinued due to adverse events, and 2 patients were discontinued due to insufficient effects. The mean change in DAS28-ESR at 4 weeks after the start of treatment was -1.75 ± 1.73 in the SAR group and -1.61 ± 0.95 in the TCZ group (P = 0.87). The mean change in DAS-ESR was -2.13 ± 0.94 in the SAR group and -2.12 ± 1.16 in the TCZ group (P = 0.99). [Conclusions] In this study, SAR improved the disease activity of RA in the same way as TCZ from the start of treatment to 12 weeks.

P2-048

Efficacy and safety of sarilumab in rheumatoid arthritis patients up to 24 weeks in clinical practice

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Conflict of interest: None

[Introduction] Sarilumab is the second IL-6 inhibitor for rheumatoid arthritis (RA), and there are few reports of real-world data. We evaluated the efficacy and safety of sarilumab in patients with RA in real-world setting. [Methods] 18 consecutive RA patients, who started to treat with sarilumab from February 2018 to March 2019, were enrolled. We examined the efficacy, which was measured by CDAI, and safety of sarilumab up to 24 weeks. [Results] The mean age was 50.4±16.1, mean disease duration was 14.1±9.5 years, mean CDAI was 27.8±10.2, and concomitant use of methotrexate was 66.7% at baseline. 3 patients were treated with sarilumab as the first bDMARD, 7 were switched from tocilizumab, 4 were from tofacitinib, 3 were from TNF inhibitors, and 1 was from abatacept, respectively. CDAI significantly decreased from 27.8 to 17.2 at 2 weeks ($p<0.05$ vs baseline), 13.4 at 4 weeks, 11.1 at 12 weeks, and 10.3 at 24 weeks. Discontinuations were 5 cases, the causes of which were 1 case of infec-

tion, 3 cases of inefficacy, 2 cases were other reasons. [Conclusion] CDAI was significantly decreased from 2 weeks after the initiation and continued the efficacy up to 24 weeks. There were few cases of discontinuation because of adverse events. The prompt effects of sarilumab was indicated.

P2-049

Effectiveness and safety of IL-6 inhibitor Sarilumab in five patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the effectiveness and safety of IL-6 inhibitor Sarilumab (SAR) in five patients with rheumatoid arthritis (RA) at 52 weeks or more. [Methods] Five patients with RA (3 women, age 66.2 (52-75) years, disease duration of 40 months, Class classification 2.2, Stage classification 2.2, TJC 6.2, SJC 6.6, CRP 3.04, 2 cases of biologics switches, concomitant methotrexate (MTX) 9mg/week [40%], and prednisolone (PSL) 5.2mg/day [60%]) who showed an inadequate response to csDMARDs (DAS28ESR 5.01 moderate disease activity) were treated with subcutaneous (200mg/2 weeks) SAR and enrolled in this 52-week, retrospective study. [Results] Remission rate of DAS28ESR, in 4 out of 5 cases at 12 weeks, was maintained until 52 weeks. DAS28ESR and other disease activity index also reached remission at 12 weeks, then, the DAS28ESR and DAS28CRP maintained remission, SDAI and CDAI also had maintained LDA. Outcome measures improved significantly, as follows; DAS28ESR from 5.01 to 1.54 ($P<0.01$). PSL use cases were also 1 case at 52 weeks (final dose 2mg/day). Side effects were the site of administration reaction and mild liver dysfunction, and no serious adverse events were observed. [Conclusions] SAR was considered to be a highly effective biologics even alone administration.

P2-050

Profiles of patients who received sarilumab therapy and registered in the Akita Orthopedic Group on Rheumatoid Arthritis registry

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Conflict of interest: None

[Purpose] Sarilumab was the second IL-6 inhibitor released in Japan in 2018, with reported effectiveness. We report cases of sarilumab administration identified from the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry. [Methods] Patient background, treatment details, and disease activity were evaluated in 10 AORA registrants in 2019 who received sarilumab therapy and had available data for analysis. [Results] Three men and 7 women (mean age, 64 y [range, 45-84 y]) were assessed; of these, 1 was naive and 9 were switched from other biologics. The reasons for switching were secondary ineffectiveness in 6 cases, inadequate effect in 2, and patient's request in 1. Only 1 patient received a single dose of 150 mg, and the rest received 200 mg. Methotrexate 6.4±2.2 mg/wk was used in 5 patients. The mean sarilumab therapy duration was 119 d (range, 27-322 d). Only 1 patient had a primary treatment failure. The mean 28-joint disease activity score for erythrocyte sedimentation rate (DAS28-ESR) was 4.01±2.05 at treatment initiation and significantly improved to 3.16±1.35 at 1 mo. [Conclusion] In clinical practice, sarilumab is frequently used as a switching agent from other biologics. The DAS28-ESR score significantly decreased at 1 mo of treatment.

P2-051

Treatment results of sarilumab for rheumatoid arthritis in our department

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Conflict of interest: None

[Objective] In February 2018, sarilumab, the second anti-IL-6 receptor antibody preparation, was launched for rheumatoid arthritis (RA). Since it has just been launched, it is necessary to accumulate sarilumab-treated cases for safe and effective RA treatment. In our department, experience of using sarilumab is accumulating, so we report the results of its use. [Methods] We analyzed eight patients who received sarilumab for RA in our department by November 2019. [ResultsOf the 8 cases, 2 cases were naive, 2 cases were relapsed after withdrawal, and 4 cases were switches. Only one patient started with sarilumab 150 mg because the patient was elderly, but the improvement was poor, so the dose was increased to the standard dose of 200 mg and CDAI remission was achieved in 3 months. In all other cases, CDAI remission was achieved at 3 months after the introduction. In addition, there were 2 cases that switched from biweekly administration of tocilizumab subcutaneous injection 162mg, all of which had good therapeutic response. We had no clinically problematic adverse events. [Conclusions] In our department, sarilumab was confirmed to have high efficacy and continuation rate as well as other biologics. Sarilumab should be started at 200 mg whenever possible.

P2-052

Seven cases of sarilumab use in RA patinets

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Conflict of interest: None

[Objective] To consider the good indication of sarilumab (SAR) reviewing 7 cases of RA patient who was treated with SAR. [Methods] Among 189 RA patients, seven used sarilumab by November 2019. The reason of indication, efficacy, continuity was retrospectively evaluated. [Results] Patients were all female, in their age of 60s-80s. Concomitant MTX was used in 4 cases (57%). Two patients used SAR for first bDMARDs/JAK inhibitor. Four patients switched from TNF inhibitors to SAR. One patient switched from tocilizumab (TCZ). There were histories of TCZ use in two cases, of which one discontinued TCZ by secondary failure, the other discontinued TCZ by local reaction to TCZ in injected site. Period of duration of SAR from initiation was up to 10 month. All the cases are continuing SAR, although one case with secondary failure to TCZ considering switch to a JAK inhibitor, because SAR showed insufficient improvement. [Conclusions] When switching to the drugs with other mode of action like TNF inhibitors, we can't point out the difference in indication between SAR and TCZ. SAR is expected for TCZ secondary failure cases, although the efficacy of SAR was limited in our case. Elderly patients may favor SAR in respect of buttonless device.

P2-053

Efficacy of Abatacept for suppressing radiographic progression of cervical lesions in patients with rheumatoid arthritis comparison with methotrexate therapy; two years of follow-up ~a Multicenter Registry Study ~

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Conflict of interest: None

[Objectives] To evaluate the efficacy of Abatacept (ABT) for suppressing the radiographic progression of RA cervical lesions comparison with methotrexate (MTX) for 2 years. [Methods] We used ABT and MTX for treating each 60 and 75 Japanese patients with active RA for at least 3 years. For evaluation of cervical lesions ADI, SAC and the Ranawat value were measured at initiation and Year 1, 2. [Results] In the patients receiving ABT (n=60) and MTX (n = 75), the mean age was 67.7 vs 63.6 years old (p=0.004), disease duration was 16.7 vs 8.0 years (p<0.001). The numbers of patients who did not showed progression in all three parameters were each 42 cases (70%) receiving MTX and 43 cases (57%) receiving ABT (p=0.130) after 3 years. The respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.20 vs 0.27mm (p=0.367), SAC: -0.12 vs -0.17mm (p=0.359) and Ranawat value: -0.15 vs -0.13mm (p=0.783). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.35 vs 0.71mm (p=0.099), SAC: -0.25 vs -0.63mm (p=0.047) and Ranawat value: -0.23 vs -0.44mm (p=0.293). [Conclusions] This study suggested that ABT treatment can be used to suppress the progression of RA cervical lesions.

P2-054

Usability of abatacept in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] In the cases of eldery Rheumatiod Arthritis (RA) patients, Abatacept is often selected by clinician. Purpose of this study is to investigate the usability of Abatacept in elderly RA patients. [Methods] Among patients who were treated with Abatacept, 49 patients were available for this study, and divided to less than 75 years old (N group: 22 cases) and the others (E group: 27 cases) The clinical effectiveness, side effects, continuation rate, were evaluated separately. [Results] The mean follow-up period was 19.8 months in Group N and 18.5 months in Group E. In both groups, DAS (disease activity score) 28-CRP and MMP (Matrix metalloproteinase) -3 were significantly decreased at the final observation compared with the baseline. There was no significant difference between the two groups at the baseline, 3 months, 6 months, 1 year, 2 years after the start of administration, and DAS28CRP, MMP-3, and continuation rate at the last observation. One patient in group N switched from Abatacept to another biologics because of stomatitis. One patient had pneumonia in both group, and thrombocytopenia in group E. [Conclusions] Even in elderly people, the same usability as non-elderly patients was confirmed.

P2-055

Clinical evaluation of Abatacept case (responder/non-responder, bio-free cases)

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Conflict of interest: None

[Objective] To find predictive factors as better responders to abatacept (ABT), a retrospective clinical analysis was carried out in patient with rheumatoid arthritis (RA) treated at our clinic. [Methods] Medical records of thirty four RA patients who had been prescribed ABT since 2013, were analyzed for patients background, disease activity (CDAI) at 0, 12, 24, 52 weeks response to ABT. [Results] Ratio of ACPA positive was 88%, and 59% of patient were not using MTX. The continuation rate of ABT was 82% at 24wks, and 71% at 52 weeks, MTX using group has achieved quicker and deeper remission with ABT. EULAR good/poor response at 12 weeks didn't point out difference in ACPA positive nor MTX use. Two cases had bio-free remission after 52weeks. Both were similar characteristics such as relatively young, shorter disease duration, MTX use, no steroid history, bio naïve. There were three drop out with adverse effect (AE), but there was no severe AE. [Conclusions] ABT was effective and safe even without MTX use, however had slower response than with MTX use.

P2-056

A case of relapse of interstitial pneumonia caused by Abatacept

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Conflict of interest: None

[Case] A 75-year-old male. In September X-2, pain in both shoulders appeared. In March X-1, he visited a clinic and was diagnosed with rheumatoid arthritis according to 2010 Rheumatoid arthritis classification criteria. RF42IU/mL ACPA (-)CRP 1.37mg/dL eGFR 41.2ml/min. KL-6 2324U/mL. He visited our hospital as a patient with rheumatoid arthritis with interstitial pneumonia and chronic renal failure. January X We treated him with Abatacept. KL-6 756IU/mL. The joint symptoms disappeared after 4months. Although there were no symptoms such as cough and respiratory distress, KL-6 2292 IU/mL increased rapidly and chest CT showed an exacerbation of the interstitial shadow. [Consideration] Interstitial lung diseases are among the most serious complications associated with systemic rheumatic diseases. bDMARDs are considered effective for elderly patients with rheumatoid arthritis, while all bDMARDs have been reported to cause or exacerbate interstitial pneumonia. In particular, treatment with abatacept, which has been reported to be useful, has exacerbated interstitial pneumonia. [Conclusion] We also need to be careful in the treatment of rheumatoid arthritis patients with interstitial pneumonia with biologics.

P2-057

A case of refractory rheumatoid vasculitis successfully treated by abatacept

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Conflict of interest: None

We report a case of rheumatoid vasculitis (RV) refractory to corticosteroids with tocilizumab (TCZ) and cyclophosphamide but successfully treated by abatacept. A 68-year-old man was diagnosed with rheumatoid arthritis (RA) with interstitial pneumonia 3 years before admission to our hospital. Despite of the potent treatment including prednisolone (PSL) 14mg, salazosulfapyridine 1000mg, and TCZ, his symptoms was not controlled. He then developed multiple lower leg ulcers and he was admitted to our hospital. His blood test showed high titer of rheumatoid factor and hypocomplementemia. Although cutaneous biopsy from his left leg could not reveal vasculitis, we diagnosed him as RV. His skin and joint symptoms and laboratory findings were initially improved by PSL 40mg but relapsed just after tapering to 30mg. We re-started TCZ and gradually tapered PSL to 15mg. But his RV was aggravated despite additional 3 courses of cyclophosphamide pulse therapy. We administrated abatacept, after 2 courses of plasma exchange, which immediately improved his skin and joint symptoms, and also gradually improved laboratory findings. The efficacy of abatacept in RV has been reported in a few case reports. Our case also suggests that abatacept is effective therapeutic option for refractory RV.

P2-058

Immuno-phenotypic Analysis of Peripheral Blood Mononuclear Cells in Rheumatoid Arthritis Patients Treated with E6011

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Conflict of interest: Yes

[Objective] Fractalkine (FKN) and its solo receptor CX3CR1 are deeply involved in the pathogenesis of rheumatoid arthritis (RA). E6011, a novel humanized FKN monoclonal antibody, suppress the migration and invasion of CX3CR1-positive cells. In this study, immunophenotyping analysis of peripheral blood before and after E6011 administration was conducted to search for E6011 pharmacodynamic markers in a phase II clinical trial in RA. [Methods] The change of peripheral CX3CR1+ immune cell was evaluated in 190 Japanese RA patients with inadequate response to Methotrexate by flow cytometry (FCM). FCM analyses were conducted within 30 hours after the blood collection by standardized method. [Results] During the E6011 treatment, the proportion of $CD16^+$ monocytes, which highly express CX3CR1 within monocytes, significantly decreased from the baseline value at 2 week after initial treatment (E6011: $p < 0.001$, placebo: $p = 0.48$) and it was sustained up to 24 week. [Conclusions] E6011 significantly decreased the proportion of $CD16^+$ monocytes in whole monocytes. CD16+ monocytes might be a sensitive marker of E6011 in peripheral blood.

P2-059

Establishment of flow cytometry-based method to measure CX-3CR1-expressing cells in human peripheral blood

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Conflict of interest: None

[Objective] E6011, a novel anti-Fractalkine (FKN) monoclonal antibody, is under clinical development in rheumatoid arthritis. To monitor the changes in CX3CR1 (FKN receptor)-expressing cells, the flow cytometry (FCM) analysis had been planned using peripheral blood samples sent from multiple facilities in phase II clinical trial. The aim of this study was to establish the stable FCM method to measure $CX3CR1^+$ immune cells by overcoming the fragility of monocytes and the instability of surface markers. [Methods] Blood samples were collected into fixative tubes (Cyto-Chex Tube, Streck), stained with antibodies and measured using flow cytometer (CantoII, BD). Regarding fourteen cell populations including monocytes, NK cells, $CD8^+$ T cells and $CD4^+$ T cells and their frequency of $CX3CR1^+$ cells, simultaneous reproducibility test, stability test, reproducibility test between devices and reproducibility test between operators were conducted. [Results] All evaluation items of monocytes met the criteria within 30 hours after blood collection. In addition, almost all lymphocyte subsets passed the evaluation criteria. [Conclusions] We established the FCM method to reproducibly measure $CX3CR1^+$ immune cells including monocytes by measuring within 30 hours using fixed cells.

P2-060

Comparison of clinical course between young-onset and elderly-onset rheumatoid arthritis

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Conflict of interest: None

[Objective] With population aging of this country, the elderly-onset rheumatoid arthritis (EORA) to develop at advanced age newly increases. The aim of this study is to assess a clinical course in EORA. [Methods] The patients with RA who visited our institution by January, 2019 from April, 2014, nd were treated with antirheumatic drugs more than six months, were divided into two groups of under 65 years old onset RA (YORA) group and the EORA group. We assessed about a patient background, the antirheumatic drug use situation, and a clinical course. [Results] Methotrexate (MTX) was a low dose in a mean maximum dose through the clinical course and the mean last dose in the EORA group than YORA group. But, as for the introduction rate and the continuation rate of MTX and biological DMARDs, there was no significant difference between both groups. About the disease activity at the time of the last follow-up, there is no significant difference in the remission achievement rate between both groups in DAS28-CRP, SDAI and CDAI. [Conclusions] The possibility that even elderly-onset rheumatoid arthritis could practice Treat to Target and Tight control like young-onset rheumatoid arthritis treatment was suggested.

P2-061

Investigation of treatment and disease status in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] In recent years, elderly population is increasing in patient with rheumatoid arthritis (RA). We investigated the disease activity and medication in elderly patients with RA. [Methods] A total of 530 patients with RA were investigated about disease activity and medication. [Results] Patients with use of methotrexate and biologics were significantly decreased according to the age. DAS28 remission rate was significantly reduced according to the age. [Conclusions] Elderly patients with RA were not well-controlled compared with younger population.

P2-062

Characteristics and treatment of elderly-onset rheumatoid arthritis (EORA)

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Conflict of interest: None

[Objective] We investigated the characteristics of elderly-onset rheumatoid arthritis (EORA) [Methods] 35 patients over 75 years old who were diagnosed with EORA from 2012 to 2018 were included. We investigated the treatment at the first and at the last observation (2 years at the most). [Results] The mean age of onset was 80.3 years and the mean age at diagnosis was 81.3 years. The primary symptoms were 13 at large joints (37.1%), 19 at small joints (54.3%), 2 others. The mean DAS28 (ESR) at the first time was 4.31. The positive rate of RF and ACPA were 62.9%, 60%, respectively. The number of patients with DAS28 (ESR) less than 3.2 increased from 18.2% at the first time to 72.7% at the last observation ($P < 0.05$). MTX, PSL and Bio were introduced into 8 (22.9%), 15 (42.9%) and 3 (8.6%) patients at the first time, respectively. At the last observation, MTX, PSL and Bio were taken in 9 (25.7%), 15 (42.9%), and 7 (20.0%) patients, respectively. [Conclusions] Similar to the previous reports, our results showed the high rates of male sex, and primary symptoms with large joints. The rate of patients who were DAS28 (ESR) less than 3.2 at the last observation was significantly improved to 72.7%. Compared with MTX and PSL, the use of Bio increased at the last observation.

P2-063

Clinical efficacy and safety of sarilumab at 24 weeks in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] We examined the clinical effects of sarilumab (SAR), changes in laboratory data, drug continuation rate, and safety in patients with rheumatoid arthritis (RA). [Methods] The subjects were 26 RA patients who had received SAR (bio switching: 19 patients, highly active: 73%). With respect to the clinical effects of SAR, changes in the DAS28-CRP and SDAI from introduction until Week 24 were investigated. [Results] The mean age was 65.1 years. The mean disease duration was 9.5 years. The rate of MTX-treated patients was 56% (mean doses of MTX were 6.7 mg/week). The DAS28-CRP and SDAI at the time of introduc-

tion were 4.94 and 31.3, respectively. Those in Weeks 4, 12, and 24 were 3.63/19.7, 2.94/14.5, and 3.07/14.8, respectively. At all points, the values were significantly lower than at the time of introduction. In Week 24, the DAS28-CRP remission rate was 31%, and the SDAI remission rate was 23%. There was a significant decrease in the neutrophil count after Week 12. The drug continuation rates in Weeks 24 were 47%. Adverse reactions, such as dermal responses in 3 patients, digestive symptoms in 1, and neutropenia in 1, required discontinuation. [Conclusion] In the RA patients, SAR therapy significantly reduced the disease activity 4 weeks after the start of administration.

P2-064

ORIGAMI study (Orencia Registry in Geographically Assembled Multicenter Investigation study), a 5-year observation of SC-abatacept (ABT) treatment for biologic-naïve RA patients

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Conflict of interest: Yes

[Objective] ORIGAMI study is a prospective observational study to evaluate the safety, effectiveness, and patient-reported outcomes of Japanese RA patients (pts) treated with ABT in a real-world setting. Here, we report pts' characteristics of the study. [Methods] A total of 325 pts from 64 facilities were enrolled (Jun 2016 to Oct 2018). Main inclusion criteria are RA pts who are biologic-naïve with csDMARDs-IR and SDAI moderate disease activity. [Results] A total of 299 pts were eligible for the analysis. The mean age was 67.1 years old and mean SDAI was 19.6. Proportions of pts with disease durations of <2, 2-10, and ≧10 years were 40.1%, 30.8%, and 29.1%, respectively. Respiratory comorbidities, cardiovascular comorbidities and diabetes mellitus were found in 23.4%, 6.7%, and 11.4% of the pts, respectively. Methotrexate was used in 32.1% of the pts with a mean dose of 9.1±3.0 mg/week and prednisolone in 29.4% with 5.0±3.6 mg/day. ACPA and RF were positive in 83.9% and 72.6% of the pts, respectively. The scores (mean±SD) of J-HAQ, pain VAS, general VAS, and EQ-5D were 1.2±0.76, 47.0±24.3, 44.7±23.5, and 0.6±0.16, respectively. [Conclusion] We reported the pts' characteristics registered in ORIGAMI study, which represents RA pts treated with ABT in a real-world setting in Japan.

P2-065

Efficacy and safety of iguratimod as first-line disease-modifying antirheumatic drug therapy for patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We studied the efficacy and safety of iguratimod (IGU) when used as a first-line daily DMARD for patients with rheumatoid arthritis (RA), prospectively. [Methods] Patients with RA who took IGU as a first-line DMARD at Niigata Rheumatic Center between April 2016 and December 2018 (IGU group) were enrolled. There were no constraints regarding the addition or withdrawal of other DMARDs. The efficacy was evaluated at week 24. The IGU group's data were then compared with 64 patients who took salazosulfapyridine or bucillamine as first-line DMARD (other DMARD group). The data are expressed as median values. [Results] 43 patients (15 males, 28 females) received IGU as a first-line DMARD. The age was 69.0 years and the duration of disease was 2.0 months in IGU group. CDAI dropped from 20.0 to 5.00 with p<0.001. Patients who achieved EULAR moderate response at 24 weeks, included 90.7% in the IGU group versus 70.5% in the other DMARD group (Fisher`s exact test, p=0.046). The retention rate of the IGU was 83.7 %, roughly equivalent to the 81.2% retention rate in the other DMARD (Log-rank test, p=0.733). [Conclusions] Our study indicates IGU is safe and effective for DMARD naïve RA patients. Starting treatment with IGU might be a new and effective strategy for RA patients.

P2-066

Remission rate and treatment regimen at 6 months in patients with rheumatoid arthritis of routine practice

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Conflict of interest: None

[objectives] Remission has become a realistic goal in patients with rheumatoid arthritis (RA). However how many and which patients can achieve remission are not well known. [Methods] The patients with early RA who visited Department of Rheumatology, Suwa central Hospital from April 2015 to 2019 were included in this study. Inclusion criteria for eligible patients were age 18 years or older and DMARDs naïve at first visit. We conducted retrospective chart review to investigate remission rate at 6 mouths and treatment. [Results] 58 patients could be followed at one year. Baseline characteristics include mean age 61.0 years, female 60%, mean disease duration 44.0 weeks and mean DAS28-ESR 4.68. The DAS28-ESR remission (<2.6) rate at 6 months was 35.6%. Methotrexate (MTX), glucocorticoid (GC) and biologic agents were given to 70%, 30% and 5% patients at 6 months. The mean MTX and GC dosages were 12mg/week and 4mg/day at 6 months. [Conclusion] In routine practice, 36% of RA patients have achieved DAS28-ESR remission at 6 months.

P2-067

Development of a database system for a rheumatoid arthritis disease registry using optical character recognition (OCR)

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Conflict of interest: None

[Objective] To develop a rheumatic disease database, diverse information needs to be integrated. Nara Medical University has developed a system that recognizes questionnaire responses using OCR software for efficient database creation. We report the operation this system. [Methods] We designed two questionnaires: A "first visit sheet" and "follow-up sheet. " We set the name, character format, and digit number for each item in the OCR system. Before entering the consultation room, the patient fills in only the patient entry columns; the doctor makes inquiries while checking them. The completed questionnaire is sent to a medical office and scanned to create the database. We prepared a screen that allows to check whether data had been read correctly. The OCR system automatically determines reading accuracy, and shows it in four stages. This reduces burden on data managers. [Results] We registered 792 questionnaires. The OCR misrecognition rate was 0.67%; it was possible to operate with only a simple visual check. [Conclusions] It can easily accumulate highly accurate data. It can be used to manage the hospital's data, and also in multi-center research collaborations such as the ANSWER cohort. We also plan to use this system to detect and report changes in disease activity in our patients.

P2-069

Decreasing methotrexate dose after remission in case of rheumatoid arthritis patients who had MTX plus BIO: a clinical course observation

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Conflict of interest: Yes

[Objective] MTX is important as a first-line in treating RA. On the other hand, it is also important to reduce MTX to reduce side effect of MTX, especially lymphoproliferative disorder (LPD), but the timing to decrease of MTX is not known in present. In patients with rheumatoid arthritis (RA) that maintained remission by MTX plus Biologic DMARD

(BIO) and got their consent, the clinical course after decreasing MTX was evaluated respectively. [Methods] Subjects were 53 patients who had MTX plus BIO from March 2014 to October 2017. Baseline characteristics were Mean age 55.5 years, mean duration of illness 66.7months, mean use period of BIO 34.8 months. Changes in the remission rate of DAS28-ESR, SDAI, and CDAI at 104W were analyzed. [Results] But remission rate of DAS28-ESR, SDAI, and CDAI at 0W were 96.2%,98.1%,98.1%, and remission rate of DAS28-ESR, SDAI, and CDAI at 104W were 83.7%,87.8%,87.8%. The treatment goal is maintained in the majority of cases after decreasing methotrexate dose of MTX at 104W.14 of 53 patients relapsed due to MTX reduction or withdrawal. [Conclusions] This study shows the possibility that decreasing methotrexate dose after remission in case of rheumatoid arthritis patients who had MTX plus BIO might be a useful option after remission.

P2-070

Use experiences of Biologics and Jakinib of RA patients in our Hospital

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Conflict of interest: Yes

Objective: this study aimed to evaluate the effectiveness of Biologics and Jakinib in patients in daily clinical practice. Method: Data were collected retrospectively in 709 RA patients.709 cases were started in our Hospital from 2003 to 2017. Result: 1) 62% RA patients were started by TNFi.2) There were many switches between the TNFi at first. But the starts from non-TNFi and Jakinib gradually increased (38%). Now the use of the non-TNFi exceeds TNFi recently. 3) The cases that continued the first Bio was 25% of the whole. The patients of the remission and discontinuation was 14.7% of the whole. 4) The duration of median time in Bio and Jakinib uses of the first was approximately two years and four months. The duration of the second and thired Biologics and Jakinib use gradially decreased. Conclusion: The achievement of the RA treatment target with the first and/or second Biologis and Jakinib is extremely important.

P2-071

Background of the patients with rheumatoid arthritis who could continue biologics spacing

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the background of the patients with RA who could continue spacing of biologics. [Methods] Retrospectively we reviewed the background of the patients who could continue biologics spacing for at least three months and continuation rate. Spacing was defined as more than one and half of the standard interval. [Results] Sixteen patients (Average 60.6 years old, 6 male, 10 female) were included in this study. The average duration of illness was 7.0 years. The average period from the onset of RA to introduction of biologics was 3.7 years. MTX was used in 15 cases (average 6.3mg/ week) and it decreased to 11 cases (average 4.5mg/ week) before spacing. Abatacept in 4 cases, tocilizumab in 4 cases, adalimumab in 3 cases, etanercept in 2 cases, golimumab in 2 cases and infliximab in one case were used. Before spacing, the mean DAS28-CRP was 2.00. Average interval was one point eight times of the standard interval and the continuation rate was 93.8%. [Conclusions] The background of the patients who continued spacing was short duration of illness, biologics introduction at early stage of RA and dose reduction of MTX before spacing. It might be possible to choose the strategy of biologics spacing for these patients.

P2-072

Drug Free Period Analysis of Molecular targeting drugs by NDB Data

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Conflict of interest: None

[Objective] To analyze the drug free period of each molecular targeting drug by Japanese National Data Base (NDB) [Methods] We analyzed naive patients with RA during 7 years (since 2010 to 2017) in NDB data. [Results] Out of 63,472 naive patients who continued at least one year administration of a molecular targeting drug, 15,002 cases (23.6%) who ceased administration were analyzed in terms of drug free period by Kaplan-Meier method. Cease continuation rate after one, two, three years are 70.8, 61.7, 57.2% respectively. [Conclusions] The highest cease continuation rate is GLM (66.1% after two years) and the lowest is CZP (52.0%). One year cease continuation rate is 70% and 60% in two years on the average, and after two years the rate does not show big decresing.

P2-073

Evaluation the subcutaneous tocilizmab administered weekly in patients with rheumatoid arthritis

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Conflict of interest: None

We investigated the current status of cases in our hospital that received subcutaneous tocilizmab (TCZ-SC) 162mg weekly (qw). There were 91 patients who received TCZ from April to December 2018 at the Rheumatoid Collagen Center, and 11 of them received TCZ-SC qw. Ten cases were considered effective and TCZ was ongoing. One patient had a diminished effect and was changed to another drug. Of the 10 patients who were effective, 3 patients were able to obtain a sufficient effect and then returned to the 2-week interval, and the effect was maintained and there was no relapse. In addition, TCZ-SC qw improved arthritis, and in some cases it was possible to reduce MTX and PSL. No serious side effects were observed from the TCZ-SC qw and safety was confirmed. Although it is a result in our center in a limited period to the last, it was thought that it was worth trying the shortening of the administration interval before the bioswitch in the case where the effect was insufficient. In addition, there was a case where it was possible to return to an interval of 2 weeks after improvement was obtained by shortened administration, which seemed to be a point of attention in terms of patient burden. We also want to present the detailed course of some cases.

P2-074

About use experience of Sarilumab for the leukopenia patient in our clinic

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Conflict of interest: None

[Objective] IL-6 inhibitors are concerned about transient neutropenia due to their mechanism of action. In one report, the clinical concern of reduced neutrophils is an increased risk of infection, and Grade 4 neutropenia continues for more than 10 days and is associated with the frequency and severity of the infection. [Methods] Efficacy and safety will be evaluated by administering salilumab to lower WBC RA patients. [Results] Case 1, 53-year-old female Stage III, Class 2, 10 years of RA patient. The patient was treated with MTX 8mg / week. There was swelling of the right hand, and MRI revealed synovial proliferation. The patient was diagnosed with synovitis associated with RA. Since blood flow signals were confirmed by joint ultrasound and the disease activity was high, introduction of biologics was examined. Considering the risk of leukopenia after administration, the initial dose was 150 mg. WBC has been around 2500, but

there has been no fever or infection. In consideration of disease activity control, risk of cytopenia, and economics, salilumab was administered at 200 mg for 3 weeks, but the WBC did not change and the blood flow signal observed by joint US was also decreasing. [Conclusions] Sarilumab could be safely used while maintaining low disease activity.

P2-075

Study for adherence of patients with rheumatoid arthritis (RA) treated with Golimumab (GOL) in our hospital

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Conflict of interest: None

[Objective] We consider the ratio of the effective dose to the total dose of the 4-week interval GOL as the adherence. [Methods] Nineteen patients with rheumatoid arthritis have been treated with GOL during from October 2011 to October 2017. Of these, 13 patients were treated with continuous GOL for 2 years. 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 and compare it over two years. [Results] In GOL, MPR ≦ 80% is 1 case, 100% is 5 cases, and 92-96% is achieved in 7 cases. MTX combined with 10 cases, MPR ≦ 80% is 2 cases. MPR> 80% is 8 cases. DAS28CRP, remission (<2.3) 8 to 10 cases, low disease activity (LDA) (2.3-2.7) 3 to 2 cases, moderate disease activity (MDA) (2.7-4.1) 2 to 1 case over 2 years. One case of GOL MPR ≦ 80% changed from remission to LDA. Two cases of MTX MPR ≦ 80% changed from MDA to MDA and from LDA to remission. [Conclusions] MPR for GOL is good enough, disease activity is controlled.

P2-077

The clinical outcome of abatacept in patients with rheumatoid arthritis in our hospital

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of abatacept in patients with rheumatoid arthritis (RA). [Methods] Thirty-three RA patients (26 females and 6 males) who were administered with Abatacept were recruited. Pacients were divided to two groups. Elderly group was over 65 years old, young group was the other. We compared with these groups. Average age of elderly group was 70.1±3.14, of young group was 53.6±9.61. [Results] DAS28ESR of elderly group (before treatment 4.93±0.86 vs at 1 year 3.09±1.07) and young group (before treatment 5.10±1.39 vs at 1 year 3.26±0.80) are significantly dicreased used by abatacept. The retention rate in elderly group was 93.3% at 1 year, in young group was 72.2. However The retention rate were not significant difference compared with both groups. [Conclusions] Abatacept inproved the disease activity of rheumatoid arthritis significantly.

P2-078

Current status of Bio/JAK remission, Bio/JAK free in RA treatment in our hospital: From the NOSRAD registry

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Conflict of interest: None

[Objective] To investigate the current status of Bio/JAK remission, Bio/JAK free in RA treatment in our hospital. [Methods] A total of 1102 patients were introduced biologic agents (Bio) or JAK inhibiter (JAK) in our hospital between May 2001 and August 2019. (1) continuation example of remission (including extended administration interval), (2) Biological preparation discontinuation (Bio/JAK free) cases, (3) Bio/JAK free dropout cases, in the number of (each) cases under Bio/JAK enforcement, were investigated. [Results] 243 cases undertook Bio/JAK Among 202 cases that were possible to do DAS calculations, 121 patients were able to obtain DAS remission. (1) During DAS remission cases, 107 patients were continuing Bio/JAK, of which the dose was reduced or administration interval was prolonged was 43 cases. On the other hand, among the 202 possible DAS calculations, there were 81 cases who did not achieve DAS remission, 26 of them underwent dose reduction and/or administration interval extension. (2) In 14 cases of Bio/JAK free, the average period from remission to drug withdrawal was 1.1 years, and the average drug holiday period up to the present was 2.4 years. (3) In 6 cases where Bio/JAK free was dropped out, 5 cases resumed the same preparation, but it was dropped out early.

P2-079

Upadacitinib versus tocilizumab in Japanese patients with moderate to severe rheumatoid arthritis (RA): A matching-adjusted indirect comparison (MAIC)

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Conflict of interest: Yes

Objectives: To compare the efficacy of upadacitinib 15mg monotherapy (UPA) with tocilizumab 8mg/kg monotherapy (TCZ) in Japanese patients with moderate-to-severe rheumatoid arthritis (RA) and inadequate response to conventional synthetic DMARDs. **Methods:** The MAIC used individual patient data from the Japanese sub-population from SELECT-MONOTHERAPY trial of UPA vs. methotrexate (MTX) and published data from the Japanese SATORI trialof TCZ vs. MTX. Patients in the UPA trial were weighted based on age, gender, and baseline DAS28-ESR score to match the SATORI trial. After matching, ACR20/50/70 and DAS28-ESR at month 3 were compared using a Wald test. **Results:** After weighting, baseline characteristics were balanced across the SELECT-MONOTHERAPY and SATORI. Patients treated by UPA had significant improvements in ACR50 compared to TCZ with a mean difference in difference (DD) versus MTX of 36.3% (95% Confidence Interval: [10.8%, 61.7%], p=0.005). Additionally, UPA showed numerical improvements in ACR20 (DD: 14.5% [-17.6%, 46.6%], p=0.375 and DAS28-ESR (DD: -0.29 [-1.26, 0.68], p=0.556 and had similar rates of ACR70 (DD: 0.2% [-19.3%, 19.7%], p=0.983). **Conclusions:** UPA 15mg monotherapy was associated with improved ACR50 response compared to TCZ 8mg/kg monotherapy for Japanese RA patients.

P2-080

Treatment of rheumatoid arthritis with renal dysfunction

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Conflict of interest: None

[Objective] Methotrexate (MTX) is positioned as the first line in the treatment of rheumatoid arthritis (RA). However, the use of MTX in patients with renal dysfunction requires caution and is difficult to treat RA. Therefore, we investigated association with the treatment status of RA and renal function. [Methods] 302 RA cases were classified into a group with compromise in renal function (group A) and a group with normal renal function (group B). Less than 60 eGFR is classified into the group A. Age,

treatment, and DAS28-ESR were compared for both groups. [Results] In group A / group B, the number of cases was 71/231, the mean age was 71.3 / 60.8, PSL combination was 28.2% / 26.3%, PSL dose was 5.9mg / 3.7mg, MTX combination was 47.9% / 71.1%, MTX dose was 9.0 mg / 9.5 mg, the combination rate of the biological DMARDs and JAK inhibitor was 36.6% / 32.8%, and the average DAS28-ESR was 3.50 / 3.04. In Group A, the proportion of TNF inhibitors was low and the proportion of Abatacept was high, the combination rate of iguratimod was high, and tacrolimus and salazosulfapyridine were equivalent. [Conclusions] RA with renal dysfunction, the MTX combination rate was significantly lower and the disease activity is higher.

P2-081

Effects of duloxetine for the relief of remnant pain of rheumatoid arthritis patient whose disease activity is remission

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Conflict of interest: None

[Objective] Pain control in rheumatoid arthritis (RA) patient is important. When pain remains even disease activity is remission, it causes deterioration of activity in daily living (ADL). Effects of duloxetine for remnant pain relief in such situation was statistically evaluated. [Methods] RA patients whose pain score with visual analog scale (PS-VAS) >30mm despite Clinical Disease Activity Score (CDAI) is <2.8, were picked up for the study. PS-VAS, CDAI, modified Health Assessment Questionnaire (mHAQ), and QOL value, at the initiation of duloxetine and at week 12 were compared with One sample T-test. Statistical significance was set less than 1%. [Results] Sixty-eight patients of 18 male and 50 female were recruited with 71.3 years of mean age, 53.6 months for time span from baseline to initiation. 80.8% of the patients sustained. Patient's global assessment (PGA) was 0.6, while the other component of CDAI were below 0.3 in average, while PS-VAS was 40.5. At week 12 when compared to baseline, CDAI was elevated significantly, however, PS-VAS and mHAQ decreased significantly. QOL value decreased with no statistical significance. [Conclusions] Duloxetine has been suggested to have effectiveness for the pain relief, for improvement of ADL, and for the contribution to QOL maintenance.

P2-082

The Relationship between Achievement Rates of Drug-Free Remission and Rates of Reduction in Rheumatoid Factor

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Conflict of interest: None

[Objective] This study examines the relationship between the "rates of Drug free remission (DFR) and relapse rates of Rheumatoid Arthritis (RA)" and the "Rheumatoid Factor (RF). " [Methods] 55 Patients treated with the Matsui method were categorized into the following three groups: (1) patients with negative RF prior to treatment, (2) patients with positive RF prior to treatment, which decreased to the normal range before the discontinuation of drug treatment, and (3) patients with positive RF prior to treatment and whose RF continues to persist at a high value at the discontinuation of drug treatment. The respective "rates of failure to achieve DFR" and "relapse rates of RA" for these 3 groups of patients were examined. [Results] Among the 17 cases in group (1), 1 case (6%) failed to achieve DFR, and there were no cases (0%) of relapse in the remaining 16 cases. Among the 24 cases in group (2), 2 cases (8%) failed to achieve DFR, and there were 4 cases (18%) of relapse in the remaining 22 cases. Among the 14 cases in group (3), 3 cases (21%) failed to achieve DFR, and there were 6 cases (55%) of relapse in the remaining 11 cases. [Conclusions] It can be concluded that there is a strong correlation between negative RF values and the achievement of DFR.

P2-083

Efficacy of Baricitinib in elderly rheumatoid arthritis patients

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Conflict of interest: None

[Objective] To investigate the efficacy of baricitinib in elderly rheumatoid arthritis patients. [Methods] 8 rheumatoid arthritis patients whom age were 65 and older, treated with baricitinib from September 2017 and could follow more than 24 weeks were recruited. Efficacy in disease activity scores and adverse events were investigated. [Results] There were 3 men and 5 women. Mean age was 76.5±6.8 years old, and mean disease duration 7.0±12.8 years. Concomitant prednisolones was used in 3 patients. Mean DAS28-CRP were, baseline: 4.66±1.34, after 4 weeks: 2.52±1.45, after 12 weeks: 2.34±1.04, after 24 weeks: 1.92±1.07, which improved from baseline rapidly. No patients had herpes zoster. Two patients canceled baricitinib treatment for upper respiratory tract infection. [Conclusions] Baricitinib in elderly rheumatoid arthritis patients is effective.

P2-084

Treatment for rheumatoid arthritis using 2 mg baricitinib in patients with normal renal function: clinical cases

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Conflict of interest: None

[Objective] Analysis of the effectiveness of the half dosage of Baricitinib (BAR) for the rheumatoid arthritis (RA) patients with normal renal function. [Methods] Herein we report cases of RA patients with a normal renal function in which a dose reduction to 2 mg is necessary for economic reasons. [Results] The total number of cases was 17, mean age was 57.5 years, mean disease duration was 12.6 years, and mean eGFR was 90.8 mL/min/1.73 m^2. The mean CDAI score was 19.3 at the start of BAR treatment. The changes in CDAI scores after starting BAR treatment were 9.5, 7.8, 8.3, 8.5, 8.8, and 7.3 at 2, 4, 8, 12, 16, and 24 weeks. The outcomes at 24 weeks were as follows: resolution of symptoms and discontinuation of BAR in one case, remission in three, low disease activity in six, moderate disease activity in two, discontinued use due to adverse event in one, termination due to ineffectiveness in zero, dose increase to 4 mg in one, and dropout in three. In 10 of 14 cases (71.4%), excluding dropout cases, disease activity was below the level of low disease activity. [Conclusions] Treatment with half-dose BAR administration can be an option for RA patients with a normal renal function in cases where normal dose BAR administration is difficult due to conditions such as economic situations.

P2-085

A comparison of the clinical courses between tofacitinib and baricitinib in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To compare the clinical courses between tofacitinib (TOF) and baricitinib (BAR) in patients with rheumatoid arthritis (RA). [Method] RA patients treated with TOF (43 cases) or BAR (26 cases) at Tama-Hokubu Medical Center and Tama Medical Center until March 2019 were included. We conducted a 52 weeks-retrospective observational study. [Result] The patient's backgrounds at baseline were similar in the TOF group and the BAR group; age (TOF 59.1, BAR 65.0 years old), disease duration (13.4, 9.3 years), rheumatoid factor positivity (76.7, 84.0%), anti-CCP antibody positivity (86.0, 98.6%), MTX combination (81.4, 69.2%), MTX dosage (9.1, 9.7 mg/week), glucocorticoid combination (57.1, 57.7%), past administration of biologic DMARDs (88.4, 88.5%), the number of bDMARDs (2.7 and 2.8) and the disease activity score 28-CRP (DAS28-CRP, 4.07, 3.84). The 24 weeks and 52 weeks-retention rates were 78.7% and 55.6% for the TOF group, 78.9% and 57.9% for the BAR group.

While the 24 weeks-DAS28-CRP remission rate was significantly higher in the BAR group (TOF 18.6, BAR 46.2%, p = 0.015), the 52 weeks-remission rate was similar in the two groups (25.0, 36.8%, p = 0.358). [Conclusion] TOF and BAR were comparable in the critical courses of patients with RA at week 52.

P2-086

Effect of Baricitinib in rheumatoid arthritis with psoriasis-like eruption after administration of biologics

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Conflict of interest: Yes

Case 1. A woman in her 70s visited our hospital due to intractable rheumatoid arthritis (RA) of 6 years history. Her disease went into remission by abatacept. However, skin rashes appeared on the extremities and trunk, and at the same time, RA exacerbated. A skin biopsy revealed a psoriasis-like lesion. Soon after abatacept was discontinued and baricitinib (BAR) 4mg was started, the rash disappeared and RA improved immediately. Case 2. A woman in her 60s developed RA with positive ACPA, RF, and anti-SS-A antibody. Abatacept was discontinued due to liver damage and skin eruption, and golimumab was also discontinued due to liver damage. In 2014, two months after the start of certolizumab pegol, skin eruption appeared on the extremities and back, and skin biopsy showed psoriasis-like lesion. It remained in the right elbow long after that. In 2018, BAR was administered because of a flare of her RA that resulted in the remission of arthritis as well as skin lesion immediately. It has been shown that type I interferon activity is elevated in secondary ineffectiveness of biologics and the development of biologics-induced psoriasis-like rash. It was considered that BAR showed a prompt effect on both RA and skin lesion by suppressing type I interferon signals by inhibiting Jak1.

P2-087

Efficacy and safety of 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 (2mg) 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 24 weeks were included in this study. We retrospectively reviewed the efficacy (DAS28-CRP), discontinuation of BAR therapy and adverse event in one-half dose (2mg group) and typical dose (4mg group), respectively. [Results] Six (2mg group) and seven (4mg group) patients were included in this study. Mean age was 70 and 68 years old and concomitant methotrexate rates are 50% and 100% (2mg and 4mg groups, respectively). Mean DAS28-CRP was 4.0 and 3.7 at baseline, and 1.4 and 1.6 at 24 weeks (2mg and 4mg groups, respectively). The number of patients who withdrew from BAR was one (2mg group) and two (4mg group). Serious adverse event is none in two groups. [Conclusion] Typical dose (4mg) but also one-half dose (2mg) 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.

P2-088

Efficacy of Baricitinib in rheumatoid arhtritis 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 24 weeks were recruited. Efficacy in disease activity scores and adverse events were investigated. [Results] There were 4 men and 14 women. Mean age was 61.1±17.1 years old, and mean disease duration 8.3±10.3 years. Mean DAS28-CRP were, baseline: 3.67±1.44, after 4 weeks: 2.25±1.14, after 12 weeks: 2.34±0.97, after 24 weeks: 2.24±1.21, which improved from baseline significantly. One patient had herpes zoster, resumed baricitinib treatment. Two patients canceled baricitinib treatment for upper respiratory tract infection. [Conclusions] Baricitinib was effective in rheumatoid arthritis treatment.

P2-089

Clinical efficacy and safety of baricitinib for patients with rheumatoid arthritis -Multicenter study-

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Conflict of interest: None

[Objective] We clarified the differences in the clinical efficacy, predictive+factors and safety of patients with rheumatoid arthritis (RA). [Methods] We investigated 79 cases of BAR newly introduced in RA patients in 3 institutions. We analyzed clinical effects and safty after 4, 12 and 24 weeks post-treatment and treatment predictors. [Results] Improvement in DAS28-CRP was observed during the entire observation period (e.g. 24 weeks: BAR: $\Delta 2.06 \pm 2.99$, $p < 0.01$). In the BAR group, the higher the anti-CCP antibody level was, the better the improvement of DAS28-CRP was observed ($p = 0.04$). [Conclusion] BAR may be effective in RA patients with high CCP antibody levels.

P2-090

Successful treatment of refractory diffuse non-scarring alopecia in systemic lupus erythematosus using baricitinib

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Conflict of interest: None

To our knowledge, the efficacy of JAK inhibitors for treating alopecia in SLE is unknown. Herein, we describe a patient with SLE who experienced substantial improvement of diffuse nonscarring alopecia following baricitinib therapy. The patient was a 27-year-old woman diagnosed with SLE at age 21, requiring prednisolone (PSL) and tacrolimus treatment. SLE disease activity had been stable after remission but relapsed at the age of 26 years (PSL 3.0 mg and hydroxychloroquine 200 mg). Along with the relapse of serum markers and proteinuria, chilblain lupus erythematosus and diffuse hair loss developed. The PSL dose was increased to 17.5 mg and mycophenolate mofetil 1500 mg was initiated. Renal involvement and serum markers improved, but skin lesions progressed. When PSL was increased to 40 mg after steroid pulse therapy, the chilblain lupus erythematosus improved but the hair loss progressed. Therefore, she was referred to our hospital at age 27 years. We introduced baricitinib 4 mg along with combination therapy with PSL and mycophenolate mofetil. Surprisingly, no progression of hair loss was observed after 4 weeks of treatment, and prominent hair regrowth was observed after 8 weeks. At 12 weeks, the PSL dose was gradually reduced to 12.5 mg, and no lesions relapsed.

P2-091

Efficacy of Chronotherapy using Baricitinib in collagen-induced arthritis mice

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Conflict of interest: None

[Objective] Diurnal variations are observed in symptoms and cytokine productions of rheumatoid arthritis, and serum cytokine concentrations of CIA mice is reported to increase under light condition. By using chronotherapy, differences in drug efficacies according to administration time of Baricitinib, a wide ranged cytokine blocker, were examined in CIA mice. [Methods] CIA mice were administered a dose of 3 mg/kg of Baricitinib once a day at zeitgeber time (ZT) 0 or ZT12 for 21 days. Phosphorylation of STAT3 in liver, expressions of IL-1β/IL-6/IL-17A/TNF/IFNγ/GM-CSF in spleen, and IL-6 and TNFα in sera were measured. Arthritis scores and histopathology were also examined. [Results] Arthritis scores of treated groups decreased from day3 as compared to untreated mice, and those of ZT0 group decreased as compared to ZT12 group from day12. In CIA mice, phosphorylated STAT3 represented diurnal variation. At ZT2, expressions of IL-6/IFNγ/TNF/GM-CSF in ZT0 group were decreased as compared to untreated mice. In ZT0 group, IL-6 and TNFα in sera were decreased for longer time than that in ZT12 group. Pathological findings and immunohistochemistry of cytokines well reflected results of arthritis scores. [Conclusions] Chronotherapy targeting cytokine secretions is effective in CIA mice.

P2-092

Drug retention rate, efficacy and safety of tofacitinib for twenty-four months in daily use for patients with rheumatoid arthritis. A single-center observational study

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Conflict of interest: None

[Objective] To evaluate the retention rate, efficacy and safety profile of tofacitinib (TOF) in patients with rheumatoid arthritis (RA) for daily use. [Methods] 130 patients were initiated with TOF from 2014 to 2018. Drug retention rate and clinical disease activity indicated by composite measures as well as adverse events (AEs) were evaluated. [Results] Baseline characteristics were as follows: age 65.2 y, female 81.5%, prior bDMARD use 49 (45.4%), concomitant of MTX 68.5% (8.5 mg/week) and concomitant of PSL 48.5% (4.7 mg/day). 49 treatment courses (37.7%) were stopped, with 19 (14.6%) due to inefficacy, 28 (21.5%) due to AEs and 2 (1.5%) due to remission. DAS28-ESR significantly decreased from 5.08 ± 1.36 at baseline to 4.07 ± 1.20 at 1 months, 3.85 ± 1.27 at 6 months, and 3.90 ± 1.21 at 24 months ($p < 0.01$, vs. baseline). 58 AEs including 16 herpes zoster (H-Z) infection occurred during tofacitinib treatment. All patients were stopped to treat with tofacitinib during anti-viral therapy and without one patient could restart after recovery. [Conclusions] Tofacitinib used in clinical practice was effective to active RA patients. Discontinuation of tofacitinib due to toxic adverse event was seemed in 21.5% of patients, but due to H-Z infection were in one patient.

P2-094

Safety and efficacy of tofacitinib for patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate the real-world safety and efficacy of tofacitinib in patients with rheumatoid arthritis (RA). [Methods] We enrolled 87 patients with RA who were administered tofacitinib and observed for more than 1 year. The mean age was 70.6 years old and the mean disease duration of RA was 14.1 years. Forty-five patients (51.7%) started at dose of tofacitinib 5mg. Thirty-one patients (35.6%) received concomitant MTX. We compared differences of the retention rate in the starting doses of tofacitinib, with or without concomitant MTX and in ages of patients. [Results] Forty-four patients withdrew from tofacitinib treatment during follow-up periods. Seventeen patients discontinued due to insufficient efficacy and 21 patients discontinued due to adverse events. The retention rate of tofacitinib was 79.3% at 1 year, 52.0% at 3 years and 45.0% at 5 years. The retention rate of tofacitinib 10mg was significantly higher than that of tofacitinib 5mg. However, there were no significant differences with or without concomitant MTX and in ages of patients. [Conclusion] Our results suggested that tofacitinib monotherapy might be useful for elderly patients with RA.

P2-095

Effects of Tofacitinib suppressed pulmonary vascular remodeling of allergic vasculitis in a murine model

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Conflict of interest: None

[Objective] We examined the effects of tofacitinib on vascular remodeling-including intraluminal myofibroblast proliferation-in a murine model of allergic vasculitis with eosinophil infiltration. [Methods] We exposed C57BL/6 mice to OVA and alum. We administered tofacitinib (0.1 g/kg) intraperitoneally to the Tofacitinib treated group of mice in parallel with daily exposure to aerosolized OVA for 7 days. We determined cell differentials and measured concentrations of IL-4, IL-5, IL-6, IL-13, and TGF-β in the BALF. We conducted semi-quantitative analysis of pathological changes in the pulmonary arteries according to the severity of vasculitis. [Results] In mice treated with tofacitinib, the number of eosinophils in the BALF was reduced significantly when compared with that of the positive control. The TGF-β concentration in the BALF of the tofacitinib-treated group was significantly decreased and intraluminal myofibroblasts in pulmonary arteries were reduced when compared with those of the positive control group. [Conclusions] By reducing eosinophil infiltration, and decreasing IL-4, IL-5, IL-6, IL-13, and TGF-β in the lung, tofacitinib suppressed pulmonary vascular remodeling in a murine model of allergic vasculitis with eosinophil infiltration.

P2-096

Intraoperative fracture during navigated total knee arthroplasty for rheumatoid arthritis

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Conflict of interest: None

[Objective] The aim of this study was to report 4 patients with rheumatoid arthritis (RA) who sustained intraoperative fracture during navigated total knee arthroplasty (TKA). [Methods] We reviewed 118 navigated TKAs for RA and identified 4 patients with 4 intraoperative fractures (3.4%). There were 1 man and 3 women with a mean age of 61 years. Fractures located in 3 femoral lateral condyles and 1 tibial medial condyle. Two fractures occurred during femoral trialing and one during tibial bone preparation, and one was identified on the radiographs 2 weeks after the operation. Three fractures were fixed with cannulated screws and 1 was treated conservatively. The mean follow-up was 3.25 years. [Results] All fractures healed clinically and radiographically. The mean Japan Orthopaedic Association (JOA) score improved from 50 preoperatively to 88 at the final follow-up. The surgical instruments were related with the fracture location. There was no fracture at the site of insertion of the navigation tracker. [Conclusions] During the same period, 732 TKAs were performed for osteoarthritis (OA) and 5 intraoperative fractures occurred (0.68%). Intraoperative fracture was 5 times more likely to occur in patients with RA than those with OA. Careful operative technique is necessary in TKA

for RA.

P2-097

Study of femoral fracture after THA and TKA in the same limb in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] When a fracture occurs after THA and TKA, it may be difficult to treat. In this study, we analyzedfemoral fracturesafter ipsilateral THA and TKA with RA. [Methods] The subjects were 9cases after THA and TKA with RA on the same limb. Mean age was 69.6 years, mean BMI was 23.5. We investigated injury mechanism, duration of RA, use of bone cement, bone density, fracture site, treatment method, medicine for RA and osteoporosis, complications, and mobility. [Results] 8 cases werefell down, 1 traffic accident. RA'saverage duration was 19Y7M. 7 cases was used bone cement in THA and TKAcases wereall. The average BMD was 0.625 and the YAM 68.2. Fractureswere THA side,4 cases, TKA side, 1 case, and 4 cases wereintermediate. The RA treatment were1 biologic, 7 MTX, and 7 steroids. Osteoporosistreatment were 2 cases. There wasnocomplication. In mobilization,5 caseswere worse. [Conclusions] The femoral fracture after THA and TKA with RA is difficult to treat due to elderly, fragility, infectively and RA. In this study, there were no cases of infection or bone nonunion, but postoperative fall prevention and osteoporosis treatment seemed to be important.

P2-099

Knee osteoarthritis requiring TKA is worse than rheumatoid arthritis in RA disease activity

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) disease assessments have been created for RA patients and have not been validated for other diseases. Knee osteoarthritis (KOA) is a comorbid disorder with RA and contributes to ADL disability. The purpose of this study was to examine which of RA and KOA is worse in RA disease evaluation. [Methods] Thirty KOA patients hospitalized for total knee arthroplasty (TKA) and 30 RA patients with symptom of knee joint were included in this study. We compared RA disease activity score (DAS28-ESR, DAS28-CRP, CDAI and SDAI) and RA dysfunction (HAQ-DI) in both groups. [Results] Mean disease duration was 14.6 (1-41) years in RA patients. BIO was used in 14 cases. There was no significant difference in age (RA: 72.7, KOA: 75.3), gender and MMP-3 (RA: 97.5 ng. ml, KOA: 66 ng/ml). In the Kellgren-Lawrence classification, there were more severe cases in KOA. There was not significant difference in DAS28-ESR (RA: 3.16, KOA: 3.43), but KOA were significantly high in DAS28-CRP (RA: 2.61, KOA: 2.93), CDAI (RA: 8.74, KOA: 12.2), SDAI (RA: 8.99, KOA: 12.39) and HAQ-DI (RA: 0.58, OA: 0.95). [Conclusions] KOA patients hospitalized for TKA were worse than RA in RA disease activity and dysfunction. Elderly RA should determine the timing of TKA considering the presence of KOA to improve ADL.

P2-102

Short-term result of SQRUM TT for Rheumatoid arthritis patients

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Conflict of interest: None

[Objective] SQRUM TT acetabular shell is available from July, 2013 in Japan. Although the short-term results of this shell for Osteoarthritis (OA) patients has reported, the report of this shell for Rheumatoid arthritis (RA) patients has not still reported yet. [Methods] We collected 103 patients (OA: 77 cases, RA: 26 cases) and evaluated the initial gap by the plain radiograph of postoperative 1 week and whether the gap disappeared at postoperative 1 year. [Results] One case experienced shell migration. Initial gap was observed in 61% (18.2% in zone 1, 36.4% in zone 2, 30% in zone3) of OA patients and 61.5% (30.8% in zone 1, 26.9% in zone 2, 38.5% in zone3) of RA patients. The gap was decreased to 9.1% (1.3% in zone 1, 6.5% in zone 2 and 3.9% in zone3) in OA patients and 23% (3.8% in zone 1, 11.5% in zone 2 and 11.5% in zone3) in RA patients by the postoperative 1 year radiograph. [Conclusions] SQRUM TT shell has 3D porous structure and anticipated to rigid initial stability. The case that we experienced shell migration had acetabular bone defect and was placed allograft bone to the defect. Initial gap was most frequently observed in zone 2 by OA patients, but zone 1 and zone 3 by RA patients.

P2-104

Bicruciate-retaining total knee arthroplasty for rheumatoid arthritis patient. -2 case report-

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Conflict of interest: None

[Objective] Traditionally, anterior or both cruciate ligaments are sacrificed when total knee arhtroplasty is performed for cases with rheumatoid arthritis (RA). Recently reintroduced bicruciate-retaining total knee arhroplasty is expected to restore native knee function by preserving both cruciate ligament. In this paper we report 2 cases of BCR TKA on RA patients. [Methods] Well controlled RA pateints were included in this seriese. Image free navigation system was used for surgery. Bone resection was performed using measured resection technique. Range of motion (ROM), quadriceps strength and 2011 Knee Society Score were recorded before and 1 year after surgery. [Results] Case1: 68 y.o. male. ROM improved -5/135° to 0/135°, and 2011KSS (symptom, satisfaction, expectation, function) improved 4, 14, 13, 11 to 23, 38, 9, 81. Case2: 64 y.o. female. ROM became 0/135° to 0/130°, 2011KSS improved 3, 16, 15, 43 to 21, 24, 9, 68. [Conclusions] BCR TKA for RA patients achieved favoroble patient reported outcome at 1 year. Closer function to the native knee is expected by preserving both cruciate ligaments.

P2-105

Total Hip Arthroplasty after Twenty-five Years Aseptic Femoral Head Necrosis Treated by Iliac Bone Graft in Systemic Lupus Erythematosus

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Conflict of interest: None

[Objective] A Vascularized pedicle iliac bone graft was performed because of ION after steroid treatment for SLE, but a total hip arthroplasty (THA) was performed 25 years after surgery due to worsening osteoarthritis. [Case] 49-year-old female, SLE developed at the age of 19, and treatment with steroids resulted in necrosis of the femoral head at the age of 24 years. After that, the course was good, but the gait disturbance occurred due to left hip pain for several years. She had left hand arthritis two years ago. Prednisolone 5 mg and 7.5 mg every other day, cyclophosphamide 100 mg, hydroxychloroquine 200 mg, methotrexate 6 mg. There was a range of motion restriction of the left hip joint and a difference in leg length of the left lower limb. C3 58mg / dl, C4 14.0mg / dl, CH50 21U / ml, anti-ds-DNA antibody 18.3IU / ml [Image findings] Left hip joint space loss and femoral head flattening were observed. [Surgery] The left hip joint was deployed in a posterior lateral approach using navigation, and after placing the acetabular component, autologous bone transplantation was performed above to correct the leg length. It is possible to walk alone by postoperative rehabilitation. [Results and Conclusion] The course is good and can be walked alone.

P2-106

Significantly higher frequency in patients with axial spondyloarthritis (axial-SpA) HLA-B54, 61, 46

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Conflict of interest: None

[Objective] The HLA class I gene of axial-SpA patients diagnosed by rheumatologists in our hospital was investigated. [Method] From 2/2015 to 9/2019, for 110 patients who were classified as axial-SpA using ASAS classification criteria by clinical symptoms and imaging findings including MRI, obtained the consent of patients HLA-B typing was performed using PCR-rSSO method. [Results] There were 31 cases of men and 79 women classified as axial-SpA. B27 is 5 cases, allyl became positive in 10 or more cases B61 is 39 cases, B54 is 28 cases, B51 is 23 cases, B7 and B46 each 16 cases, B35 and B60 each 14 cases, B62 13 cases, B52 was 11 cases. As a result of testing the positive rate of allyl using the Chi-square test with the general Japanese of HLA laboratory, significant difference was observed in B61, B54, B46. (B61: p.0075, B54: p.0015, B46: p.0460). [Consideration] HLA-B61 has been reported to be strongly associated with AS and other SpA in the world. B54 and rheumatic patients associated with silicosis in Japan, Buerger's disease, the association with type 1 diabetes is known. B46 in PsA patients of the Japanese, is considered a risk factor for severe sacroiliac arthritis. Our findings suggest that HLA-B54, 61, 46 can be a risk factor in the expression of Axial-SpA.

P2-107

A case of ulcerative colitis complicated with IL17 inhibitor therapy

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Conflict of interest: None

A 74-year-old female came to my department of our hospital, because of lumbago and axial motor disturbance, she was diagnosed to have ankylosing spondylitis. Before the therapy colonoscopy was performed, because of her symptom of diarrhea, no abnormality was observed. IL17 inhibitor therapy was started. After the therapy, diarrhea recurred, and second colonoscopy revealed newly finding of ulcerative colitis. IL17 inhibitor therapy was stopped immediately after CF. But axial symptom reappeared gradually, IL17 inhibitor therapy was restarted, but again diarrhea recurred and IL17 inhibitor were changed to TNFα inhibitor. We must pay attention to UC complicated with IL17 inhibitor therapy.

P2-108

A case of high disease activity axial-spondyloarthritis patient treated with TNF inhibitor drugs

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Conflict of interest: None

A 49-year-old male aware of neck pain and shoulder pain on May 2018. Because of severer general pain he hardly disturbed ADL on Jan. 2019. But for the medication the symptoms were continued and he admitted our hospital on April. Coincide with the symptoms he had eye floaters and diagnosed uveitis at the ophthalmic clinic. For severe inflammatory back pain it is difficult for him to gait, take a deep breath and spinal bending. Dactylitis, psoriasis, urinary tract disease and IBD were not observed. CRP and ESR level were elevated. RF, ACPA and HLA-B27 were negative. Radiographic findings were normal. MRI of the pelvis demonstrated high-intensity lesions in the S-I joint in STIR images. Axial-spondyloarthritis was diagnosed and SSZ and MTX were started. Symptoms were continued and the liver dysfunctional and proteinuria were observe. After stop of treatment with SSZ and reduce of MTX, previous findings were improved. We started the TNF inhibitor (IFX 5mg/kg) 8 weeks after initial examination and prompt improvement of symptoms and decrease of CRP and ESR were observed. Despite continuation of IFX (2nd, 3rd) the flair up of the inflammatory findings were observed. After change of IFX to ADA the previous findings were improved gradually. The symptom of uveitis was improved similarly.

P2-110

Examination of 12 cases of SAPHO syndrome in our hospital

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Conflict of interest: None

[Objective] SAPHO syndrome is most commonly seen in the anterior chest wall of the sternum and clavicle, but also in the sternum and sacroiliac spine. In this study, we examined clinical symptoms and imaging findings (bone scintigraphy, MRI) of 12 cases of SAPHO syndrome experienced in our hospital. [Methods] In 12 cases of SAPHO syndrome diagnosed at our hospital between June 2016 and October 2019, we analyzed clinical features, laboratory findings, and therapeutic drugs. [Results] The average age at diagnosis was 52.5 years, and the sex was 1 male and 11 females. Skin lessions were palmoplantar pustulosis in 5 cases. 7 cases had no skin lesions. Regarding osteoarthritis, 11 cases of sternoclavicular arthritis, 6 cases of spondyloarrthritis (including 2 cases of cervical vertebrae, 5 cases of thoracic vertebrae, 3 cases of lumber spine), 1 case of knee arthritis, and 1 case of ankle arthritis were observed. RF was negative in all cases, antinuclear antibody was positive in 3 cases. Increased mild red sedimention and CRP were observed in 6 cases. Treatment was all NSAIDs, 11 methotrexate, 1 salazosulfapyridine, 1 adalimumab, and 2 tonsillectomy. [Conclusions] A spinal lesion with SAPHO syndrome can be found in the cervical spine and requires careful serch.

P2-111

Cutibacterium acnes isolated from the skull in a patient with SAPHO syndrome

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Conflict of interest: None

[Case] A 58-year-old woman with palmoplantar pustulosis showed exacerbation of pustulosis and high CRP levels two years ago. Since then, high CRP levels persisted for two years. Cervical pain appeared a year ago and csDMARDs were administered. However, cervical pain did not improve, and headache was appeared three months ago. Bone scintigraphy showed increased uptake in the skull, and contrast-enhanced MRI showed a contrast effect on the bone marrow at the same site. The skull biopsy showed fibroblasts, lymphocyte infiltration, and granulation tissue. Furthermore, *Cutibacterium acnes* (*C. acnes*) was detected in bone culture. Then, she was diagnosed with SAPHO syndrome. After starting loxoprofen, pain VAS decreased slightly. However, headaches and high CRP levels had persisted. Six weeks after minocycline administration, VAS improved to 0 mm and CRP levels decreased. [Discussion] SAPHO syndrome is commonly characterized by lesions involving the anterior chest. It has been reported previously that *C. acnes* could be involved in the pathogenesis of SAPHO syndrome. However, there are no reports about *C. acnes* detected from the skull. This is the first report of SAPHO syndrome limited in the skull and detected *C. acnes* from the skull.

P2-112

A case of SAPHO syndrome following calcium pyrophosphate deposition disease (CPPD) involving a lumber facet joint

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Conflict of interest: None

A 68-year-old women suffered from lumbago for ten years and a slight fever for one year. She detected exacerbation of the lumbago and fever

more than 37.5 degrees Celsius in June, then small bouton appeared to a whole body. So she was hospitalized in July. Right L4/L5 intervertebral joint showed liquid effusion by MRI, and after puncturing it, there was not the bacterial body, and a phagocytosis image of the pyrophosphate calcium crystal was confirmed, and CPPD was diagnosed. We administered celecoxib, but lumbago, fever and the CRP increase were not improved and small bouton spread more widely. L2-L5 vertebra showed inflammation by bone scan and sacroiliitis was detected in pelvis MRI, then we had a diagnosis of SAPHO syndrome. After changing celecoxib to diclofenac, the symptom was improved remarkably and left the hospital. Because she was complicated with tonsillitis, tonsillectomy is performed in otolaryngology and passes without recurring to date. We experienced rare one patient whom CPPD of the lumbar vertebrae intervertebral joint and the SAPHO syndrome developed in at the same time. Since there were many common point in two disease, the diagnosis was difficult. But SAPHO syndrome was able to be diagnosed by a merger of pustulosis palmaris et plantaris.

P2-113

A case of pustulotic arthro-ostitis complicated by IgA nephropathy

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Conflict of interest: None

A 61-year-old woman visited our hospital with clavicular pain, back pain. She had been diagnosed with IgA nephropathy 19 years earlier, and diagnosed with palmoplantar pustulosis (PP) seven years before visiting. Laboratory studies showed an elevated erythrocyte sedimentation rate and serum C-reactive protein level. Urinalysis showed proteinuria and occult blood. Rheumatoid factor and anti-cyclic citrullinated peptide antibody were negative. Bone-scintigraphy revealed multi-hot accumulation. She was diagnosed with pustulotic arthro-ostitis (PAO) and had been treated with Celecoxib. Five months after our hospital visiting, she was performed tonsillectomy combined with steroid pulse therapy following by oral steroid administration for six months, because microhematuria, proteinuria, palmer eruption, and back or/and clavicular pain were disappeared. Her all symptoms had temporarily gone into remission immediately after those combined therapy, however, her back pain relapsed as steroid reduced gradually. Tonsillar focal diseases, such as PP or IgA nephropathy, are reported that a different disease is often complicated each other. To our knowledge, PAO complicated by IgA nephropathy were not many reported previously, and we include an additional review of the literatures to a report.

P2-114

Assesment of tibia trabecular bone structure of patients with rheumatoid arthritis using 3T-MRI

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Conflict of interest: None

[Objective] Bone fragility is one of the most important issues for patients with rheumatoid arthritis (RA) because it leads to bone fracture. We examined whether bone microstructure can be evaluated in RA patients using a clinical 3T-MRI system. [Methods] Twenty RA patients were examined. Patient background includes age, gender, disease duration, bone density, bone metabolism marker, osteoporosis drugs, CRP, ESR, use of methotrexate, PSL, biological DMARDs, and JAK inhibitor. MRI images of subchondral bone were taken using Achieva 3.0T TX (Philips, The Netherlands) for bone microstructure imaging, and trabecular volume ratio (BV/TV: Bone Volume/Total volume), trabecular number (TbN), trabecular thickness (TbTh), and trabecular spacing (TbSp: Trabecular separation) were investigated. [Results] All patients were female, with an average age of 67.8 ± 8.9 years and an average duration of 16.8 ± 14.3 years. The values were CRP 0.63 ± 0.96 mg/dL, ESR 34.6 ± 17.7 mm/h, TRACP-5b 435.4 ± 232.4 mU/dL, and total P1NP 63.1 ± 42.8 ng/mL. The bone structure parameters were BV/TV 0.585 ± 0.241%, TbN 0.913 ± 0.308 /mm, TbTh 0.681 ± 0.331 mm, TbSp 0.514 ± 0.383 mm. [Conclusions] Using clinical MRI, it was possible to evaluate the trabecular structure of the subchondral bone of RA patients.

P2-115

Postoperative anti-osteoporosis therapy among the RA patient with the fragility fracture

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Conflict of interest: None

[Objective] The purpose of this study is to investigate retrospectively the postoperative anti-osteoporosis therapy among the patients with rheumatoid arthritis (RA). [Methods] This study included 149 patients who underwent the open reduction internal fixation for the fragility fractures (126 hip fractures, 17 distal radial fractures and 6 proximal humerus fractures). We investigated clinical information, pre- and post-operative osteoporosis therapy, and the occurrences of secondary fractures from the medical record. [Results] The mean duration of RA was 13.9 years. Of 149 cases, 55 cases were treated by MTX, 16 cases were treated by bDMARDs and 80 cases were treated by glucocorticoid. 89 cases had the history of fragility fracture. The proportions of the pre- and post-operative anti-osteoporosis therapy were 34.2% (51 cases) and 63.8% (95 cases), respectively. Only 10 cases changed the therapy regardless of fragility fracture. 31 cases (20.8%) occurred the secondary fracture. [Conclusions] Although the strategy of treatment for the RA patients with the frequent fragility fracture has not been established, the change of therapy should be considered at the occurrence of fragility fracture.

P2-116

Glucocorticoid use decreases the continuation of denosumab

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Conflict of interest: None

[Objective] The usefulness of denosumab (DMAb) for osteoporosis is clear, but treatment is interrupted in many cases. Therefore, we investigated the rate of DMAb continuation and tried to identify risk factors leading to treatment interruption. [Method] One hundred and seventy four (158 women, 91 rheumatoid arthritis patients, age 73.5 ± 9.5 years, BMI 20.7 ± 3.9 Kg/m^2, lumbar spine BMD 0.668 ± 0.147 g/m^2 and hip BMD 0.582 ± 0.086 g/m^2) were included, the hazard ratio (HR) of candidate factors was determined using the Cox proportional hazard model. [Results] Fifty six patients (32.2%) dropped out with an average of 22.1± 17.4 months. In the Cox proportional hazards model adjusted by age, gender and BMI, the high level of femur BMD (HR; 0.006, 95% CI 0.000-1.004, p=0.050) for continuation and the glucocorticoid (GC) dose (HR; 1.161, 95% CI 1.052-1.282, p=0.003) for discontinuation were identified for significant predictors. Reasons for dropout were self-discontinuation, referral to another hospital, and death. [Conclusions] In this study, GC use was a risk factor for discontinuing of DMAb treatment, and efforts to reduce the amount of GC use might be necessary to continue treatment. There was no clear reason for the effect of baseline height hip BMD for continuation of treatment.

P2-117

A status report of consciousness about osteoporosis in patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] In rhuematoid arthrisis (RA), the complication rate of os-

teoporosis was very high. But its treatment rate was low. In this study, we researched the consciousness about osteoporosis in patients with RA. [Methods] We checked 98rheumatic patients, average 60.1±12.5years old. There were 18males, and 80females. We performed 3closed questions whether they had 1: previous fracture histories, 2: medical treatments for osteoporosis, 3: consciousness about osteoporosis. Rates of patients who responded yes to each question were investigated and we compared rates in aspect of their age, duration of RA, body height, body weight, disease activity of RA, mHAQ, dose of glucocorticoid, and density of bone. [Results] 17.3% of RA patients had previous fractures, 25.5% of patients had medical treatments, 23.5% of patients had consciousness about osteoporosis. Each group responded yes to each questions had different characters in every aspect. Only 52.0% of patients having medical treatment had the consciousness about osteoporosis. [Conclusions] We researched the consciousness about osteoporosis by using 3questions. RA patients may have consciousness about osteoporosis in different aspects from doctors'.

P2-118

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 (ROM) for 6 months in patients with rheumatoid arthritis complicated with osteoporosis. [Methods] 9 patients received continuous ROM 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 months and bone turnover markers, PINP, TRACP-5b and corrected serum calcium level at 1, 3 and 6 months. [Results] Gender of patients are 8 female and 1 male. The mean age was 71.2±7.9 years old; disease duration was 23.0±14.2 years; BMI was 18.8±2.6; DAS28-CRP 3.42±0.70; LS-BMD was 0.795 ± 0.148 g/cm^2; LS-T score was -2.77 ± -1.48; TH-BMD was 0.539±0.091 g/cm^2; TH-T score was -3.28±-0.69; P1NP was 54.1±23.7μg/l; TRACP-5b was 441±185mU/dL and 9.6±0.6 mg/dl. The change of PINP, TRAC-5b and corrected serum calcium level from baseline to 1, 3 months were 54.1→101.8→110.7 μg/l, 441→347→433 U/dL and 9.6→9.2→9.2 mg/dl. [Conclusion] The changes in bone turnover markers after the start of ROM showed a so-called dual effect. In this presentation, we will also report the LS and TH-BMD increase rate and changes in turnover markers at 6 months.

P2-119

Effect of anti-TNF and non-anti-TNF agents on spine/proximal hip BMD and hip geometry for rheumatoid arthritis patients

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Conflict of interest: None

[Objective] We examined fracture protective effect of DMARD especially focused on anti-TNF and non-anti-TNF patients. [Methods] We extracted RA patients with remission or low disease activity without osteoporosis theraputic agents among RA patients followed in NHO Osaka Toneyama medical center and JCHO Osaka Hospital from 2018 Mar. to 2019 Oct. We devided into three groups treatet with csDMARD (cs DMARD group), anti-TNF agent (TNF group) and non-anti-TNF agents (non-TNF group). We examined changing rate and degree of lumber BMD and priximal hip BMD and hip geometry assessed by advanced hip assessment, which is considerd as a new indicator oh hip fracture [Results] CsDMARD group (45 patients,6 male, mean age 69, DASCRP 2.51), TNF group (15 patients,4 male, mean age 65, DASCRP 2.23), nonTNF group (12 patients,2 male, mean age 69, DASCRP 2.24) were involved in DXA examination more than 1 year follow up. Lumber BMD showed 2.1/2.9/1.1, proximal hip BMD showed -0.13/0.94/1.1, bone strength index showed -0.08/-0.07/0.11. NonantiTNF group indicated significant improvement in bone strength of proximal hip estimated by AHA. [Conclusions] Biologic agent especially nonantiTNF agents may be effective from the view point of hip fracture risk.

P2-120

Effects of denosumab on bone metabolism and bone mineral density with disease modifying anti-rheumatic drugs in osteoporosis with rheumatoid arthritis

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Conflict of interest: None

[Objective] The aim of this retrospective study was to evaluate the differences in outcomes of denosumab with DMARDs in osteoporosis (OP) patients with RA. [Methods] We investigated 105 RA patients started and continued with denosumab for more than 2 years at our department (12 males and 93 females, mean age; 72.1 years, csDMARDs-treated group; 53, TNF-treated group; 18, TCZ-treated group; 22, ABT-treated group; 12 cases). We measured TRACP-5b and assessed BMD of the lumbar vertebrae and femoral neck at baseline, 12 and 24 months. [Results] The percent change of BMD of lumbar from baseline was 4.6 at 12 months, and 6.5 at 24 months in the csDMARDs group, 2.6 and 5.9 in the TNF group, 3.6 and 7.8 in the TCZ group, 2.0 and 4.8 in the ABT group, respectively. The percent change of femoral neck was 2.5 and 3.4 in the csDMARDs group, 3.9 and 7.0 in the TNF group, 2.6 and 6.1 in the TCZ group, 0.8 and -0.4 in the ABT group, respectively. The percent change of TRACP-5b was -42.2 and -30.7 in the csDMARDs group, -37.0 and -36.1 in the TNF group, -45.6 and -50.4 in the TCZ group, -39.5 and -32.2 in the ABT group, respectively. There were no significant differences in the percent changes among the groups. [Conclusions] Denosumab might be useful for OP patients with RA regardless of treatments.

P2-121

Efficacy of discontinuing risedronate for patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] We investigated the effectiveness of discontinuation of risedronate for female patients with systemic lupus erythematosus (SLE) treated with glucocorticoid (GC). [Methods] The participants were patients with SLE treated with prednisolone (PSL) ≧2 mg/day and risedronate for at least 3 years. Lumbar spine and total hip bone mineral density (BMD), and bone turnover markers were measured during 48 weeks. [Results] 23 patients discontinued risedronate. The age was 45 years (42-58 years), the duration of GC treatment was 11 years (5.7-24 years), the dose of PSL was 7 mg/day (5-10 mg/day), and the duration of risedronate was 5.4 years (3.3-7.5 years). Fifteen patients showed decreased BMD at 48 weeks after discontinuation of risedronate, with lumbar spine BMD decrease of 1.3% and total hip BMD decrease of 1.1% (p=0.13, 0.022). Serum tartrate-resistant acid phosphatase 5b (TRACP-5b) ≧ 309 mU/dl at baseline was a risk factor for decreased total hip BMD at 48 weeks compared (p=0.023). One patient developed a clinical fracture of the lumbar spine at 20 weeks. [Conclusions] Discontinuation of risedronate treatment in patients with SLE who had received GC therapy led to decreases in lumbar spine and total hip BMD, particularly in patients with high baseline serum TRACP-5b levels.

P2-122

Study of romosozumab for osteoporosis patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We report on the effects on disease activity of patients

with osteoporosis with RA who used romosozumab. [Methods] We compared changes in disease activity and bone density in 47 osteoporosis patients with RA among 193 patients who were treated with romosozumab. In addition, we also compared the impact on bone density and occurrence of side effects in 47 patients with RA and 146 patients with non-RA. [Results] Of the 47 cases, 3 were male and 44 were female, with an average age of 71.7 years (51-89 years). There were 29 patients using biologics (including JAK inhibitor). The average value of DAS28-CRP before romosozumab treatment was 2.62 (± 0.96) and SDAI was 11.29 (± 8.07). At 6 months after treatment with romosozumab, DAS28-CRP was 2.77 (± 0.79) and SDAI was 10.25 (± 4.98), indicating no deterioration in disease activity. The results of bone density by DXA after 6 months, RA patients (n=28) showed YAM values of lumbar spine + 3.96% and total hip + 1.47%. Non-RA patients (n=67) had YAM values of lumbar spine + 5.21% and total hip + 0.47%. There was no obvious difference in effect. [Conclusions] It was suggested that osteoporosis patients with RA can be expected to have the same therapeutic effects as non-RA patients and do not affect disease activity.

P2-123

The association between FTO gene and bone health in Japanese community dwelling population, Nagasaki Island Study

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Conflict of interest: None

[Objective] To examine the association of the FTO gene (Fat Mass and Obesity associated gene #610966 on OMIM) with bone health. [Methods] This cross-sectional study was nested in Nagasaki Islands Study, which is a prospective cohort in Goto City, in islands of Japan. Participants were recruited at medical check-ups for community dwelling population. Bone mass of the calcaneus was evaluated using a quantitative ultrasound measurement. Peripheral blood mononuclear cells were obtained from 1,601 subjects. The SNP rs1421085 was genotyped using hydrolysis probe. The chi-squared test was used to determine whether the variants was in equilibrium in that population. All analyses were carried out using SPSS 23. [Results] Subjects were 1,601 community-dwelling persons (mean age was 68.5 years in men and 68.1 years in women). There was a significant association between the genotype and obesity (OR 1.52, 95%CI 1.07 2.14, p=0.02 in men, OR 1.48, 95%CI 1.16 1.95, p=0.01 in women). Logistic regression analysis showed a significant association in men after an adjustment for age and BMI (OR 1.60, 95%CI 1.13 2.42, p=0.01 in men, not significant in women). [Conclusions] Our study indicated that the FTO gene might associate with bone health in community dwelling population.

P2-124

The impact of continuous administration of corticosteroid on geriatric locomotive function scale-25

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Conflict of interest: None

[Objective] The corticosteroid is used for treatment of various diseases, however, its use causes glucocorticoid induced osteoporosis and insufficiency fracture, declining ability of daily life (ADL). In current study, we evaluated the clinical impact of corticosteroid on ADL using GLFS-25. [Methods] 238 female patients, over 65 years old, were included. They were evaluated by GLFS-25, occurrence of radiographic vertebral fractures (RVFs), and bone mineral density (BMD) using DEXA in lumber spine and proximal femur. [Results] Patients were classified into two groups. A group was contained patients received the administration of corticosteroid (45 cases; Group P1), and another one (193 cases; Group N1). The scores of GLFS-25 in Group P1 (34.4 points) was significantly higher than Group N1 (23.0 points). On the other hand, there was no significance in the occurrence of the RVFs, and BMD among the 2 group; 26 patients of Group P1 who were evaluated BMD (Group P2) and 71 of Group N1 (Group N2), while significantly higher GLFS-25 score was shown in Group P2 (27.4 points) than Group N2 (17.4 points). [Conclusions] It was considered that the administration of corticosteroids causes to increase the scores of GLFS-25 without significantly higher occurrence of RVFs or decreasing of BMD.

P2-125

One-year denosumab and bisphosphonate treatment in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the efficacy of denosumab and bisphosphonate treatment for 1 year to osteoporosis in patients with rheumatoid arthritis (RA). [Methods] Patients with RA received subcutaneous injection of denosumab 60mg (n = 23) at baseline, 6 months and 12 months and oral bisphosphonate (n = 11) 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 +7.7% ($p < 0.01$) and +2.6% ($p < 0.05$), respectively. While mean changes with bisphosphonate were +3.6% ($p = 0.130$) and +4.2% ($p = 0.248$), respectively, there were no significant differences. [Conclusions] In patients with RA, denosumab treatment for 1 year provided favorable benefits.

P2-127

The serum 25 (OH) vitamin D density in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the srum vitamin D density and the sufficiency degree in patients with rheumatoid arthritis (RA). [Methods] The 122 RA patients comprised 112 women and 10 men with a mean age of 70.8 years and a mean duration of disease of 18.7 years. Serum 25 (OH) vitamin D density measured it by ECLA method. The BMD measured at femoral neck and lumbar spine. We measured disease activity, bonemetabolism marker, other renal function, liver function and CRP. [Results] The mean of thevitamin D density was 14.9ng/ml. Vitamin D deficiency was found in 100 patients, vitamin D insufficiency was found in 19 patients, vitamin D was found in 3 patients. We accepted serum vitamin D density and a positive correlation of age, Cre, and BUN, but the concentation was not

seen with bone density and the disease activity. [Conclusions] Vitamin D density was a deficiency state in many of RA patients. It was thought that sufficiency of the vitamin D density was mportant to treatment of osteoporosis and the fall prevention.

P2-128

Treatment Outcomes of Multi-target Therapy Using Tacrolimus and Mycophenolate Mofetil on Lupus Nephritis Presented as Rapidly Progressive Glomerulonephritic Syndrome

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Conflict of interest: None

[Objective] Although the multi-target therapy using tacrolimus and mycophenolate mofetil are reported to be effective on lupus nephritis (LN), its efficacy on LN presented as rapidly progressive glomerulonephritis syndrome (RPGN) has not been well reported. [Methods] Patients who were presented as RPGN, diagnosed as LN by renal biopsy, and treated by multi-target therapy in our department were retrospectively analyzed. Data are expressed as mean ± SD (range). [Results] Five patients (3 female), age 36.6±13.5 years old (19-56) were treated by multi-target therapy. Renal biopsy at treatment revealed Class IV (A) in 2, Class IV (A+C) in 1 and Class IV (A)+V in 2. Crescent formation was 23.1±25.4% (2.0~61.5). eGFR and proteinuria at the initiation of treatment were 46.8±11.5 mL/min/1.73m^2 (38.2-61.0) and 7.7±3.4 g/gCr (4.3-13.4), respectively. Steroid pulse therapy followed by 0.8-1.0 mg/kg of prednisolone (PSL) were used. At 6 months, eGFR and proteinuria improved to 72.9±11.3 (57.9-85.7) and 0.19±0.13 (0.04-0.36). At 12 months, patients were treated by 6.6±1.5 mg/day (5-8) of PSL and eGFR and proteinuria further improved to 76.8±7.8 (65.3-84.9) and 0.10±0.07 (0.04-0.21), respectively. [Conclusions] Multi-target is effective to LN which is presented as RPGN.

P2-129

Lupus Low Disease Activity State as a Treatment Endpoint for Systemic Lupus Erythematosus (SLE): a Prospective Validation Study in Japanese Patients

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Conflict of interest: None

[Objective] We aimed to validate the lupus low disease activity state (LLDAS) in our Japanese SLE patients prospective cohort. [Methods] Patients aged 18 years or older with SLE were recruited and followed prospectively. Patients with at least 2 visits over the study period no more than 6 months apart were included in the longitudinal analysis. Patients with no visits in the final year of the study were censored from their last visit. Attainment of the LLDAS was assessed at each visit. The primary outcome measure was accrual of irreversible end-organ damage, defined as at least a 1-point increase in the SDI. We used time-dependent hazard regression models to measure the association between LLDAS (attainment at any timepoint, and cumulative time in LLDAS) with accrual of irreversible end-organ damage or flare. [Results] 121 patients were included. Attainment of LLDAS at any timepoint was associated with reduction in damage accrual (HR 0.46, 95% CI 0.13-1.62) and subsequent flare (HR 0.61, 95% CI 0.34-1.69). Patients with at least 50% of observed time in LLDAS had reduced risk of damage accrual (HR 0.55, 95% CI 0.14-2.16) and flare (HR 0.39, 95% CI 0.19-0.78). [Conclusions] LLDAS attainment is associated with protection against flare and damage accrual in Japanese patients with SLE.

P2-130

The characteristics and renal prognosis in systemic lupus erythematosus patients with anti-ribosomal P antibody

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Conflict of interest: None

Objective: Anti-ribosomal P antibody (Anti-P) is detected in patients with systemic lupus erythematosus (SLE). It has been reported that anti-P were associated with lupus nephritis (LN) and had better renal prognosis. By contrast, some studies showed that anti-P was not related to LN. In this study, we investigated the association between anti-P and the characteristics of SLE and renal prognosis. Methods: Ninety-seven patients who were admitted to our hospital for treatment of SLE from 2008 to 2018. Anti-P was detected by an immunoblot assay. Laboratory and clinical data at admission, 6 months, 1 year, 3 years, and 5 years after starting the treatment were analyzed. Results: Twenty-eight patients had anti-P, fourteen patients progressed to chromic kidney disease (CKD), and one patient developed end-stage renal disease. Patients with anti-P showed younger-onset of SLE, severer hypocomplementemia and were treated with higher dose of glucocorticoid compared to those without. Anti-P was not related to the presence of LN, LN remission, the development of CKD, relapse, survival rate. Conclusion: Anti-P was not associated with LN and better renal prognosis. Anti-P could be a marker of severe disease activity, but the treatment response was same between patients with and without anti-P.

P2-131

Study on the effectiveness of renal re-biopsy in patient with lupus nephritis

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Conflict of interest: None

[Objective] In Japan's SLE Clinical Practice Guidelines 2019, re-biopsy for lupus nephritis is useful because the class may often change. In this study, we examined the significance of re-biopsy for lupus nephritis in our department. [Methods] In our renal biopsy registry, We extracted 16 cases in which re-biopsy was performed among 213 cases diagnosed as lupus nephritis from December 1990 to October 2019. [Results] Among the 16 cases, male: female = 5: 11, the mean age at the time of the re-biopsy was 49.1 ± 17.4 years old, and the average interval until the re-biopsy was 90.6 ± 61.3 months. Initial tissue type is type III: type IV: type IV: mix type = 1: 6: 4: 5, tissue type at the time of re-biopsy is type III: type IV: type IV: mix type = 0: 4: 4: 9 cases. Histological changes were observed in 10 cases, with an increase in the mix type. One case was nephrotic syndrome due to diabetic nephropathy. Treatment was reinforced for each histological type, and cases with no activity received nephroprotective therapy and reduced doses of immunosuppressive drugs. [Conclusions] More than half of the cases showed histological changes, suggesting that re-biopsy is useful for determining an appropriate treatment strategy.

P2-132

The clinical significance of anti-ribosomal P protein antibody in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] Previous studies have shown conflicting results regarding the association of anti-ribosomal P protein antibody (anti-P) with neuropsychiatric systemic lupus erythematosus (NPSLE). We investigated the clinical characteristics of anti-P-positive SLE patients. [Methods] We retrospectively reviewed the clinical features of 101 SLE patients who were

admitted to our department from January 2006 to October 2019. [Results] Anti-P was detected in 32 patients (32%). There was no significant difference in age and gender between anti-P positive and negative patients. No significant difference was found in the percentage of NPSLE between the two groups. In addition, there was no imbalance in the specific manifestations of NPSLE such as aseptic meningitis and cognitive dysfunction. Cytopenia was more frequent (91% vs. 71%; p=0.04), and anti-Sm antibody was more frequently detected (50% vs. 25%; p=0.02) in anti-P-positive patients. There was no significant difference in mortality between the two groups. [Conclusions] The frequency of NPSLE was 25% in anti-P-positive SLE patients. Further accumulation of cases is required to establish the clinical picture of anti-P-positive SLE patients.

P2-133

The association of antiphospholipid antibody and avascular necrosis of the femoral head in the patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] Avascular necrosis of the femoral head (ANF) is a major complication of systemic lupus erythematosus (SLE). High-dose steroid therapy and antiphospholipid antibody (aPL) are known to be associated with ANF. Some SLE patients have no history of thrombosis or habitual abortion even if aPL has been positive once or more times. The aim of this study was to compare the incidence of ANF with aPL-negative patients after dividing aPL-positive SLE patients into two groups according to the presence of history of thrombosis or habitual abortion. [Methods] Among SLE patients treated at our department from April 2008 to September 2019, those in whom aPL was measured once or more were examined retrospectively. Baseline demographic data, contents of treatment, history of thrombosis or abortion and that of symptomatic ANF were obtained. [Results] There were 205 aPL-negative patients, 32 of the 100 aPL-positive patients with a history of thrombosis or abortion, and the remaining 68 without the history. The incidence rate of ANF was 9%, 22%, and 15%, respectively. There were no significant differences in initial steroid dose or steroid pulse therapy rate. [Conclusions] When aPL is positive in SLE patients, ANF may develop frequently regardless of a history of thrombosis or habitual abortion.

P2-135

Usefulness of MRI for multiple plexiopathy in SLE: A case report

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Conflict of interest: None

A 36-year-old woman was admitted to our hospital with a 3-month history of neuropathic pain in bilateral upper extremities and muscle weakness of extremities. Over a few days prior to admission, she had progressive muscle weakness and acute severe pain in the extremities. Physical examination showed severe proximal and distal muscle weakness with atrophy, anesthesia and loss of tendon reflexes in the extremities. Based on photosensitivity, oral ulcer, serositis, arthritis, positive ANA, high titer anti-ds DNA antibodies, and low levels of complements, a diagnosis of SLE was made. MRI showed high intensity signals on brachial and lumbosacral plexuses and muscles. Nerve conduction studies and sural nerve biopsy were consistent with axonal denervation changes. With these findings, the multiple plexopathy was considered to be a manifestation of SLE. Treatment with corticosteroids, plasmapheresis, and cyclophosphamide resulted in clinical and radiological improvements. Generally, it is difficult to localize the neurological lesion in diagnosing plexopathy due to the complicated structure of the plexus. This is the first report of MRI findings in a case of lupus plexopathy. This case highlights the potential of MRI for detecting plexopathy and denervated muscles in SLE.

P2-136

A case of clinically mild encephalopathy with a reversible splenial lesion (MERS) associated with neuro psychiatric systemic lupus erythematosus (NP-SLE)

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Conflict of interest: None

[Objective] The transient reversible lesion in the splenium of the corpus callosum (SCC) is caused by various rare conditions such as drug, infection, alcohol, metabolic disorder and SLE. [Methods] A 31-year-old woman was diagnosed with SLE four years ago. Despite of steroid therapy, her skin lesion and high anti-dsDNA antibody titer, hypocomplement continued. She was absent from work about 2 weeks ago due to fever and fatigue and transferred our hospital because of consciousness disturbance. She had high fever and butterfly rash. MRI showed hyperintensity in the SCC by diffusion-weighted imaging and deep and subcortical white matter small hyperintensity by fluid attenuated inversion-recovery. Cerebrospinal fluid IL-6 was remarkably high at 1680 pg/mL. Her status was acute confusional state. We selected therapy for steroid pulse, plasma exchange and IVCY. At three days, MRI re-examination revealed that the abnormalities of SCC disappeared, the consciousness level became clear. [Results] MRI findings of the SCC due to NPSLE disappeared in a short time after immunosuppressive therapy. [Conclusions] In the cases that SLE patients have SCC lesions, we should care for other causes and can be expected to promptly improve and good prognosis by immunosuppressive therapy.

P2-137

Tacrolimus effectively reduced proteinuria in a patient with membranous lupus nephritis without steroid therapy

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Conflict of interest: None

A 54-year-old Japanese female with systemic lupus erythematosus was referred due to worsening of edema. Her condition was generally stable so that she did not take any medication prior to her admission. Her blood tests on admission showed hypoalbuminemia and hyperlipidemia, but anti-ds DNA antibody was negative and hypocomplementemia was not observed. Massive proteinuria (12.15 g/g·creatinine) was detected by urinalysis. The diagnosis of membranous lupus nephritis (MLN) was made based on pathological evaluations of renal biopsy. In terms of treatments, the patient strongly refused prednisolone (PSL) therapy, so that mycophenolate mofetil (MMF) was selected as an initial immunosuppressive agent. However, MMF was not effective and failed to reduce proteinuria even though the dose of MMF was step-wisely increased. Then, tacrolimus (TAC) was added on MMF and fortunately proteinuria was remarkably reduced. Although MLN is a relatively rare type of LN, we should consider possibility of MLN in patients who manifest proteinuria even without positive anti-ds DNA antibody and hypocomplementemia. Although moderate dose of PSL (0.5 mg/kg/day) in addition to MMF is generally recommended as a remission induction therapy against MLN, TAC could be an alternative.

P2-138

A case of NP-SLE and lupus nephritis complicated with idiopathic basal calcification (Fahr's disease)

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Conflict of interest: None

A 76-year-old woman visited an emergency department because of poor appetite and disturbance of consciousness from 2 weeks ago. She was diagnosed with SLE 14 years ago and started treatment with prednisolone

(PSL) 45mg per day. She had no symptoms after she stopped taking PSL. Head CT showed marked calcification in both basal ganglia and cerebellar dentate nuclei. Brain MRI showed high signal in diffusion-weighted images in deep white matter around the bilateral ventricles. We suspected the strokes. Because of the characteristics calcification, Fahr's disease was also considered. But relapse of SLE was apparent from high anti-DNA antibody levels, hypocomplementemia, nephritis, and hemophagocytic syndrome. She received steroid pulse and IVCY. She gradually recovered. PSL was reduced from 50mg per day, and hydroxychloroquine and tacrolimus were added. IVCY was administered 3times. She was discharged on the 113th hospital days. Fahr's disease is a rare disease which is associated with symmetrical brain calcification and exhibits various CNS symptoms. The treatment has not been established. On the other hand, NP-SLE also exhibits various CNS symptoms. This case was diagnosed as NP-SLE because the symptoms improved with immunosuppressive therapy.

P2-139

A case of systemic lupus erythematosus with remarkable hypertriglyceridemia

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Conflict of interest: None

<case>A 18-years-old man with nine-year history of hypertriglyceridemia presented with thrombocytopenia. One year before, photosensitivity occurred and thrombocytopenia progressed. Physical examinasion revealed photosensitivity. Labolatory data showed pancytopenia, autoimmune hemolytic anemia, hyocomplementemia, anti-nuclear antibody 160 ×, positive Ds-DNA antibody, positive cardiolipin antibody and hypertriglycedemia with hyperchylomicronemia and decreased LDL activity. Based on above findings, systemic lupus erytematosus (SLE) was diagnosed. Treatment with predonisolone 30mg/day was started and subsequently hypertriglyceridemia improved. <consideration>It has been previously reported that 63% of pediatric SLE patients have hypertriglycedemia and that autoimmune hypertriglyceridemia might cause by lipoprotein lipase antibody. In our case we suspected that he could have autoimmune hypertriglyceridemia, because hyperchylomicronemia improved by prednisolone.

P2-140

A case of SLE patient who died of myocardial infarction due to coronary artery spasm with reversible cerebral vasospasm syndrome (RCVS)

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Conflict of interest: None

It is known that patients with SLE have more cardiovascular events than healthy individuals. Until now, it has been assumed that the causes are inflammation, arteriosclerosis due to the use of steroids, and hypercoagulation due to antiphospholipid identity syndrome. Involvement of vasospasm due to disability has also been pointed out. Reversible cerebral vasospasm syndrome (RCVS) is characterized by thunderheadache and reversible cerebral vascular stenosis. Atherosclerosis, arterial dissection, vasculitis, etc. Unlike vasospasm, stenosis was caused by vasospasm, suggesting the possibility of vascular endothelial damage. This time, SLE patients with a history of RCVS experienced death due to myocardial infarction. Catheter examination was performed and vasospasm was proved in the catheter. We report this with a review of the literature in order to find similarities between SLE coronary spasm and RCVS.

P2-141

Two cases of elderly-onset SLE that met the diagnostic criteria for TAFRO syndrome

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Conflict of interest: None

[Case 1] A 76-year-old man. Increased CRP levels and thrombocytopenia were observed, and CT showed bilateral pleural effusion, multiple lymphadenopathy. Hypocomplementemia and high anti-dsDNA antibody level were recognized, and diagnostic criteria of SLE and TAFRO syndrome were satisfied. After mPSL pulse therapy, treatment started with PSL and hydroxychloroquine. Since platelet count did not improve, tacrolimus was added, and platelet count increased. [Case 2] A 62-year-old female. Increased CRP levels, anemia and thrombocytopenia were present. A CT scan showed lymphadenopathy and bilateral pleural effusion. She had rapid progressive glomerulonephritis and nephrotic syndrome. The diagnostic criteria for SLE and TAFRO syndrome were met, and renal biopsy showed signs of lupus nephritis. After mPSL pulse therapy, treatment with PSL and cyclosporine was started. Since thrombocytopenia remained, rituximab was introduced and the platelet count improved. [Conclusion] The two cases that met the diagnostic criteria for SLE and TAFRO syndrome were both older-onset SLE, requiring poor treatment for thrombocytopenia and requiring enhanced treatment. In the treatment of SLE with TAFRO syndrome, treatment guidelines for TAFRO syndrome may be useful.

P2-142

Secondary antiphospholipid syndrome caused by splenic marginal zone lymphoma and resolved after the splenectomy

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Conflict of interest: None

A 66-year-old woman with no significant medical history or abortion developed splenic infarction with acute abdominal pain. The titer of anticardiolipin IgG antibody (aCL) was high, then antiphospholipid syndrome (APS) was diagnosed. Anticoagulant therapy quickly improved the abdominal pain and was continued for prophylaxis. Splenomegaly and pancytopenia gradually worsened. Splenectomy was performed for diagnosis and treatment of presumed splenic malignant lymphoma. Prior to the surgery, thrombocytopenia refractory to platelet transfusion developed, which seemed to be caused by hypersplenism and anti-HLA antibody production. To increase the platelet count for splenectomy, glucocorticoid therapy, intravenous immunoglobulin therapy and HLA-matched platelet transfusion were conducted. After the splenectomy, pancytopenia quickly improved and aCL disappeared. Splenic marginal zone lymphoma (SMZL) was histopathologically diagnosed. Anticoagulation therapy was stopped but there has been no recurrence of the thrombotic event. This is a rare case that developed splenic infarction with aCL induced by SMZL. When APS is diagnosed in an elderly patient, the possibility of malignancy-induced APS should be considered. It may be cured by the treatment for the malignancy.

P2-143

Monocyte CD64 expression as a biomarker for disease activity of systemic lupus erythematosus during pregnancy

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Conflict of interest: Yes

[Objective] It is sometimes difficult to assess the disease activity of systemic lupus erythematosus (SLE) during pregnancy. Biomarkers that can quickly assess the disease activity are needed. We have previously reported a correlation between monocyte CD64 (mCD64) expression and disease activity of SLE. In this study, we investigated the usefulness of mCD64 as a disease activity marker for SLE during pregnancy. [Methods] The study sample comprised patients with SLE during pregnancy who were examined at the Osaka Women's and Children's Hospital between May 2016 and October 2020. The mCD64 expression levels were quantitatively measured in first, second, and third trimester, and postpartum. [Results] 21 patients were enrolled. The median mCD64 expression levels were not significantly different between each trimesters in inactive SLE patients (SLEDAI<6). The median mCD64 expression levels during pregnancy were 34,384 (IQR, 26,075-35,602) molecules/cell in active SLE (SLEDAI≧6), and 23,361 (IQR, 19,633-27,562) molecules/cell in inactive SLE ($p = 0.027$). [Conclusions] These results suggest that mCD64 expression levels are highly upregulated in active SLE during pregnancy. The mCD64 expression level may be a useful biomarker for assessing the disease activity of SLE during pregnancy.

P2-144

A case of primary antiphospholipid syndrome with triple positivity

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Conflict of interest: Yes

Case: 17-year-old male Medical history: A urinary protein (1+) and serum Cr 1.30 mg/dL were pointed out in July X-1. In May X, serum Cr elevated 1.53 mg/dL, and he was admitted to our hospital. Urinary protein (4+, 2.5 g/gCr) was observed. Hematuria and nephritic cast were negative. APTT was extended. Lupus anticoagulant, anticardiolipin antibody and anti-β2GP1 antibody were positive (triple-positivity). Brain MRI revealed old cerebral infarction. There was no physical finding or hematologic abnormality associated with collagen disease. We diagnosed him as primary antiphospholipid syndrome (APS) and started Aspirin and Warfarin. In August X, due to drug-induced liver injury, they were changed to Clopidogrel and Apixaban. In April X+1, he developed right cerebellar infarction. Transesophageal echocardiography showed vegetation in the mitral valve. After starting Heparin, vegetation disappeared. To strengthen therapy, Warfarin was restarted and increased, paying attention to liver damage. Treatment continues without recurrence of infarction and vegetation. Clinical significance: The superiority of warfarin over Novel Oral Anticoagulants (NOAC) has been reported in triple positivity cases of APS. This case was suggestive in considering the treatment policy in high-risk cases of thrombosis.

P2-145

A case of a patient with systemic lupus erythematosus presenting with pseudo-pseudo Meigs' syndrome

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Conflict of interest: None

A forty-four-year old woman was referred to our hospital because of the presence of pleural effusion, ascites and raised CA-125 levels. There is no evidence for the diagnosis of solid tumor according to the results of imaging modality. The test results showed peripheral lymphopenia, proteinuria, hypoproteinemia, renal dysfunction, elevated CA 125, low C3 and C4 levels and antidouble-stranded DNA antibodies was positive. The patient was diagnosed as having pseudo-pseudo Meigs syndrome. Pseudo-pseudo Meigs' syndrome is a newly emerging manifestation of systemic lupus erythematosus, characterized by the presence of pleural effusion, ascites and raised CA-125 levels. Up to now, only approximately 10 reports about pseudo-pseudo Meigs syndrome have been published. Here we report a case of a patient with systemic lupus erythematosus presenting with pseudo-pseudo Meigs' syndrome.

P2-146

The case reports of three systemic lupus erythematosus patients, treated with belimumab and got good management by the decease of steroid

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Conflict of interest: None

SLE is a chronic autoimmune disorder involving multiple organs and having diverse clinical manifestations. Clinical features range from involvement of skin and joints to severe debilitating complications at later stages, like infections and problems of renal, cardiovascular, and central nervous system. Belimumab is not recommended for patients with severe active lupus nephritis and CNS manifestations. However the another difficult conditions exist like the flares of lupus and various side effect of steroids. To reduce the steroid dose, we applied belimumab for management of the disease activity and avoiding the adverse effect of steroids in three lupus patients. First case had moderate diabetes due to steroids, severe interstitial pneumonitis and infection. Second case was suffered from aseptic necrosis and osteoporosis related high dose of steroids, severe discoid eruptions, alopecia, enteritis, and cystitis. Another case had obesity and diabetes due to daily high dose of steroids against flares of lupus. Now belimumab is the only approved biological against SLE, and is also indicated as an add-on therapy for the treatment of adult patients with active, autoantibody-positive, SLE, receiving standard therapy.

P2-147

Constrictive pericarditis with rare calcification in a patient with SLE and Sjogren's syndrome: A case report

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Conflict of interest: None

Chronic pericardatitis is reported in SLE, but with calcification is rare. We herein report a rare calcification of constrictive pericardatitis in a patient suffered from SLE and Sjogren's syndrome. [Case] A 62-year-old man presented to our hospital after 3 months of the onset of exertional dyspnea, to refer for cardiac catheterization associated with pulmonary hypertention. Medical history included stasis dermatitis and a suspect of autoimmune hepatitis in thirties have been refused steroid treatment. He had Sjogren's syndrome for finger joint pains, reported that per-oral methotorexates had begun for about one year prior. Another medication was diuretics, which were started as cirrhosis because medical checkup X-ray found a pleural effusion when 56 year-old. On admission, a right heart catheterization showed "dip and plateau patern" and pulmonary hypertention. CT scan revealed calcification on pericardium. After another 3 months, fever and joint pains continued for one month, in addition, dyspnea were exacerbated. Blood tests revealed a pancytopenia, a low complement and positive of anti-dsDNA antibody. Thus, he was diagnosed as SLE to treat with predonisolone (0.5mg/kg/day), his symptoms expeditiously disappeared. Followed-up a right heart catheterization showed normalized.

P2-149

A role of circulating immune complex in untreated systemic lupus erythematosus patients

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Conflict of interest: None

[Objective] To study a role of circulating immmune complex on disease activity in untreated patients with systemic lupus erythematosus (SLE), and to investigate an association between autoantibodies and IC. [Methods] All the patients with a diagnosis of SLE visiting during April 2009 and July 2019 and were included. Clinical data were retrospectively extratcted: age, sex, IC, complement, anti-ds DNA, anti-DNA (RIA), an-

ti-RNP, anti-Sm, anti-Ro/SSA, anti-La/SSB, anti-cardiolipin, anti-beta 2 GPI antibodies, lupus anticoagulant, and SLEDAI. A comparison of SLEDAI was conducted between 3 groups: High IC (>3.0 μg/mL), Intermediate IC (1.5-3.0), and Low IC group (<1.5). Multivariate Logistic model was used to investigate antoantibodies significantly associated with detection of IC (High and Intermediate group). [Results] 43 cases (36 female) were included, and mean age (SD) was 41.0 (17.2) years. The SLEDAI were significantly high in High and Intermediate IC groups than in Low group. Anti-dsDNA, anti-DNA (RIA) antibodies, and hypocomplementemia were significantly frequent in high and intermediate groups than in low group. Anti-ds DNA and anti-Ro/SSA antibodies independently predicted detection of IC. [Conclusion] Our result suggests that IC may have a role of disease activity of SLE.

P2-150

Perforation of the appendix associated with vasculitis in a case of neuropsychiatric SLE

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Conflict of interest: None

A 26-year-old woman was admitted to a nearby mental hospital in January 2019 because of mood disorders and anorexia. She was transferred to our hospital in June because of high fever and pancytopenia. She was diagnosed with SLE due to the low complement levels, positive antinuclear antibody, and anti-double-stranded DNA and antiphospholipid antibodies, and arthritis. Enhanced brain MRI showed a high-signal area from the bilateral coronary canal to the basal ganglia in the FLAIR-weighted image. Her cerebrospinal fluid IL-6 concentration was elevated. Nerve conduction studies revealed mononeuritis multiplex. We diagnosed NPSLE. The day after starting treatment with PSL 1 mg/kg/day, she developed an acute abdomen and underwent surgery. During surgery, a perforated appendix was noted. After surgery, histopathological examination revealed that the perforation was caused by SLE vasculitis. Few other reports exist linking lupus-associated vasculitis with appendix perforation. In our case, her acute appendicitis was initially considered a non-SLE-related cause of the acute abdomen. We thus report a rare case of NPSLE complicated with perforation of the appendix associated with vasculitis.

P2-151

A case of MMF and IVCY-resistant class V lupus nephritis who was successfully treated by Cyclosporin A

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Conflict of interest: None

[Case] A 44-year-old woman was admitted to our hospital with complain of hair loss and oral ulcer in July 2016. Laboratory tests revealed hypocomplementemia and positive of ANA and anti-Sm Ab. She fulfilled criteria for SLE. She was treated with prednisolone (PSL) 30 mg/day and hydroxychloroquine (HCQ). In September 2017, she developed leg edema and proteinuria (3.5 g/gCre). The finding of renal biopsy revealed class V lupus nephritis (LN) and we started induction therapy with PSL 60 mg/day, mycophenolate mophytyl (MMF) 2000 mg/day, and HCQ. Since proteinuria (6 g/gCre) was prolonged even 1 month after the therapy, tacrolimus (TAC) was added. TAC was gradually increased to 3 mg/day, but LN did not improve. In May 2018, MMF was switched to cyclophosphamide intravenous therapy (IVCY) (500mg/2) for a total of 5 courses, but proteinuria was prolonged. TAC was switched to cyclosporine (CsA), starting from 2 mg/kg and increasing gradually, proteinuria decreased. In May 2019, a complete renal remission was achieved with 4 mg/kg CsA, and has be maintained with 2mg/kg CsA for 1 year. [Conclusion] In SLE guidelines, MMF and IVCY are recommended for remission induction in class V LN. We report a successful treatment with CsA in a patient whose class V LN was resistant to MMF and IVCY.

P2-152

A refractory case of MPO-ANCA-positive lupus nephritis despite of early intervention with intensive remission induction therapies

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Conflict of interest: None

[Introduction] Myeloperoxidase anti-neutrophil cytoplasmic antibodies (MPO-ANCA) positivity in lupus nephritis (LN) is rare and is likely to be associated with chronic inflammation such as extend interstitial fibrosis and tubular atrophy. [Case report] 49-year-old woman with 2-months history of edema was admitted. Laboratory data showed that serum albumin 1.9 g/dL, serum creatinine (Cre) 1.94 mg/dl, urinary red blood cells >50/HPF, urinary protein 4.61 g/g·Cre, Anti-ds-DNA IgG 127 U/ml, and MPO-ANCA 54.0 U/ml. Renal biopsy revealed active LN class IV-G (A) along with tubular atrophy and interstitial fibrosis. We started multi-target therapy (prednisolone, mycophenolate mofetil and tacrolimus) without a favorable efficacy and subsequent development of protein-losing enteropathy. Therefore, we introduced 3 cycles of intravenous cyclophosphamide administration. Second renal biopsy exhibited disappearance of active LN with progressive chronic change of glomeruli and persistent tubulointerstitial findings. Serum Cre and the amount of urinary protein excretion achieved minimal improvement. [Conclusion] Our case suggested that MPO-ANCA-positive LN is likely not to respond to the standardized induction therapy for LN. Further investigations will be needed to confirm the result.

P2-153

Recurrence subdural hematoma caused by acquired hemophilia B in antiphospholipid syndrome patient: a case report

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Conflict of interest: None

Case presentation: A 58-year-old male was diagnosed with antiphospholipid syndrome (APS) about 30 years ago. He had taken warfarin (WFN). He suffered from headache and fever in July 2019 and computed tomography (CT) scan revealed right sided subdural hematoma, so he was admitted to our hospital. Because his fever went down and hematoma got smaller after discontinuation of WFN, he received WFN again on the 12th day. However, fever and headache appeared again. On the 51st day, new bilateral subdural hematoma and ground glass opacity on bilateral lung field was detected by CT. Later, blood test showed positivity of anti-factor IX inhibitor, so it was suggested that he had acquired hemophilia B. After he started taking prednisolone and cyclophosphamide, his fever and activated partial thromboplastin time (APTT) was improved. Discussion: It is known that lupus anticoagulant prolong APTT but in vivo it gets higher risk of thrombosis, not bleeding tendency. In this case, we considered that acquired hemophilia B caused recurrence subdural hematoma. Past report showed that acquired hemophilia B was associated with autoimmunity disease such as systemic lupus erythematosus (SLE). Acquired hemophilia B is rare disease, and accompanied with APS is also very rare, so we report this case.

P2-154

A case of refractory skin ulcer due to calciphylaxis in patients with systemic lupus erythematosus and anti-phospholipid syndrome

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Conflict of interest: None

Case: A 40s woman, who had 24 years history of systemic lupus erythematosus (SLE), was previously treated with prednisolone (PSL) for malar rash, and arthritis. 22 years before the presentation, aspirin was initiated

for the treatment of microthrombosis of pulmonary artery. 9 years before the presentation, aspirin was switched to warfarin due to the development of anti-phospholipid syndrome (APS), and tacrolimus was added for SLE disease flare. She was hospitalized for a 2-month history of progressive skin ulcers with severe pain requiring opioids. On physical examination, ulcer with surrounding purpura in size of 120 mm by 80 mm appeared on left lower leg. Skin biopsy showed ring calcification of small-sized vessels within the subcutaneous fatty tissue without vasculitis or thrombosis, which was consistent with calciphylaxis. Warfarin was switched to unfractionated heparin because warfarin is one of the risk factors of calciphylaxis. Sodium thiosulfate, hyperbaric oxygen therapy, hydroxychloroquine were added and the dosage of PSL was tapered. Severe pain resolved and ulcer gradually diminished 50 days after hospitalization. **Clinical significance:** Skin biopsy should be performed to distinguish calciphylaxis in patients with SLE or APS developing refractory ulcers and severe pain.

P2-155

Association between smoking and disease activity of systematic lupus erythematosus: cross sectional study: from LUNA registry

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Conflict of interest: None

[Objectives] We aimed to examine whether smoking is associated with the disease activity of SLE. [Methods] The research design was cross-sectional study. 739 SLE patients who satisfied ACR criteria were targeted. They were registered in databases currently being constructed at 10 Japanese hospital. The exposure factor assumed it smoking, the definition if there were past smokers and current smokers. The main outcome was SLEDAI. The secondary outcomes were complement level and anti ds-DNA antibody. The linear regression analysis was performed to analyze the association between smoke and the disease activity. Confounding factors were sex, age, present corticosteroid dosage and present immunosuppressant use. [Results] The median age was 45 years old. 88% was female. The median corticosteroids dosage was 5mg. Immunosuppressant use was 73%. The median SLEDAI was 4. Nonsmokers were 487 / 739. Smokers were 252 / 739. No significant difference was observed between the 2 groups in Kruskal Wallis test and no significant difference was observed in multiple regression analysis. [Conclusions] We did not show the association between smoking and disease activity of SLE.

P2-156

What is the predictor of the onset of alveolar hemorrhage due to SLE?

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Conflict of interest: None

[Cases] He developed antiphospholipid antibody syndrome caused by deep vein thrombosis and pulmonary thromboembolism at the age of 41. He was also diagnosed with systemic lupus erythematosus (SLE) by proteinuria at the age of 51 and anti-DNA antibody positive. Despite the administration of steroids and various immunosuppressive agents, he has repeated alveolar hemorrhage five times so far. When he had bloody sputum and dyspnea and visited our hospital, there was no suggestion of increased activity serologically. The chest CT was observed diffuse frosted glass shadow in both lung fields. In 10 years, patients who developed alveolar hemorrhage by SLE patients in our hospital is three cases. Except for this case, three cases showed disease activity such as an increase in anti-DNA antibodies and low complement levels. The causes of alveolar hemorrhage were due to SLE and vascular vulnerability due to long-term steroid administration, as well as easy bleeding due to warfarin and severe sleep apnea syndrome. [Conclusions] There are no prognostic factors for alveolar hemorrhage associated with SLE. However, in addition to disease activity, psychiatric disorder and renal disorder, each environmental factor may be deeply involved.

P2-157

A case of Lupus-associated protein-losing enteropathy diagnosed by renal biopsy

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Conflict of interest: None

A 40-year-old woman was admitted to the hospital with a complaint of abdominal pain and malaise since 10 days ago. Upon admission, Blood tests showed hypoalbuminemia (2.2 mg/dl), hypercholesterolemia (343 mg/dl), hypocomplementemia (CH50<10U/ml, C3 24mg/dl, C4 1.6 mg/dl). Urine protein creatinine ratio 0.6 g / gCr and anti-nuclear antibody (ANA) was 40 times (SPECKLED, CYTOPLASMIC) but ds-DNA antibody, Sm antibody, and U1-RNP antibody were all negative. Stool α1-antitrypsin clearance was high, and gastrointestinal scintigraphy (99mTc-HSA-D) revealed protein leakage from the small intestine. Based on the above, hypoalbuminemia due to protein losing enteropathy were suspected. But renal biopsy was performed because exudative pleural effusion was detected by thoracentesis. Renal biopsy revealed Lupus nephritis class II Met and excluding drugs and infections, Lupus-associated protein-losing enteropathy was diagnosed. [Clinical significance] This case can be classified as lupus erythematosus (SLE) by renal biopsy results and ANA to the 2012 SLICC, but can't be classified to the new criteria of EULAR/ACR in 2019. Since this may still be difficult for the diagnosis of atypical SLE, we report this case with a literature review.

P2-159

Association of CD300H gene polymorphisms and systemic sclerosis (SSc) in Japanese patients

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Conflict of interest: None

[Objective] SSc is characterized by fibrosis of the skin and internal organs and microvascular injury. Endothelial injury is induced by the actions of free radicals or environmental factors with immune activation. A novel immunorecepter CD300H is one of CD300 family molecules is identified in 2015. CD300H is expressed on $CD16^{+}$ monocytes and myeloid dendritic cells, and that mediates neutrophil chemoattractant production. In previous study, we reported that the frequency of rs905709 A allele was significant higher in SSc than healthy control (P=7.32e-7). In this study, we examined whether *CD300H* polymorphisms are associated with clinical background of SSc. [Methods] We investigated 102 SSc patients. Single nucleotide polymorphism (SNP) rs905709 was determined using TaqMan SNP genotyping assay. We analyzed the association of clinical data and autoantibodies with *CD300H* gene polymorphisms of SSc. [Results] There were no association between *CD300H* gene polymorphisms and clinical data and autoantibodies of SSc. However, the frequency of SSc who had anti RNP antibody was tend to be higher in A/A genotype and G/A genotype group than G/G genotype (P=0.066). [Conclusions] Our results suggest *CD300H* polymorphism may be associated with susceptibil-

ity to anti RNP antibody positive SSc.

P2-160

Crosstalk between ADAM17 and BMPR2 in systemic sclerosis

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Conflict of interest: Yes

[Objective] The aim of this study is to investigate the expression and the function of A disintegrin and metalloproteinase (ADAM17) and Bone morphogenetic protein receptor type II (BMPR2) in systemic sclerosis (SSc). [Methods] We measured the levels of BMP-2 and ADAM17 in serum from the patients with SSc using ELISA. The expression levels of BMPR2 and ADAM17 in TNF-α stimulated HUVEC were measured by Western blotting, ELISA and qPCR. To block the expression of ADAM17, HUVEC were transfected with siRNA against ADAM17, and we analyzed BMPR2 expression by Western blotting. [Results] The levels of ADAM17 in serum from the patients with SSc were higher than healthy control and positively correlated with the levels of BMP2. In the HUVEC, the expression of ADAM17 was increased by TNF-α stimulation and the expression of BMPR2 was decreased by TNF-α stimulation. The expression of BMPR2 in HUVEC was increased by knockdown of ADAM17. [Conclusions] These data indicates that ADAM17 and BMPR2 crosstalk might be involved in the pathogenesis of SSc.

P2-161

A case of Eosinophilic fasciitis with hardening of skin including fingers requiring the differential diagnosis of systemic scleroderma

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Conflict of interest: None

A 39-year-old man had suffered from edema on limbs and hardening of the skin on the wide-area for one year. He visited our hospital due to the development of the restricted motion of the fingers. Even though nail fold capillary changes, Raynaud phenomenon, anti-nuclear antibodies, and scleroderma-related autoantibodies were all negative, he fulfilled the 2013 ACR/EULAR classification criteria and The Japanese Dermatological Association diagnostic criteria for systemic scleroderma (SSc) because of the skin thickening on wide-area (mRSS 36). After 3 months, he had shown softening of the skin and hardening of the subcutaneous tissue. MRI revealed fascia thickening in the bilateral thigh. Muscle biopsy from the left thigh lateral vastus muscle revealed fascial fibrous thickening and plasma cell infiltration. We diagnosed him with eosinophilic fasciitis (EF) in accordance with The Japanese Dermatological Association diagnostic criteria for EF. Under administration, the treatment with prednisolone 50 mg/day improved his skin thickening [mRSS 26] and the motion of joints. This case emphasizes the need to include the EF in the differential diagnosis when patients with the hardening of skin don't show any other symptoms of SSc.

P2-162

Anti-Th/To antibody positive systemic sclerosis complicated with myositis and immune thrombocytopenia

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Conflict of interest: None

Serum anti-Th/To antibody was detected in 2-5% of systemic sclerosis (SSc) patients, almost of whom have limited cutaneous SSc. Patients with this antibody frequently develop either interstitial lung disease (ILD) or pulmonary arterial hypertension (PAH). We describe here a diffuse cutaneous SSc patient with anti-Th/To antibody complicated with myositis and immune thrombocytopenia. A 62-year-old woman was admitted to our hospital with diffuse scleroderma, muscle weakness and petechiae. Modified Rodnan skin score was 27 points. Laboratory tests showed elevated serum muscle enzymes and thrombocytopenia. Anti-Th/To antibody was positive. Upper gastrointestinal endoscopy showed reflex esophagitis. Muscle magnetic resonance imaging showed typical inflammatory myopathy. Bone marrow examinations revealed no abnormalities in cellularity, number of megakaryocytes, erythropoiesis and myelopoiesis. She was diagnosed as SSc complicated with myositis and immune thrombocytopenia. Thus, our case indicated that anti-Th/To antibody might be associated with some clinical features such as myositis other than ILD or PAH.

P2-163

One case of systemic sclerosis patients with anti-centriole autoantibodies complicated by pulmonary arterial hypertension

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Conflict of interest: None

Scleroderma is generally positive for antinuclear antibodies, and anti-scl-70 antibody, anticentromere antibody, and anti-RNA polymerase III antibody are known as specific antibodies. The anti-centriol antibody-positive scleroderma reported by Brenner et al. In 1980 is said to be negative for antinuclear antibody, a cytoplasmic antibody, and to exhibit localized skin sclerosis. Although few cases have been reported, fingertip ulcers and pulmonary arterial hypertension are associated with high probability. We experienced a 73-year-old woman. Anti-centriol antibody was suspected and retested, so it was positive, and anti-centriol antibody-positive scleroderma was diagnosed. There were limited medical institutions reporting anti-centriol antibody-positive scleroderma in the literature. It is speculated that there are cases that have been overlooked unless they are scleroderma because they are positive for anti-cytoplasmic antibodies. We report on the course of pulmonary hypertension with a review of the literature.

P2-164

Mycophenolate mofetil (MMF)+Prednisolone (PSL) combination therapy for 4 cases with Systemic sclerosis-associated interstitial lung disease (SSc-ILD) which will progress to extensive lung fibrosis

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Conflict of interest: None

[Purpose] In SSc-ILD, it is important to select cases that are predicted to have a high risk of progression to end-stage lung disease and introduce appropriate disease-modifying therapy. Several reports on progression predictors and therapies have been made, and we will examine the SSc-ILD cases that have undergone treatment intervention. [Method] 1) Disease duration; within 7 years after the appearance of non-Raynaud symptom, 2) Fibrosis lesions on HRCT, 3) dcSSc, 4) % FVC≧40%, 5) KL-6 ≧ 1000U/ml, (6) CRP positive. MMF and PSL combination therapy was introduced to patients who met these conditions, and 4 cases that had been followed for more than 12 months were subject to% FVC, % DLco, KL-6, SP-D, CRP, mRSS) was evaluated. [Results] Three women, age 50-71 years, disease duration 9-60 months. Anti-Scl-70 antibody was positive in 3 cases. % FVC 68.8-97.6%, % DLco 51.4-78.7%, KL-6 1269-5324U / ml, SP-D 112-472ng/ml, CRP 0.165-0.804mg/dl, mRSS 9-19. The change from baseline at 12 months was improved in 1 case, worsened in 1 case, and unchanged in 2 cases. KL-6 decreased in 3 cases and increased in 1 case. mRSS improved in all cases. [Conclusion] MMF and PSL combination therapy for SSc-ILD may be able to suppress the deterioration of lung function and improve skin sclerosis.

P2-165

A case of systemic scleroderma with pulmonary arterial hypertension treated with epoprostenol for the surgery of colon cancer and switched to selexipag after the surgery

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Conflict of interest: None

[Case] A 59-year-old woman with systemic scleroderma (SSc), interstitial pneumonitis and pulmonary arterial hypertension (PAH) has been treated with tadalafil, bosentan, and beraprost for PAH. She developed colon cancer and open colectomy was selected. She was admitted to our hospital to introduce epoprostenol (EPO) during the perioperative period. Beraprost was switched to 2ng/kg/min of EPO 16 days before surgery. Two days before surgery, EPO was gradually increased to 9.5 ng/kg/min. A right hemicolectomy was performed under general anesthesia. Selexipag (SXP) was started on the 19th postoperative day. EPO gradually decreased and SXP gradually increased from 0.4mg/day to 1.2mg/day. On the 30th postoperative day, EPO was completely switched to SXP. She was discharged on the 40th postoperative day. [Discussion] Considering the exacerbation of PAH due to postoperative invasion and the prolonged fasting period, it may be useful to introduce EPO on the perioperative period with switching to SXP after the operation. [Conclusions] We experienced and reported an example of successful introduction of EPO as a perioperative management of PAH in SSc patients and switching to postoperative SXP.

P2-166

A case of systemic sclerosis-associated gastric antral vascular ectasia successfully treated with intravenous cyclophosphamide

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Conflict of interest: None

A 79-year-old woman was admitted to our hospital because of anemia. She was diagnosed with systemic sclerosis based on sclerosis of the fingers and below the knee. Simultaneously, she was diagnosed with systemic sclerosis-associated gastric antral vascular ectasia (GAVE). We treated her with proton pump inhibitors, oral iron supplementation, and argon plasma coagulation. We also stopped the anticoagulant. Unfortunately, these treatments were insufficient, and she required frequent blood transfusion therapy. Then, she started to receive intravenous cyclophosphamide at monthly intervals, for a total of six months. After that, no further blood transfusions were necessary over the one-year follow-up period. Additionally, her hemoglobin levels normalized. We successfully treated systemic sclerosis-associated GAVE with cyclophosphamide. Previously, the efficacy of cyclophosphamide for patients with systemic sclerosis-associated GAVE has been reported in only seven cases.

P2-167

A case of acute exacerbation of interstitial lung disease with anti-Ro antibody positive systemic sclerosis successfully treated with tocilizumab

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Conflict of interest: None

[Case] A 62-year-old lady with history of polymyositis, who had been in drug-free remission for 20 years presented with edema and redness on extremities lasting for 3 months. She had skin sclerosis distal to elbow and ankle with fine crackles heard on the bilateral chest. Autoantibody was positive only for anti-Ro. Chest CT showed interstitial lung disease (ILD) with NSIP pattern. We diagnosed her as systemic sclerosis (SSc) based on skin sclerosis (TSS: 29 points) and ILD. She was initially treated with prednisolone (PSL) 30mg qod, mizoribine 100mg qd, tacrolimus 1mg qd, leading to worsening of ILD. She started subcutaneous tocilizumab (SC TCZ) biweekly from 2 month after the initial visit, with tapering PSL to 5mg qod. 2 month later, CT showed remarkable improvement of ILD. Skin thickness had also improved (TSS: 21 points). [Clinical Implication] ILD is a leading cause of death in SSc, sometimes refractory to treatments. A recent study showed efficacy of weekly SC TCZ for SSc especially on the decline in FVC (*Arthritis Rheumatol.* 2018; 70 (suppl 10).). In this case, acute exacerbation of SSc-ILD was successfully treated with biweekly SC TCZ. Further research is needed to examine whether TCZ can improve SSc-ILD flare, as well as the difference between weekly and biweekly dosing.

P2-168

A case of anti-TIF1-gamma antibody positive dermatomyositis relapsed during complete remission of malignant lymphoma

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Conflict of interest: None

A 40-year-old woman visited our department with complaints of skin symptoms, muscle pain, and weakness in July X-2. Dermatomyositis was diagnosed based on Gottron's sign, CK elevation, proximal muscle weakness, and EMG. Blood tests showed positive anti-TIF1-γ antibody, elevated soluble IL-2 receptor, and CT revealed multiple lymphadenopathy. Lymph node was performed from the left axilla and malignant lymphoma was confirmed. Since dysphagia was also observed, treatment for dermatomyositis was started from PSL 60 mg / day. For malignant lymphoma, 6 courses of R-CHOP were conducted, and complete remission in January X-1. PSL gradually decreased due to good progress of dermatomyositis and was discontinued in July X-1. After that, both dermatomyositis and malignant lymphoma were stable for about 1 year, but Gottron's symptoms worsened in July X, myalgia and muscle weakness became apparent from August, and it was judged that dermatomyositis relapsed. Treatment resumed at PSL 10 mg / day. At that time, although the anti-TIF1-γ antibody re-elevated, the soluble IL-2 receptor did not increase, and CT showed no evidence of relapse of malignant lymphoma. We experienced a case in which only dermatomyositis relapsed in a favorable malignant lymphoma course.

P2-169

A case of immune-mediated necroticzing myopathy which is suspected to be caused by 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) inhibitor

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Conflict of interest: Yes

[Case] A 51-year-old man. In X-4 years, Statins were started for dyslipidemia. From May X, extremital myalgia appeared. A blood test showed an increase in myogenic enzyme, and rhabdomyolysis was suspected. However, his symptoms were not improved after discontinuation of statins, he visited our hospital in July X and was admitted to the hospital in August X. Myogenic enzymes were significantly high, and muscle MRI showed abnormal high intensity areas in the extremital muscles, suggesting polymyositis. However, the results of muscle biopsy showed necrosis of myofiber and regenerative fiber, which was diagnosed as necrotizing myopathy. The anti HMGCR antibody test was positive, suggesting a diagnosis of immune-mediated myopathy. After taking high-dose corticosteroids, some improvement in symptoms and in myogenic enzymes were observed, but no further improvement was observed. [Consideration] Immune-mediated necrotizing myopathy is clinically manifested as a proximal muscle weakness and difficult to differentiate from polymyositis. The diagnosis is based on myopathological findings, and the response to corti-

costeroids is generally insufficient. Measurement of anti-HMGCR antibody is also useful as a diagnostic aid, and some positive cases may be associated with statins.

P2-171

A rare case of anti-Ku antibody-positive polymyositis associated with hypothyroid myopathy

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Conflict of interest: None

A 70-year-old Japanese man with ten-year history of hypertension and atrial fibrillation presented with polymyalgia. Physical examination revealed myalgia in the shoulders, waist and thighs. Laboratory examination revealed CPK was 1348 U/L. TSH, free T3, and free T4 were 186.1μIU/mL, 1.83pg/mL, and 0.32ng/dL, respectively. hypothyroid myopathy was initially diagnosed. Thyroid hormone replacement therapy started and CPK level decreased with thyroid hormone normalization. However, CPK level was not completely normalized. Electromyogram shows myogenic changes. Muscle biopsy specimen revealed inflammatory cell infiltration in the muscle. Serological tests revealed positive anti-Ku antibodies. Based on above findings, anti-Ku antibody related polymyositis. Treatment with PSL 30 mg/day was started and polymyalgia and CPK level improved. We herein a rare case of anti-Ku antibody-positive polymyositis associated with hypothyroid myopathy. Initially, the elevated CPK level due to hypothyroidism made polymyositis difficult to diagnose. In cases of anti-Ku antibody-related polymyositis, there had previously been a report of the case complicated with Graves' disease, but there was no report of the association of hypothyroid myopathy.

P2-172

Predictive factors of dysphagia in dermatomyositis

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Conflict of interest: None

[Objective] Clinical prediction of dysphagia in dermatomyositis (DM) is still challenging, although several risk factors have been reported. In this study, we assessed the association between the swallowing impairment and clinical and laboratory features. [Methods] We retrospectively reviewed the medical records of 24 patients with DM treated at our department from 2009 to 2019. Every patient fulfilled the revised criteria for the diagnosis of DM which proposed by the Japanese Ministry of Health, Labour, Welfare (2015). [Results] There were 11 patients with dysphagia (dysphagia group) as determined by videofluoroscopic swallow study and 13 patients without dysphagia (non-dysphagia group). The number of patients over 60 years old (p=0.047) and the frequencies of V-Neck sign (p=0.038), Shawl sign (p=0.008) and internal malignancy (p=0.003) were significantly higher in dysphagia group than non-dysphagia group. Each finding with significant difference was assigned a score of 1 point and dysphagia prediction score was calculated (minimum score 0, max score 4). At the score 2, the sensitivity and the specificity were 81.8% and 92.3%, respectively (AUC=0.916). [Conclusions] Dysphagia in DM may be predicted by age (over 60 years old), V-Neck sign, Shawl sign and internal malignancy.

P2-174

Clinical characteristics in patients with anti-ARS antibodies: A single center study

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Conflict of interest: None

[Objective] Anti-aminoacyl transfer RNA synthetase (Anti-ARS) antibody positive patients show various manifestations. The aim of this study is to elucidate clinical characteristics in patients with anti-ARS antibodies. [Methods] We retrospectively reviewed medical records of anti-ARS antibody positive patients who were admitted to our hospital between April 2015 and October 2019. [Results] Twenty patients were enrolled in this study. Among the 20 patients, 8, 6, 4 and 2 patients were positive for anti-EJ, anti-Jo-1, anti-PL-7 and anti- PL-12 antibodies, respectively. The patients included 9 with dermatomyositis, 6 with polymyositis and 5 without myositis. All patients had lung disease, and were treated with oral prednisolone in combination with calcineurin inhibitors. All patients survived during the study period. Five patients relapsed and 4 of them were more than 65 years old. Compared with patients with Anti-Jo1 antibodies, those with Anti-EJ antibodies showed higher diffusion impairment (62.5%) and recurrence rate (37.5%). And they also showed lower rates of arthritis (25%) and muscle weakness (25%). [Conclusions] This study indicates that early combination therapy of prednisolone and calcineurin inhibitors may improve their prognosis. Large-scale and long-term studies are required.

P2-175

Elevated blood level of tacrolimus might be attributed to accidental intaking furanocoumarins -A case of anti-aminoacyl tRNA antibody positive interstitial pneumonia

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Conflict of interest: None

[Case] A 48-year-old women was diagnosed with anti ARS antibody positive myositis, for that prednisolone and tacrolimus were prescribed for one month. Nevertheless, she presented subacute exacerbation of interstitial pneumonia and was hospitalized. Before admission, her blood concentration of tacrolimus was 6.7 mg/dl. She was continued with the same 4 mg of tacrolimus, treated with methylprednisolone 1000 mg for 3 days subsequently prednisolone 50 mg daily, and introduced intravenous cyclophosphamide pulse therapy. High dose corticosteroid caused her stomach pain so that lansoprazole was administered. During hospitalization, the blood concentration of tacrolimus was monitored and observed the aggressively increase from 22.1 mg/dl to 43.6 mg/dl without any adverse event. The patient was found that she accidentally took Citrus natsudaidai almost every day provided as hospital meals. Under the sufficient informed consent, she took 2 mg daily of tacrolimus and lansoprazole without any citrus fruit, and then the reasonable blood concentration of tacrolimus was obtained (3.2 mg/dl). [Discussion] Citrus natsudaidai contains furanocoumarins which inhibit the metabolic activity of CYP3A4, that may result the abnormal increase in the blood concentration of tacrolimus.

P2-176

Clinical statistical examination of the dermatomyositis case in our department in the last 24 years

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Conflict of interest: None

[Background] In recent years, there are many opportunities to experience dermatomyositis patients. Increasing incidence of dermatomyositis has been reported in the United States and Japan. [Method] We retrospectively examined the trends and clinical features of new dermatomyositis patients to our department. [Results] There were 38 dermatomyositis patients between 1995 and 2018, and annual number of patients increased significantly after 2007 compared to pre-2006. There were many trends in 2006-2007, 2012-2013 and 2017-2018. Mean age of onset was 56.0 years, with many women. There were 9 autoantibody positive cases. 17 cases had interstitial pneumonia and 11 cases had malignant tumors. Compared with the general population, smoking rate of dermatomyositis patients was high, and cases that smoked had significantly more malignant tumors and

interstitial pneumonia. Prognosis was poor in cases with malignant tumors. Comparing 2005-2011 and 2012-2018, smoking rates were similar, but rate of interstitial pneumonia was significantly higher in 2012-2018. [Conclusion] Number of patients with dermatomyositis is increasing. It was suggested that smoking may be involved as an acquired environmental factor for the onset of dermatomyositis associated with interstitial pneumonia and malignant tumors.

P2-177

Clinical Characteristics of secondary Thrombotic Microangiopathy in Patients with Polymyositis/Dermatomyositis

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Conflict of interest: None

[Objective] Thrombotic microangiopathy (TMA) is sometimes associated with connective tissue disorders. Although systemic lupus erythematosus and systemic sclerosis are reported as underlying condition of TMA, it is rarely accompanied by polymyositis/dermatomyositis (PM/DM). The aim of this study is to clarify the clinical features of secondary TMA in patients with PM/DM. [Methods] PM/DM patients who visited our Hospital were screened for secondary TMA. Autoantibodies were identified by immunoprecipitation assays and all clinical data were collected retrospectively. ILD is diagnosed based on findings of computed tomography. Clinical and immunological features of TMA with PM/DM patients were assessed. [Results] Three patients with anti-PL-7 antibody positive PM/DM who had concomitant TMA were identified. Two were DM and remaining 1 was PM. All 3 patients had sclerodactyly with the exacerbation of myositis at the time of the TMA onset and taking a calcineurin inhibitor. After we made a diagnosis of secondary TMA, we discontinued a calcineurin inhibitor and plasma exchange was initiated in two patients resulting the improvement of TMA. [Conclusions] These results suggest that sclerodactyly and anti-PL-7 antibody positivity are closely associated with secondary TMA in patients with PM/DM.

P2-178

Clinical characteristic and prognosis of anti melanoma differentiation associated gene 5 antibody positive dermatomyositis with interstitial lung disease in our hospital: A retrospective cohort study

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Conflict of interest: None

[Objective] To evaluate clinical characteristics and prognosis of anti melanoma differentiation associated gene 5 antibody (MDA5) positive dermatomyositis with interstitial lung disease in our hospital. [Methods] We reviewed medical records of anti MDA5 antibody positive dermatomyositis patients in our hospital database from November 2014 to July 2019. [Results] 8 patients (2 male and 6 female) were recruited in this study. The mean age was 60.5±10.0 years. All patients were treated with glucocorticoids, calcineurin inhibitors and intravenous cyclophosphamide combination therapy, and had consolidation or ground glass opacity in lower lobe by CT scan. 4patients (1 male and 3 female) died of rapidly progressive interstitial lung disease within 6 months after the appearance of skin lesions. There were no differences between survivals and deaths in levels of serum ferritin, serum KL-6, C-reactive protein and serum albumin. 3survivors were administered with mycophenolate mofetil and Rituximab. [Conclusions] It is thought high serum ferritin level develope poor prognosis in patients with anti MDA5 antibody positive dermatomyositis, but there is no difference between survivals and deaths in our study. It is likely that mycophenolate mofetil is useful for refractory case.

P2-179

Three cases of dermatomyositis with severe dysphagia by IVIG therapy

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Conflict of interest: None

[Introduction] Dermatomyositis (DM) is an autoimmune inflammatory myopathy. In patients with dysphagia or rapidly progressive interstitial pneumonia, it is necessary to start treatment strongly and promptly. In addition to steroid treatment, the effectiveness of intravenous intravenous immunoglobulin (IVIG) has been shown for steroid-resistant refractory myositis. [Case] A 64-year-old woman, a 77-year-old woman, and a 72-year-old woman. All three cases were steroid-resistant refractory myositis and had dysphagia. Blood sampling data also showed high CPK and severe muscle weakness. Specific autoantibodies were positive for anti-TIF1-γ, Mi2 and SRP antibody, respectively. In addition to steroids, treatment with immunosuppressants and IVIG therapy improved all patients to oral intake. There has been no relapse for several years after treatment, and the course is still good. [Discussion] Various autoantibodies have been reported in DM, with various symptoms. Among them, the prognosis of myositis associated with dysphagia is considered to be poor. There have been many reports on the effectiveness of IVIG therapy for refractory myositis. We report on the effectiveness of IVIG therapy for refractory myositis based on three cases of successful IVIG therapy for myositis with dysphagia.

P2-180

Two cases of treatment-resistant anti-MDA5 antibody-positive dermatomyositis interstitial pneumonia improved with plasma exchange (PE) and tofatinib (TOF)

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Conflict of interest: None

[Case1] 55-year-old male [Present medical history] Skin eruption (Gottron sign, heliotrophic rash) appeared, visited a doctor. CT showed extensive ground glass and infiltrative shadows. Treatment was started with steroid pulse (mPSL), Cyclophosphamide IV, Tacrolimus. Image findings continued to deteriorate, he was transferred to our department. [Progress after hospitalization] PE was started. CT showed a tendency to exacerbate shadows, so we started TOF. Since then, the disease has gradually improved. [Case2] 17-year-old male [Present medical history] Visited a local doctor with chief complaints of cough. Visited another hospital with no antibacterial improvement. CT showed frequent frosted glass shadows. Blood samples showed positive anti-MDA5 antibody. He was referred to our department and was hospitalized. [Course after hospitalization] Treatment was started with PSL, IVCY, Cyclosporine. Mediastinal emphysema appeared. The ground shadow of the lung field was unchanged, but exacerbation of mediastinal emphysema was confirmed. The disease state was judged to be aggravated, and TOF10mg/day was started. The disease was not stable and remission was obtained when PE was started. [Conclusion] We report two cases of combined treatment with PE and TOF for dermatomyositis interstitial pneumonia.

P2-181

Amerlioration of acute renal failure in a patient with dermatomyositis having hypercytokinemia following initiation of immunosuppressive therapy

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Conflict of interest: None

A 63-year-old woman, suffering from persisitant fever 38°C and cough, was introduced to us in mid July, 201X. Past medical history: appenditis (operated), glaucoma, osteoporosis, hypertension. On admission, physical examinations showed V-neck sign, nailfold bleeding, and muscle

pain. Laboratory evaluation revealed CRP 30 mg/dl, aldolase elevation and positive for anti-ARS antibody and anti-centromere antibody. Heliotrope rash was suspected by dermatologist in August. We diagnosed her with dermatomyositis (DM). She also had anemia, decrease in platelet, elevation of ferritin and soluble IL-2 receptor. Marked increase in serum IL-6 level of 28.70 (referenece level<4.00 pg/ml) was noted on admission. She gained 8 kg of her body weight in one week with edema. Treatment was initiated with 1g intravenous methyprednisolone for 3 days, followed by 50mg/day of predonisolone (PSL) and 5 mg/day of tacrolimus. She had gone continous hemodiafiltration shortly after the admission due acute renal failure with anuria (Cr4.51mg/dl). She was withdrawed from dialysis in October (Cr1.08mg/dl). PSL was reduced. We had to quit tacrolimus due to pancreatitis and elevation of liver enzymes. We restarted tacrolimus with lower dose. It was rare to have acute renal failure in DM patient with hypercytokinemia.

P2-182

A case of dermatomyositis diagnosed eight years after surgery for lung cancer with comorbid sarcoidosis

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Conflict of interest: None

<Case> A 63-year-old woman was diagnosed with lung cancer (poorly differentiated adenocarcinoma) and sarcoidosis (non-caseating epithelioid cell granulomas) concomitantly eight years ago by the pathological findings of the right upper lobe and lymph nodes (LN), respectively. Five years ago, lung segmentectomy was performed due to the recurrence of adenocarcinoma. Epithelioid cell granulomas were also found in the LNs. Three years later, lower permeability and multiple nodular shadows on the bilateral lungs were observed. Transbronchial lung biopsy for the nodules revealed non-caseating granuloma formation, suggesting sarcoidosis. She then presented with erythema, heliotrope rash, myalgia and the elevated levels of serum CPK and aldolase. Myositis-associated autoantibodies were negative. She was diagnosed with dermatomyositis based on the pathological findings of the skin and muscle. After starting prednisolone (1 mg/kg), both her symptoms and bilateral lung shadows improved. <Discussion>There are many reports on the comorbidity of sarcoidosis and malignancy, as well as that of dermatomyositis and malignancy. However, cases of sarcoidosis complicated by dermatomyositis are rare. In this case, biopsy was indispensable for the differentiation of dermatomyositis from sarcoidosis.

P2-183

A case of dermatomyositis associated with cancer of unknown primary

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Conflict of interest: None

[Case] A 70-year old woman visited our hospital with dyspnea and hip pain. She was diagnosed as dermatomyositis (DM) with positive Anti Jo-1 antibody. Computed tomography (CT) scan revealed only enlarged paraaorta lymph node, and other screening for malignancy was unremarkable. Open abdominal biopsy was too invasive, and we decided to follow up. She was treated with predonison (1mg/kg/d) and tacrolimus because of interstitial pneumonia, and showed the improvement in muscle weakness as well as reduction of muscle enzyme. After 9 month, CT scan revealed whole body lymph node enlargement. She underwent biopsy from left sided axillary lymph node which showed poorly differentiated carcinoma. Age appropriate screening was repeated, but all test was unremarkable. So, we concluded the diagnosis as cancer of unknown primary (CUP). Because she had not been wanted aggressive treatment for cancer, we planned palliative care. She died after 12month from diagnosis of DM. [Clinical importance] Although many malignancies are associated with DM, the associateon between DM and CUP has not been well understood. All patients newly diagnosed with DM should be evaluated for the possibility of an underlying malignancy, but we should be careful for sometimes it happens as CUP.

P2-184

Current treatment status of microscopic polyangiitis and granulomatosis with polyangiitis in Japan assessed by the intractable disease database

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Conflict of interest: None

[Objective] In Japan, clinical personal record of intractable disease, including MPA and GPA, is compiled into a database, reflecting medical treatment throughout our country. Previous study using this database reported that cyclophosphamide (CY) was used less commonly especially in MPA. We performed this study to understand identify current treatment status and the change of the treatment regimen from previous survey. [Methods] Using the database of 2012 and 2013, MPA and GPA with new onset fulfilling the diagnostic criteria were extracted and analyzed. [Results] We analyzed 1278 MPA and 215 GPA patients. The average age was 72, 63 years-old, respectively. Renal involvement and interstitial pneumoniae were significantly frequent in MPA and mucous, membrane and eye involvement and ear, nose and throat involvement in GPA. Glucocorticoid (GC) pulse therapy was used in 51% of MPA, 41% of GPA, and the initial GC dose was 39.8 mg/day in MPA and 44.7 mg/day in GPA. Concomitant CY was used in 23% of MPA and 56% of GPA. Younger age, bloody sputum, low serum creatinine and higher CRP level were independently related to CY use in MPA. [Conclusions] More MPA cases were registered. Compared to GPA, MPA patients was older and lower frequency of CY usage, showing the same as in the previous survey.

P2-185

The associations between BAFF/APRIL levels and disease activity/outcomes of AAV patients treated with rituximab

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Conflict of interest: None

[Objectives] Disease activity of ANCA-associated vasculitis (AAV) correlates to B cell activation and rituximab is effective for AAV via B cell depletion. BAFF/APRIL are cytokines associated with the proliferation and differentiation of B cells. We aimed to assess the associations between BAFF/APRIL levels and disease activity/outcomes of AAV patients treated with rituximab. [Methods] We enrolled 18 AAV patients treated with rituximab. The serum BAFF/APRIL levels of AAV patients and healthy controls were measured by ELISA. In AAV patients, the levels were measured before treatment, at 2 months after treatment, and at the time of B cell recovery if applicable. We also assessed baseline characteristics and outcomes of AAV patients. [Results] The median serum BAFF before treatment was 2312pg/ml, and APRIL was 12ng/ml. The median serum BAFF at 2 months was 1642pg/ml, and APRIL was 10ng/ml. The BAFF level in AAV patients was significantly higher than those in healthy controls. The serum BAFF level correlated with serum CRP level but not ANCA titer nor BVAS. B cells were recovered in 6 patients but there was no association between B cell recovery and the BAFF level. [Conclusions] The serum BAFF level might be associated with the disease activity of AAV.

P2-186

Clinical characteristics and prognosis of ANCA-related Vasculitis in Japan

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Conflict of interest: None

[Objective] Among ANCA-related vasculitis (AAV), clinical features of MPO-ANCA-positive granulomatosis with polyangiitis (GPA) differs from that of PR3-ANCA-positive GPA. Some reports have suggested that the clinical phenotype (GPA vs microscopic polyangiitis, MPA) is more important than the ANCA pattern in predicting the prognosis. Studies in Japan are limited, and we performed a retrospective chart study of GPA and MPA at our hospital. [Methods] Patients who had visited our department from April 2003 to March 2019 and classified as GPA or MPA by the European Medicines Agency algorithm (PR3-GPA: 15, MPO-GPA: 17, MPO-MPA: 26 cases) were included. Clinical features were compared using data from medical records. ANCA negative patients and patients diagnosed at other hospitals were excluded. [Results] The age of onset was PR3-GPA: 58.3±17.8, MPO-GPA: 71.0±11.0, MPA: 74.4±9.2 years old (p=0.0006). The proportion of females was 8/15 (53%) for PR3-GPA, 12/17 (71%) for MPO-GPA, and 19/26 (73%) for MPA. MPO-GPA was less likely to have bloody nasal discharge compared to PR3-GPA (4/17 vs 10/15, p=0.03), and the relapse rate tended to be lower. MPO-AAV had a lower relapse rate compared to PR3-AAV (p=0.01). [Conclusions] Clinical features and prognosis of MPO-GPA differs from PR3-GPA.

P2-188

A case of propylthiouracil-induced Otitis Media with Antineutrophil Cytoplasmic Antibody-associated Vasculitis, with refractory progress

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Conflict of interest: None

A 42-year-old woman who was treated with Propylthiouracil (PTU) for Basedow's disease was aware of bilateral hearing loss and fever, and she visited a nearby doctor. She was given antibiotics, but was referred to our hospital because her hearing loss worsened. Because of clinical findings such as advanced severe inner ear deafness, long-term history of PTU, bilateral otitis media, high MPO-ANCA, we diagnosed her with PTU-induced Otitis Media with ANCA-associated Vasculitis (OMAAV). We discontinued PTU and performed treatment with prednisolone (PSL) at 1.0mg/kg/day. However, due to insufficient hearing improvement, rituximab (RTX) 600 mg was administered 4 times a week. After treatment, her hearing improved slightly, but ANCA did not improve well, and her hearing did not improve beyond a certain level. Since hearing deteriorated again in the process of PSL gradual decline, we added RTX600mg twice. However, the reaction is still inadequate, and she has followed an intractable course. PTU-induced AAV generally has a good prognosis. Several cases of PTU-induced OMAAV have been reported in the past. In almost all cases, the prognosis was good, such as improvement with PTU discontinuation. We consider this case to be a rare case with an intractable course.

P2-189

Two cases of ANCA-associated vasculitis with pachymeningitis that were difficult to distinguish from IgG4-related disease

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Conflict of interest: None

[Case 1] An 81-year-old woman visited our hospital with gait disturbance. Brain contrast MRI revealed a hypertrophic dura mater with enhancement. Laboratory findings were as follows: CRP 1.0 mg/dL, PR3-ANCA 2.5 U/mL, MPO-ANCA 54.1 U/mL, and IgG4 269.0 mg/dL. Dural biopsy tissue showed fibrosis, a dense inflammatory infiltrate rich in IgG4-positive plasma cells, the disappearance of endothelium and fibrin deposition in some capillaries, and infiltration of neutrophils. She was diagnosed with ANCA-associated vasculitis (AAV) and treated with prednisolone (PSL) and rituximab (RTX). [Case 2] A 77-year-old man visited the hospital complaining of weight loss, headache, high fever, and some cranial nerve disturbances. Brain contrast MRI showed an enhanced hypertrophic dura mater. Laboratory findings were as follows: CRP 17.1 mg/dL, MPO-ANCA 22.2 U/mL, and IgG4 263.0 mg/dL. Histopathological findings of the dura mater revealed a dense inflammatory infiltrate rich in lymphocytes and IgG4-positive plasma cells, necrotic tissue with leukocytoclasia, and gathering epithelioid cells surrounded by multinucleated giant cells. He was diagnosed with pachymeningitis due to AAV and treated with PSL and RTX.

P2-190

Efficacy and safety of combined glucocorticoid and immunosuppressant therapy for elderly-onset ANCA-associated vasculitis

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Conflict of interest: None

[Objective] Combined glucocorticoid (GC) and immunosuppressant therapy (combined therapy) is effective for ANCA-associated vasculitis (AAV), but its efficacy and safety for elderly-onset AAV are not established. We aimed to investigate the efficacy and safety of combined therapy for elderly-onset AAV. [Methods] Seventeen patients (aged ≧70 years) diagnosed with AAV at our hospital from 2011 to 2019 were selected. Patient characteristics, laboratory data, remission rate, relapse rate, survival period, and infection incidence rate were retrospectively reviewed. [Results] Six patients were treated with combined therapy and 11 with GC monotherapy. Further, most patients in both groups had microscopic polyangiitis. The rate of symptoms involving major organ systems and disease activity were not significant between the two groups. Moreover, remission rate was higher, relapse rate was lower, and mean survival period was longer in the combined therapy group than in the GC monotherapy group. The infection incidence rate was higher in the combined therapy group; the incidence rate of severe infection was not significant. [Conclusions] Combined therapy is effective for elderly-onset AAV; however, this therapy should be cautiously selected in patients with higher infection rate.

P2-191

A case of Microscopic Polyangiitis with Multiple Primary Cancers

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Conflict of interest: None

A 78-year-old-man presented with exertional dyspnea and swallowing discomfort. Four years ago, he was diagnosed of microscopic polyangiitis (MPA) based on interstitial pneumonia, high titer of myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) and pathological findings of small vasculitis at resected specimen of sigmoid colectomy for stage I sigmoid colon cancer. Vasculitis was located nearby well-differentiated adenocarcinoma. On this admission, a blood test showed CRP 6.03mg/dl, KL-6 466.6U/ml and MPO-ANCA <1.0U/ml, CT scan showed pleural effusion, pulmonary opacity at left lower lobe and right pharyngeal mass. There were no findings which suggested getting worse of vasculitis including exacerbation of interstitial pneumonia. Poorly differentiated adenocarcinoma cells were detected in pleural effusion and pharyngeal biopsy specimen showed moderately differentiated squamous cell carcinoma. PET/CT revealed FDG uptake of right pharynx, left lower lung and pleura. From these results of images and pathological findings, metastatic cancer was unlikely, we diagnosed triple primary cancers. This case suggests a relationship between vasculitis and cancer because of vasculitis located nearby tumor and triple primary cancers, we also analyze other patients at our institution.

P2-192

Three cases with hypertrophic pachymeningitis followed by ANCA-related vasculitis

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Conflict of interest: None

Hypertrophic pachymeningitis (HP) is inflammatory disease which causes intracranial hypertension and cranial neuropathy. We encountered three patients with HP followed by ANCA-related vasculitis (AAV). Case1: 71-year-old man was referred to our department because of nausea, anorexia, and remarkable elevation of C-reactive protein. He had a headache and MPO-ANCA was positive. MRI revealed hypertrophy of dura mater. He was diagnosed as HP and otitis media with AAV because of refractory otitis media and glomerulonephritis. Case2: 82-year-old man was diagnosed with polymyalgia rheumatica because of fever and neck pain, and was treated with 30mg of prednisolone (PSL). The illness repeatedly relapsed at 15mg of PSL and MPO-ANCA was positive, so he was referred to our department. He had a headache and MRI revealed hypertrophy of dura mater. He was diagnosed as HP with AAV resistant to moderate dose of PSL. Case3: 72-year-old woman with AAV was suffered from a heavy headache in January, and she didn't have a cerebral hemorrhage. In July she had hoarseness and difficulty swallowing and was admitted to our hospital. MRI revealed hypertrophy of dura mater and there was neuropathy of left recurrent nerve, glossopharyngeal nerve, and hypoglossal nerve. She was diagnosed as HP with AAV.

P2-193

A case of Granulomatosis with Polyangiitis with Bilateral Chronic Subdural Hematoma

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Conflict of interest: None

[Case] 75 years old female [Chief complaint] General malaise, Fever [Medical history] Left pleuritis, gastric cancer, Pleomorphic adenoma in parapharyngeal space [Present illness] In February 2018, she was diagnosed as otitis media and CRP elevation was observed in laboratory examination. Head MRI in July 2018 showed right subdural hematoma. In July 2019, she was admitted to our hospital with 2-months history of fever. We diagnosed her with granulomatosis with polyangiitis (GPA) from a high serum titer of MPO-ANCA, proteinuria, and crescentic glomerulonephritis with necrotizing vasculitis in renal biopsy. We treated her with high dose prednisolone and rituximab. Remission was promptly induced and we gradually decreased the dose of prednisolone. Head CT in July 2019 showed bilateral chronic subdural hematoma and hematoma size increased, although head CT in September 2019 after remission induction therapy of GPA showed decrease of bilateral hematoma size. [Discussion] She had no history of trauma and antithrombotic therapy. Subdural hematoma was observed with otitis media which is thought to be the first symptom of GPA. It was suggested that bilateral chronic subdural hematoma was associated with GPA.

P2-194

IL-6 inhibitor prevent the progression of ANCA associated vasculitis in a rheumatoid arthritis

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Conflict of interest: None

[Case] 86-year-old woman [Clinical course] She visited our hospital for the examination of both hands, feet, knees, shoulder joint pain on September, 201X. She was diagnosed with rheumatoid arthritis (RA) (CRP 7.7 mg/dl, RF 165 U/ml, ACPA-negative MPO-ANCA 163 IU/ml, urine protein 0.1g/day). TNF-α inhibitor was started against active RA. Since then, the increase in proteinuria and the progression of renal dysfunction were observed, and MPO-ANCA was increased 231 IU/ml. Renal biopsy was performed in January, 201X+1 and crescentic glomerulonephritis was revealed. We changed IL-6 inhibitor only for avoiding the combination of steroids and biologics because of the ageing and the history of nontuberculous mycobacterial disease. Thereafter the activity of RA calmed down and urine findings and renal function improved. MPO-ANCA became negative after two years. [Discussion] ANCA-related nephropathy was induced by the use of TNFα inhibitors in non-explicit ANCA-positive patients, while the use of IL-6 inhibitors caused a decrease in ANCA and improved nephropathy. It was suggested that suppressing TNFα leads to the progression of nephropathy through increased production of ANCA levels, but inhibitting IL-6 leads to the improvement of nephropathy by suppressing the production of ANCA.

P2-195

The patient/disease characteristics in combined pulmonary fibrosis with emphysema (CPFE) on the chest computed tomography (CT) in the patients with microscopic polyangiitis (MPA)

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Conflict of interest: None

[Objective] To clarify the associations between combined pulmonary fibrosis with emphysema (CPFE) on the chest computed tomography (CT) and patient/disease characteristics in patients with microscopic polyangiitis (MPA). [Methods] We retrospectively identified 150 MPA patients whose chest CT images before treatment were available. We determined the presence of a total of 22 CT imaging components for interstitial lung lesions, airway lesions, emphysematous lesions, pleural lesions. We determined whether the global pattern of abnormalities in each case fits into a typical idiopathic interstitial pneumonia (IIP) pattern. We analyzed associations between these lung lesions/patterns and disease characteristics. [Results] Usual interstitial pneumonia improved in 11 MPA patients, nonspecific interstitial pneumonia in 3, CPFE in 6. Honeycombing improved in 34, Emphysematous lesions improved in 56. In the patients of CPFE, mean age was 68.5 years old, and male was 5. 5 of 6 patients had a history of smoking, pack-years of smoking 55.9. Median follow-up period was 80 weeks (Interquartile range 54-112) and 1 patient died, no patient had lung cancer. [Conclusions] The CPFE patters can be identified in the patient with MPA who had never smoking history.

P2-196

The clinical courses of patients with granulomatosis with polyangiitis (GPA) receiving Rituximab (RTX) as remission induction therapy: a single center experience

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Conflict of interest: None

[Objective] To clarify the clinical courses of GPA patients receiving RTX as remission induction therapy. [Methods] We retrospectively examined the clinical courses of patients with GPA who had received RTX as induction therapy at Nagaoka Red Cross Hospital. [Results] Six patients received RTX as induction therapy (4 males and 2 females with an average age of 53.6 years; MPO-ANCA positive 2, PR3-ANCA positive 4). RTX was used as the initial induction therapy in 2 patients [adverse event or resistance to cyclophosphamide (CY) therapy] and as re-induction therapy in 4 patients (relapse after CY induction therapy). After RTX induction therapy, prednisolone monotherapy (n=1) with azathioprine (AZA) (n=1), methotrexate (MTX) (n=1) or RTX (n=3) was employed as maintenance therapy. Three patients without RTX maintenance therapy all suffered relapse (at an average of 10.3 months after the last administration of RTX) and were re-treated with RTX. Two of the 3 patients receiving regular RTX

maintenance therapy have maintained remission. One patient in whom RTX maintenance was stopped because of remission relapsed 18 months after RTX withdrawal and was re-treated with RTX. [Conclusions] Regular RTX maintenance therapy might be necessary for patients with GPA receiving RTX as induction therapy.

P2-197

Changing diagnosis from EGPA to GPA during the treating course

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Conflict of interest: None

In January 2018, 60-year-old man presented with small blisters and pustules in his head and lower extremities and abdominal pain. His past medical history was bronchial asthma. Laboratory tests showed increased numbers of eosinophils and double negative of ANCA. A chest CT showed ground-glass opacity, and skin biopsy showed extravascular granulomas. He fulfilled the Lanham's criteria of eosinophilic granulomatosis with polyangiitis (EGPA). The treatment with immunosuppressants and prednisolone (PSL) resolved eosinophilia and improved clinical symptoms. However, purpura in his trunk, otitis media and thickening of nasal mucosa appeared with the dose tapering of PSL in November. In July 2019, chest CT showed multiple nodules and lung biopsy showed necrotizing granulomatous vasculitis with neutrophils. He fulfilled the ACR diagnostic criteria for GPA. Rituximab reduced lung nodules. Both GPA and EGPA are characterized by granulomatous inflammation. GPA is characterized with the respiratory tract lesions, EGPA is characterized with eosinophilia and bronchial asthma. There are a few reports that shows symptoms of both GPA and EGPA at the same time. There are no report of changing diagnosis from EGPA to GPA during the treating course and we will report this time.

P2-198

Correlation of Serum IL-5 Level to Disease Severity of Eosinophilic Granulomatosis with Polyangiitis (EGPA)

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Conflict of interest: None

[Objective] To elucidate the association of serum IL-5 level with the disease activity of EGPA [Methods] Patients of EGPA were searched on the electric records in our hospital for recent 10 years. We collected their history of the disease and the results of physical examination, blood tests, imaging and peripheral nerve assessment. Symptoms at the onset of EGPA, eosinophil count, CRP, IgE and IL-5 before and during treatment were compared among the eligible cases. [Results] A total of 28 EGPA patients (21 females and 7 males) with well-documented history, laboratory data and medication history were selected. Almost all patients developed peripheral neuropathy. Fever occurred in 28% (female) and 16.7% (male), nasal symptoms in 27% (female) and 66.7% (male) and, purpura in 50% (female) and 28.6% (male). 5.3% of female and 14.3% of male patients developed glomerulonephritis. There was a marked increase in peripheral eosinophil count (10639±9615/μL), CRP (4.2±3.2mg/dl), serum IgE (1514±1358ng/ml) and serum IL-5 (94.1±101.1pg/ml). 15.4% of the patients showed positive ANCA (75% MPO-ANCA, 25% PR3-ANCA). Initial IL-5 levels correlated to initial CRP ($r=0.86$, $p=0.0006$) and to the presence of purpura ($p=0.0303$). [Conclusions] Serum IL-5 is a promising measure for severity of EGPA.

P2-199

Eosinophilic Granulomatosis with Polyangiitis (EGPA) treated with Mepolizumab in our hospital: 3 cases report

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Conflict of interest: None

[Objective] Recently, efficacy of Mepolizumab for treatment to refractory EGPA was reported and approved in japan. In this study, we report 3 cases treated with Mepolizumab in our hospital. [Case 1] A 68-year-old woman was diagnosed EGPA at 44-year-old. She was treated with prednisolone (PSL), cyclophosphamide (CY). However, she had had relapses four times during PSL tapering. This time, during PSL tapering to 6mg/day, she suffered wheeze. She received Mepolizumab and improved her symptom. After 5 months, she had been tapered PSL to 3mg/day without relapse. [Case 2] A 48-year-old woman was diagnosed EGPA at 36-year-old. She developed otitis media with ANCA associated vasculitis (OMAAV) at 37-year-old. She was treated with PSL and other immunosuppressants. However, she had had relapses three times. This time, otitis media growed worse therefore she received Mepolizumab. [Case 3] A 72-year-old woman was newly diagnosed EGPA and treated with PSL and intravenous CY, however not achieve remission. She received Mepolizumab but not effect therefore discontinued. She switched to Rituximab and achieved remission. Conclusion: In 3 cases received Mepolizumab, 2 cases were effective but one case was not. We need discuss about optimal patient for mepolizumab.

P2-200

The incidence of venous thrombosis in the patients with eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] To analyze the frequency of venous thromboembolic events (VTE) in the patients with eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] Twenty three patients (Male: 16, Female: 7), those who were diagnosed with EGPA from 2010 to 2019 in our hospital, were enrolled. Data were collected retrospectively from their charts. Data were indicated as median (1/4 interquartile range - 3/4 interquartile range). [Results] Age at diagnosis was 61.0 (40.5 - 75.0) years old. During a follow-up of 37.8 (15.5- 92.1) months, seven among 23 (30.4 %) EGPA patients developed VTE (lower-limb deep venous thrombosis in 4, pulmonary embolism in 2, and superior mesenteric vein thrombosis (SMVT) in 2 patients). All atients with SMVT had the history of abdominal surgery due to the perforation caused by EGPA. [Conclusions] Our results confirm a high risk of VTE in patients with EGPA. SMVT may be associated with abdominal surgery.

P2-201

Mepolizumab for eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] To investigate the treatment of eosinophilic granulomatosis with polyangiitis (EGPA) and evaluate the clinical benefit from treatment with mepolizumab. [Methods] The subjects were consecutive cases of EGPA hospitalized in our department and in Osaka Medical College from 2002 to 2018. We evaluated clinical data, treatment, and prognosis, and the safety and efficacy of mepolizumab. [Results] There were 49 cases of EGPA, 41 cases that could be analyzed (27 females), and the mean age of onset was 56.4 years. The ANCA positive was 31.7%, and the affected

sites were peripheral nerve 92%, central nerve 17%, skin 51%, ENT symptoms 39%, lung 29%, heart 22%, digestive organs 12%, kidney 15%. Remission induction therapy included 41 patients with PSL (100%), PSL pulse 16 (39%), IVCY 17 (41%), RTX 4 (10%), IVIG 22 (54%), AZA 22 (54 %), MTX 4 (10%), MMF 2 (5%), MIZ 1 (2%), MEPO 1 (2%), Maintenance therapy PSL 41 cases (100%), AZA 21 (51%), MTX 6 (15%), MMF 2 (5%), MIZ 3 (7%), and MEPO 10 (24%). Of the 10 patients of mepolizumab, the ANCA positive was 40%, improving PSL dose before administration to 9.5 mg and the after 5.5 mg. There was no EGPA relapse and no adverse events. [Conclusions] The treatment with mepolizumab for EGPA showed prednisone withdrawal and tolerability.

P2-202

Two cases who developed superior mesenteric vein thrombosis during the treatment with eosinophilic granulomatous polyangiitis

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Conflict of interest: None

[Case1] Fifty year old man, who had been treated with bronchial asthma for 2 years, was suffered from diarrhea and leg pain. He was diagnosed as eosinophilic granulomatosis with polyangiitis (EGPA) because of eosinophilia and mononeuritis multiplex. He was treated with mPSL pulse therapy followed by oral PSL. He had a rigid abdomen during these treatment, he was diagnosed as bowel perforation and performed emergency surgery. Although he was successfully treated with PSL and IVIg after the surgery, superior mesenteric vein (SMV) thrombosis was demonstrated by CT scan. [Case2] Twenty-nine year old man developed fever, asthma, and lower abdominal pain. Laboratory finding showed eosinophilia, and positive MPO-ANCA. Being suffered from mononeuritis multiplex, he was diagnosed as EGPA and treated with mPSL pulse therapy followed by oral PSL. Two month later, he developed small intestine perforation, and emergency surgery was performed. Although he was treated successfully with PSL, IVCY, and IVIg after surgery, he had severe abdominal pain and CT scans revealed SMV thrombosis three month later. [Conclusion] Patients with EGPA are known at a high risk of deep vein thrombosis and pulmonary embolism. SMV thrombosis is also the matter to be attended to, especially after abdominal surgery.

P2-203

Rapid and successful remission induction with mepolizumab in a refractory case of eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

A 47-year-old man with a past medical history of bronchial asthma and eosinophilic sinusitis was admitted to our hospital because of asthma exacerbations, abdominal pain, and painful legs with purpura. Blood test revealed marked eosinophilia (15,225/μl) and highly elevated levels of myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) (>134IU/ml). He was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). Initial treatment with high dose prednisolone (60mg/day) and intravenous cyclophosphamide (IVCY) followed by additional intravenous pulses of methylprednisolone was partially efficacious with only temporary decrease of peripheral blood eosinophil count. After starting treatment with mepolizumab (300mg), however, all symptoms and eosinophilia immediately subsided. He was discharged 3 weeks later and prednisolone was reduced to 6 mg/day without relapse on mepolizumab. Mepolizumab has been shown to prevent relapse and allow for sparing glucocorticoids but its efficacy in the remission induction remains unknown. The role of mepolizumab in inducing remission of EGPA will be discussed with some literature review.

P2-204

Coronary vasculitis in a young male with eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Background] Eosinophilic granulomatosis with polyangiitis (EGPA) presents vasculitis of not only small vessels but also medium ones, but its coronary involvement is rare. [Case] 33 year-old man was suffered from asthma and a painful digital ulcer 8 years before. Because of a remarkable eosinophilia, a diagnosis of EGPA was made and steroid therapy was started. 10 days before, the digital ulcer and hypereosinophilia developed, so he was admitted to our hospital to evaluate those abnormalities. Physical examination revealed cold sensation on his extremities and weakness of peripheral arterial pulses. Catheter angiography showed peripheral arterial narrowing and coronary aneurisms. Further examinations detected intestinal ulcers and infarctions in brain white matter, so we concluded that the vessel involvements are one of the manifestations of EGPA. [Discussion] Coronary vasculitis can be crucial because it leads myocardial infarction (MI). Underestimation of its incidence can occur because it is asymptomatic until developing MI. Another important issue is that 2011 revised Five Factor Score doesn't include coronary vasculitis in its definition of cardiac involvement. [Conclusions] Physicians need to pay attention to coronary vasculitis in EGPA with medium vessel involvements.

P2-205

Chest hypertrophic pachymeningitis from Eosinophilic granulomatous polyangiitis

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Conflict of interest: None

A 58-year-old man was admitted to our hospital with bilateral leg paralysis for one month. Two years before admission, he initially presented with eosinophilia, asthma, and multiple mononeuropathy and had frequently relapsing illness with a history of eosinophilic granulomatous polyangiitis, which was indicated by elevated proteinase 3 anti-neutrophil cytoplasmic antibody (PR3-ANCA). He developed optic neuropathy associated with cerebral hypertrophic pachymeningitis, and was treated with immunosuppressive agents including high-dose prednisolone, cyclophosphamide, and rituximab. He was on maintenance therapy with prednisolone 0.4 mg/kg/day when paralysis began. He presented with flaccid paraplegia, sensory paralysis below the chest, and bladder disorder. Gadolinium-enhanced magnetic resonance imaging (MRI) showed chest hypertrophic pachymeningitis from spinal cord levels T4 to T8 consistent with his symptoms. He was treated with high dose orednisolone and monthly subcutaneous mepolizumab, which improved his symptoms. Hypertrophy of the thoracic dura, shown by follow-up MRI, completely disappeared after 1 month of treatment. This is a rare case that chest hypertrophic pachymeningitis from eosinophilic granulomatous polyangiitis.

P2-206

A case report of small intestine perforation associated with Eosinophilic Granulomatosis with Polyangiitis during treatment with corticosteroid and Mepolizumab

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Conflict of interest: None

A 26-year-old woman was admitted to our hospital with pyrexia, abdominalgia, diarrhoea, vomit, and numbness in lower limbs in June 20XX. Due to allergic rhinitis/asthma, elevated eosinophil count, multiple erosions in large intestine and mononeuritis multiplex, she was diagnosed with EGPA. Steroid pulse therapy and IVIG was started for rapidly evolving neuropathy. However, since eosinophil count and neuropathy remained, Mepolizumab 300 mg was added on two weeks later resulting in nerve conduction study improvement. 56 days after discharge, she visited the hospital with abdominalgia. Enhanced CT scan showed free air at abdominal cavity. Emergency partial small intestine resection was conducted for small intestinal perforation. As eosinophilic infiltration and active vasculitis were not found in the pathological tissue, besides antibiotics, steroid was reduced due to the risk of infection and ruptured suture. Intestinal perforation in EGPA mostly develops in small intestine, which is difficult to be observed with endoscopy. Although acute inflammation change can be improved with steroid therapy, intimal fibrosis of vessels is irreversible that remains as a risk of intestinal perforation. Capsule endoscopy and angiography would be desirable to evaluate the risk of perforation.

P2-207

Small bowel pseudo-obstruction and necrosis caused by intestinal vascular AA amyloidosis in the course of polyarteritis nodosa (PN)

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Conflict of interest: None

Gastrointestinal tract and kidney are common organ systems involved in AA amyloidosis, however, vascular involvement is relatively rare. Here, we report an exceptional case who developed small bowel pseudo-obstruction followed by necrosis due to intestinal vascular AA amyloidosis. A 51-year old man was admitted because of abdominal pain and vomiting for several days. When he was 35 years old, he suffered from paralytic ileus and diagnosed as polyarteritis nodosa (PN) from the findings of dilatation and stenosis of renal and celiac arteries. He also had a history of rupture of left renal artery aneurysm at the age of 48. His PN was controlled with oral prednisolone 7mg/day and anti-platelet therapy. On this admission, he was diagnosed as viral enteritis, but developed small bowel pseudo-obstruction. On his 20th hospital day, he had small bowel perforation and an emergency surgery showed almost all small intestine necrotic and resected. Histopathological examination of the small intestine revealed no amyloidosis in lamina propria but broad deposition inside the blood vessels with occlusion. When patients with PN complicated with bowel pseudo-obstruction, it is important not only to consider intestinal ischemia due to vasculitis activity, but also to consider vascular amyloidosis.

P2-208

Two cases of polyarteritis nodosa diagnosed by lower limbs MRI and FDG-PET/CT

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Conflict of interest: None

[Introduction] Polyarteritis nodosa (PN) is an inflammatory disease in the small and medium arteries, and no clinical symptom except for fever are observed. We have reported two cases PN suspected by lower limbs MRI and FDG-PET/CT (PET-CT). [Case1] An 81 year-old man had weakness in the lower limbs and developed fever, and was admitted with high CRP level. Vasculitis was suspected, but no other clinical symptoms were observed on contrast-enhanced CT. Lower limbs MRI showed a high signal intensity along the blood vessel on STIR images. Muscle biopsy was not performed because of normal levels of ANCA and myogenic enzymes, so that we have diagnosed as PN. PSL (35mg/day) was started. [Case2] A 78 year-old man was hospitalized because of unknown origin of fever. No abnormalities were detected on CT. Giant cell arteritis was suspected due to fever, bilateral headache and high CRP level. PET-CT was performed because the temporal arterial echo images was normal. FDG accumulation was found on the bilateral popliteal artery, and we diagnosed PN. Steroid pulse treatments were started, and PSL (50mg/day) treatment continued. [Discussion] Even if no symptom is observed, lower limbs MRI and PET-CT should be done before angiography during the diagnosis of small and medium vasculitis.

P2-209

A case of localized nodular polyarteritis with muscle biopsy useful for diagnosis

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Conflict of interest: None

[Case] A 93-years-old man [Chief complaint] Both lower leg swelling [Progress] From August 2019, both lower leg swollen. On September 27, he was hospitalized for the purpose of examining the cause of lower leg swelling. Antibiotic treatment was started as cellulitis on the first day of the disease, but tenderness in lower legs were not improved. Necrotizing fasciitis was suspected by MRI in the lower leg muscles. On the 14th day, the right gastrocnemius and right soleus fasciotomy and muscle biopsy were performed. Pathological findings showed inflammatory cell infiltration around the artery wall and occlusion of the vascular lumen. On the 23rd day, treatment with PSL 45 mg was started. The symptoms of swelling of the gastrocnemius and tenderness improved, and the increase in inflammatory response also improved. The course of treatment was good, and the gradual decrease of PSL was started from the 37th disease day. [Consideration] The affected sites of polyarteritis nodosa vary from case to case, and many cases have been reported that are restricted to specific organs such as the skin, gallbladder, appendix, and genitals. We experienced a case of polyarteritis nodosa confined to the muscles, so we report it with a literature review.

P2-210

A case of polyarteritis nodosa with gastrointestinal perforation and peritonitis just after immunosuppressive treatment that we were able to save by emergency surgery

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Conflict of interest: None

The case is a 56 years old man. He had a stomachache, fever and anorexia from August, 2018. He was taken a wait-and-seeapproach though CRP was high and he had splenic infarction. He was hospitalized from the end of January, 2019, and cystography CT showed renal infarct newly. We performed angiography because suspected PAN, and it showed significant vascular irregularity and many microaneurysms with stenosis and expansion of the vascular diameter of a celiac artery, a superior mesenteric artery, both renal arteries. We started to administer mPSL pulse and IVCY every two weeks, but stomachache relapsed one week later, CRP rose to 39.87, and gastrointestinal perforation was suspected. We diagnosed the onset of intestinal perforation and peritonitis with polyarteritis nodosa, confirmed perforation in proximal jejunum by urgent abdominal operation, then performed small intestinal resection and constructed an artificial anus. The condition was settled down once, but we confirmed perforation of the transverse colon in CF and performed again transverse colon segmental resection by abdominal operation. It is said that advanced age and a gastrointestinal lesion are poor prognostic factor in PAN.

P2-211

The clinical features and characteristics of adult IgA vasculitis in our hospital

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Conflict of interest: None

[Objective] This study investigated the clinical features and characteristics of adults with IgA vasculitis (IgAV) in our hospital. [Methods] We retrospectively analyzed patients aged 18 years or older, diagnosed with IgAV and treated at our hospital between April 2013 and March 2018. The diagnosis of IgAV was based on meeting at least one criterion of the American College of Rheumatology (1990) and the European League Against Rheumatology / Pediatric Rheumatology International Trials Organization / Pediatric Rheumatology European Society classification criteria (2010). [Results] We identified 49 patients with IgAV. The mean age of the patients was 57.8 years, and 51% were male. Manifestations included skin lesions (89.8%), joint involvement (JI) (16.3%), gastrointestinal involvement (GI) (26.5%), and proteinuria/hematuria (67.3%). Renal complications (RC) identified by renal biopsy were present in 36.7%. Corticosteroids were used in 77.8% of patients with RC and 30% of those without RC. In cases without RC, corticosteroids were used in 42.9% of patients with JI and in 40% of those with GI. [Conclusions] The percentage of patients with JI and GI tended to be lower than in previous studies. Corticosteroids were used for the treatment of arthritis in 42.9% of patients with JI.

P2-212

Two cases of primary and secondary urticarial vasculitis in whom complement measurement led to diagnosis

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Conflict of interest: None

[Case 1] A 60-year-old male developed polyarthritis in March 2019. Leukopenia (3,700 /μl), CRP 3.1 mg/dl, antinuclear antibody x160, anti-ds-DNA antibody 236 IU/ml, CH50 <12.0 U/ml, pleural effusion was confirmed, and systemic lupus erythematosus (SLE) was diagnosed. Skin biopsy of urticaria lasting more than 24 hours showed leukocytoclastic vasculitis (LCV), and urticarial vasculitis (UV) secondary to SLE was diagnosed. [Case 2] A 67-year-old male suffered from urticaria for 20 years. He repeated fever lasting for several days after 2016. He was referred to our department in June 2019. Elevated CRP (1.41 mg/dl) and hypocomplementemia (CH50 11.0 U/ml) were observed. Skin biopsy showed LCV. No other cause, including other autoimmune diseases and drugs, was identified and he was diagnosed as having idiopathic UV and treated with prednisolone and tacrolimus. [Discussion] The proportion of idiopathic UV is reported to be high in 69-75% among reported UV. Making diagnosis is difficult in primary UV that has no other organ lesions than chronic urticaria. In our both cases, detection of hypocomplementemia despite high inflammatory response was led to the diagnosis. It is meaningful to make it known that measuring complement value leads to diagnosis in cases of chronic urticaria.

P2-213

Association between statin use and incidence of relapse in anti-neutrophil cytoplasmic antibody-associated vasculitis: a single-center retrospective cohort study

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Conflict of interest: None

Background: Little information is available about the impact of statins on relapse in antineutrophil cytoplasmic antibody-associated vasculitis (AAV). **Methods:** This single-center retrospective cohort study included 98 consecutive patients with newly diagnosed AAV from Aichi Medical University Hospital, Japan between March 2009 and December 2017. **Results:** During the follow-up period (median, 24 months; interquartile range, 9-50 months), 35 (97.2%) patients in the statin group achieved remission, whereas 56 (90.3%) patients achieved remission in the non-statin group (P=0.201). After achieving first remission, 9 (25.7%) patients in the statin group and 29 (51.8%) patients in the non-statin group had at least one relapse. Multivariate Cox proportional hazard models revealed that non-statin use was significantly associated with a higher incidence of relapse compared with statin use (multivariate-adjusted hazard ratio=2.44, 95% confidence interval: 1.08-5.47; P=0.031). **Conclusions:** Statin use was significantly associated with a lower risk of relapse in AAV. Our results should be assessed in well-designed randomized controlled trials.

P2-214

Significance of MR sialography in Sjogren's syndrome

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Conflict of interest: None

[Objective] Diagnosis of Sjogren's syndrome (SS) is made by oral, ophthalmological, serological examinations and labial salivary gland biopsy. Among several diagnostic methods, MR sialography is one of the least invasive test. In this study, we studied the significance of MR sialography in evaluation of SS. [Method] 49 SS patients who diagnosed by 1999 revised Japanese diagnostic criteria for SS from 2010 to 2019 were subjected for the study. The relationship of MR sialography findings (Rubin & Holt classification) with oral, ophthalmological, serological tests and labial salivary gland biopsy was analyzed. [Results] The MR stage assessed by Rubin & Holt classification was 0.88±3.4, the focus score was 1.39±3.4. There was a strong correlation between the MR sialography stage and the focus score (correlation coefficient 0.66, p=0.0004). Saxon test, ophthalmological examination and the autoantibody titer had little correlation with the MR sialography. [Conclusions] These findings suggest that MR sialography is useful technique not only for diagnosis but also for histological evaluation in SS.

P2-215

Improvement in xerostomia and salivary gland ultrasonography findings after steroid administration in secondary Sjogren syndrome

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Conflict of interest: None

[Introduction] Steroids are usually not administered for xerostomia in Sjogren syndrome (SS). We describe two patients with secondary SS who showed improvement in xerostomia and salivary gland ultrasonography (SGUS) findings after prednisolone (PSL) treatment for other conditions. [Case 1] A 42-year-old woman with systemic lupus erythematosus developed xerostomia and dry eyes 5 years before admission. She presented for lupus nephritis treatment and was also diagnosed with SS. She received PSL (40mg), mycophenolate mofetil, tacrolimus, and hydroxychloroquine. Xerostomia disappeared 6 months later. Power Doppler signals (PD) on SGUS changed from moderate to weak, and the 14-item Oral Health Impact Profile (OHIP-14) score reduced from 28 to 18. [Case 2] A 45-years-old woman who received etanercept and tacrolimus for rheumatoid arthritis developed xerostomia 6 months prior to presentation and was diagnosed with SS. She received pilocarpic acid, which was discontinued owing to ineffectiveness. PSL (7.5mg) was administered for polyarthritis. Xerostomia reduced 2 weeks later and disappeared 3 months thereafter. PD changed from high to weak, and the OHIP-14 score reduced from 38 to 18. [Conclusion] PD on SGUS successfully predict the efficacy of PSL to treat xerostomia in secondary SS.

P2-216

The study of ACR / EULAR 2016 classification criteria for Sjogren's syndrome using ultrasonography of salivary glands

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Conflict of interest: None

[Objective] The revised criteria for the diagnosis of SS proposed by the Japanese Ministry of Health (JPN criteria) and it has been reported that sensitivity is 79.6% and specificity is 90.4%. Though the 2016 ACR-EULAR classification criteria (The 2016 criteria) were published, it is difficult to perform salivary gland biopsy in all cases. In recent years, the development of imaging has been remarkable, and we have retrospectively examined whether US can be used instead of biopsy. [Methods] The study subjects were 64 patients (Pt). All patients had been assessed for ocular, oral, blood test and imaging. The clinical diagnosis by the physician in charge was set the 'gold standard'. [Results] JPN criteria were sensitivity 42.8% and specificity 100%. The 2016 criteria were sensitivity 76.2% and specificity 90.9%. When US grade 2 or higher instead of biopsy, the sensitivity increased further to 81.0% and specificity 91.9%. 8 Pt that were clinically diagnosed but were negative for the 2016 criteria, 2 Pt were positive for the anti-centromere antibody and all Pt were US grade 1 or less. [Conclusions] Although the 2016 criteria had high sensitivity and specificity. US improved diagnostic ability. The limit is that there is no case of biopsy, and the problem is whether it can be instead of biopsy.

P2-217

Effects of hydroxychloroquine treatment on ESSPRI and ESSDAI in patients of primary Sjogren's syndrome with cutaneous lupus erythematosus

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) is commonly used to treat arthralgia and fatigue of primary Sjogren's syndrome (pSS) in western countries. However, its efficacy in treatment of pSS is in dispute, and insurance coverage of HCQ are limited to SLE and CLE in Japan. The aim of this study was to evaluate the effect of HCQ on ESSPRI and ESSDAI in pSS with CLE. [Methods] Twenty-two pSS patients with CLE were studied. The clinical indexes were evaluated by ESSDAI, ESSPRI, IgG and CH50 before and after HCQ treatment. [Results] Four of 22 patients had adverse effects of cutaneous eruption. The total ESSPRI, ESSPRI fatigue and pain domain were significantly decreased after HCQ treatment than before HCQ treatment (ESSPRI: 4.26±1.56 vs 3.56±1.64, p=0.02, fatigue: 5.00±2.17 vs 3.89±2.08, p=0.02, pain: 3.44±2.06 vs 2.22±1.70, p=0.01). HCQ treatment was associated with a decrease in total ESSDAI, ESSDAI articular and biological domain (ESSDAI: 9.00±3.74 vs 6.56±3.93, p=0.003, articular: 1.00±1.24 vs. 0.44±0.86, p=0.03, biological: 1.00±0.84 vs 0.78±0.94, p=0.046). IgG level after HCQ treatment was also significantly lower than before HCQ treatment (1898±621 vs 1800±601, p=0.008). [Conclusions] HCQ treatment was effective in reducing fatigue and pain with immunological improvement in pSS with CLE.

P2-218

Saxon test results and VAS evaluation of patients with SjÖgren syndrome - based on antibody values and medication

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Conflict of interest: None

Purpose: we conducted Saxon tests in patients with Sjögren syndrome through coordination with medical institutions. **Methods:** We created a tabulation based on five sets of results: Saxon test results, antibody test results, dose information found in medication records, patient VAS (discomfort, difficulty speaking, difficulty eating, or difficulty sleeping due to dry mouth), and questionnaires about the effectiveness and side effects of drugs for treating xerostomia as well as adherence to taking them as prescribed. **Results:** The mean Saxon test result was 1.76 g with 203/331 patients showing results of 2.0 g or less. We observed a weak correlation between the Saxon test and patient VAS. Regarding the relationship between xerostomia drugs and patient quality of life, we found that patients freely adjust their own dosages due to side effects even when they feel the effectiveness of the medication. Thirty percent of patients have regularly gargled, worn masks, or used dietary restrictions since their symptoms appeared. **Conclusion:** Since the Saxon tests produces results easily in a short period of time, it can be used to gain a mutual understanding of a patient's dry-mouth situation together with them. Verifying the effectiveness of medication is also a simple matter.

P2-219

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.

P2-220

Sjögren syndrome accompanied with idiopathic CD4 lymphocytopenia and disseminated cryptococcosis

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Conflict of interest: None

A 39-year-old woman was referred to our hospital because of a 3-month-history of back pain, and a 2-week-history of cough. Laboratory findings showed a white blood cell count of 5,900/μL, with a lymphocyte count of 620/μL, and C-reactive protein level of 11.6 mg/dL. CT scan revealed a lung nodule, subcutaneous mass, and multiple osteolytic lesions. Cultures of the subcutaneous mass and lung tissue yielded *Cryptococcus neoformans*. Her CD4 T-cell count was only 33/μL without HIV infection. We diagnosed her with idiopathic CD4 lymphocytopenia (ICL) and disseminated cryptococcosis. The coexistence of Sjögren syndrome (SS) was recognized due to positive results of anti-SS-A antibodies, Schirmer's test, and gum test. We initiated treatment with liposomal amphotericin B and switched to fluconazole. Her clinical condition remains stable although her current CD4 T-cell is low. We continue to follow her and there is no extraglandular manifestation of SS so far. ICL is a rare disease characterized by marked loss of CD4 T-cell without HIV infection. One report showed that 5.2% of SS patients was accompanied with ICL. We should consider a possibility of the coexistence of ICL if an opportunistic infection occurs in SS patient without use of glucocorticoid or immunosuppressive therapy.

P2-221

A case of steroid resistant protein leaking gastroenteropathy (PLGE) associated with Sjogren's syndrome (SS)

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Conflict of interest: None

[Case] 43-year-old woman was referred because of facial edema and positive ANA test. Since she gradually gained weight (7kg/month) and dyspnea and edema of extremities were started, she was admitted. [Course] Hypoalbuminemia (1.8g/dL) was observed, and CT scan showed existence of ascites and pleurisy. However, urinary test revealed normal and no evidence of malignancies were observed. Protein leakage was detected at small intestine by the scintigraphy. As an underlying disease, she was diagnosed as SS based on positive anti-SS-A antibody, Saxon test, and salivary gland scintigraphy findings. Taken together, the diagnosis of PLGE associated with SS was made. Then 1mg/kg/day of PSL was started, but she was refractory. So IVCY, albumin supplementation, and ascites filtration concentration reinfusion were introduced, but hypoalbuminemia was still progressed. At day 111 after PSL initiation, albumin was begun to rise eventually and reached to 3.1g/dL at day 131. Her symptom was also improved when discharged. [Conclusions] In general, PLGE with CTDs has good response to glucocorticoid, suggesting involvement of inflammation. However, it should be noted that some are refractory and need a few months to normalize and multidisciplinary approach including long-term immunosuppression.

P2-222

Clinical presentation of two cases with IgG4-related coronary periarteritis successfully treated with corticosteroid

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Conflict of interest: None

[Case 1] An 83-year-old woman. She had the prominence of the aortic arch pointed out by a medical examination of January, 2019 and visited our hospital cardiovascular surgery. IgG4 was1,090 mg/dl shown by a blood test, and soft part shadow to occur around a chest abdominal aorta and coronary arteries frequently was found in computed tomography scan. She became the hospitalization in our department in March. We started 30 mg of prednisolone on April, and the reduction of the soft part shadow around the coronary arteries was detected. [Case 2] A 70-year-old man. Myocardial infarction developed in 2018 and was treated in another hospital. Coronary angiography showed soft part shadow around a left coronary artery in November, and IgG4 was 544 mg/dl shown by a blood test. He was hospitalized in our department in July 2019. We started 30 mg of prednisolone in July, and the reduction of the soft part shadow around the coronary arteries was detected. [Discussion] There are the reported cases such as rupture, and the like of the coronary artery aneurysm by steroid administration for the coronary lesion due to the IgG4 associated diseases. It is thought that careful follow-up will be necessary for the disorder in future.

P2-223

A case of IgG4-related urethral tumor emerging during the long-term clinical follow-up without any medication after extirpating bilateral lacrimal gland

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Conflict of interest: None

[Objective] IgG4-related disease with urethral lesion [Methods] Case report [Results] A 67-year-old woman was admitted to our hospital with complaints of dysuria. She had been diagnosed as IgG4-related Mikulicz disease from specimen obtained by bilateral lacrimal gland excision 5 years ago. SHe had multiple lymphadenopathy and multiple renal nodules, which was relieved after the surgery. So, we administered neither corticosteroids nor immunosuppressants. She realised difficulty urinating, and her computed tomography showed soft tissue surrounding her urethra. Urologists biopsied the lesion, wihich was compatible with IgG4-related disease, including prominent infiltration of eosinophils and plasma cells, IgG4/IgG ratio >80%, obliterative phlebitis. We administered prednisolone 15mg and her dysuria was resolved. [Conclusions] IgG4-related disease is an autoimmune disease with high serum IgG4 level and plasma cell-rich mass lesion in various organs. Although it is well known that the disease affect lacrimal glands, salivery glands, and pancreas, a urethral lesion is not common. We report the case with several literature review.

P2-225

Deep vein thrombosis due to periarteritis and intraabdominal mass caused by IgG4-related diseases

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Conflict of interest: None

[Case] A 78-year-old male without particular past medical history. He became aware of redness, swelling, and pain of the entire left lower limb. The laboratory data showed elevation of D-dimer level, and contrast-enhanced CT scan revealed pulmonary embolisms and DVT from the left iliac vein to the IVC. We placed an IVC filter and started rivaroxaban. The CT scan also showed periarterial inflammation from the aorta to the bilateral iliac arteries and a 6mm irregular mass in the mesentery. Serum IgG4 levels increased, so we suggested that thromboembolism was caused by vein compression due to a periarteritic mass, one of the lesions of IgG4-related diseases (IgG4-RD). For the intraabdominal mass, a laparoscopic biopsy was performed, and it revealed a result consistent with IgG4-RD, including severe fibrosis, infiltration of lymphoid and plasma cell, the elevation of IgG4/IgG ratio. Periarteritis and intraperitoneal masses spontaneously showed disappearing tendency. [Discussion] There were many reports of deep vein thrombosis due to retroperitoneal lesions of IgG4-RD, but thrombosis due to periarteritis was very rare. In the case of IgG4-RD, immediate treatment is required for important organ lesions, but there is no clear treatment consensus for other lesions like our case.

P2-226

A case of IgG4-related disease diagnosed by renal biopsy accompanied with slowly progressive insulin-dependent diabetes mellitus

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Conflict of interest: None

A 74-year-old man was admitted to our hospital because of jaundice and elevated cholestatic liver enzymes. Abdominal contrast enhanced computed tomography (CT) scan showed the intrahepatic bile duct dilatation, a swelling of pancreas, and multiple local and diffuse patchy lesions in the bilateral renal parenchyma. In addition, serum IgG4 level was remarkably elevated. Then, we speculated IgG4-related disease (IgG4+RD). Renal biopsy for definitive diagnosis was performed, although his urinalysis and renal function were normal. Renal biopsy showed the infiltration of IgG4-positive plasma cells with storiform fibrosis in the interstitium. On the other hand, carbohydrate metabolism disorder and impaired insulin secretion with serum anti- glutamic acid decarboxylase antibody had been observed, as a result of being diagnosed as slowly progressive insulin-dependent diabetes mellitus (SPIDDM). Oral prednisolone for IgG4+RD and intensive insulin therapy for SPIDDM were administered, resulting in normalization of serum bilirubin and improvement of cholestasis and glycemic control. This is the rare case of IgG4+RD accompanied with SPIDDM, suggesting that immunological disorders associated with IgG4-

RD were related to the pathogenesis of SPIDDM.

P2-227

A case with rapid progression of pulmonary nodules and elevated serum IgG4 level

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Conflict of interest: None

A 63-year-old woman with a history of pulmonary nodules and hilar lymphadenopathy presented a year ago with bilateral salivary and lacrimal gland swelling. Her serum IgG4 level was increased and Saxon test was positive. She was started on 10mg/day of prednisolone (PSL) following which her symptoms of swelling improved. During admission in our hospital, she developed high fever, left blepharitis, salivary and lacrimal gland swelling, and increased level of CRP. She had a CT scan which showed multiple pulmonary nodules and bilateral hilar lymphadenopathy. Bronchoscopy was performed. While we tried to exclude other disease that may show IgG4-related disease (IgG4-RD)-like manifestations, hypoxia developed due to the rapid progression of pulmonary nodules. She was given high dose of intravenous methylprednisolone, followed by oral glucocorticoid therapy (PSL 1mg/kg), and responded promptly to the treatment. The hilar lymph node biopsy previously provided by another hospital was assessed and did not fulfilled diagnostic criteria for IgG4-RD and different diagnostic disease. This case provides an unusual presentation of IgG4-RD. When we see the patients showing the characteristics with tumor-like lesions at multiple sites, histopathologic examination should be performed immediately.

P2-228

A case of IgG4 related lymphadenopathy with an orbital tumor

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Conflict of interest: None

[Case] A 68-year-old male came to our hospital due to right ocular proptosis and right cervical mass. CT revealed a lymph node enlargement in the right neck, and MRI showed an orbital tumor around the upper ocular vein. IgG4 was 240 mg/dL. Lymph node biopsy revealed follicular hyperplasia and eosinophil infiltration in the interfollicular region. And it also revealed infiltration of IgG4-positive plasma cells into the germinal center, and the ratio of IgG4-positive cells to total IgG positive cells was 40% or more in the entire lymph node. Based on these results, we diagnosed IgG4-related lymphadenopathy (Progressively transformed germinal centers-type). We considered that an orbital tumor was a part of IgG4-related disease, and steroid administration (prednisolone 30 mg/day) was started. The right ocular proptosis was improved within 1 week, and we tapered the steroid dose gradually. However, the recurrence of the orbital tumor occurred twice over the next 3 years. After the second recurrence, we added azathioprinea and successfully reduced steroid dose without recurrences. [Conclusion] We experienced a case of IgG4-related lymphadenopathy with an orbital tumor. We report the clinical course of this case with a review of the literature.

P2-230

Comparison of serum biomarkers for the diagnosis of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis during tocilizumab therapy

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Conflict of interest: None

[Objective] This study aimed to compare the accuracy of serum biomarkers for the diagnosis of macrophage activation syndrome (MAS) complicating systemic juvenile idiopathic arthritis (s-JIA) during tocilizumab therapy. [Methods] Serum cytokine levels of neopterin, IL-18, CXCL9, soluble tumor necrosis factor receptor (sTNFR)-I, and sTNFR-II were determined by ELISA in 37 patients with MAS complicating s-JIA, including 13 patients receiving tocilizumab. [Results] The levels of all serum cytokines at MAS diagnosis were significantly lower in the tocilizumab-treated group than in the tocilizumab-untreated group. In contrast, the serum sTNFR-II/I ratio at MAS diagnosis was comparable between the tocilizumab-treated and the tocilizumab-untreated groups. The ROC analysis revealed that the area under the curve and cut-off values of sTNFR-II/I ratio were 0.9796 and 4.71, respectively. The serum sTNFR-II/I ratio was correlated positively with disease activity. [Conclusions] These findings suggest that the serum sTNFR-II/I ratio might be a useful indicator to evaluate disease activity in MAS complicating s-JIA even in tocilizumab-treated patients and might be considered a useful diagnostic marker for the transition from active-phase s-JIA to MAS during tocilizumab therapy.

P2-231

A case of refractory adult transition systemic juvenile idiopathic arthritis (sJIA) successfully treated with Canakinumab

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Conflict of interest: None

[Case] 22-year-old male [Principal complaint] Fever [Progress] Diagnosed as sJIA at age 14. He received Infliximab (IFX), Methotrexate (MTX), Prednisolone (PSL), but their effects were poor. He consulted in X-3. He was changed to Tocilizumab (TCZ) in September due to fever and CRP rise. However, fever and CRP were not negative. In X-2 he was suspected in macrophage activation syndrome. He was taken PSL 1mg/kg. When the dose of PSL gradually decreased, fever was observed, and we changed TCZ to IFX, MTX, Tac. After that, CRP did not become negative, and administration of Golimumab 100 mg in April X-1 was ineffective. In August X, the disease did not improve, and he was treated with TNFi and TCZ but considered to be resistance. Therefore, Canakinumab (CAN) 300mg was administered. It was administered 4 times, and CRP was improved to 0.5mg / dl, and no fever or joint pain was observed. [Discussion] This case was considered to be IL-18 dominant. CAN has been applied to sJIA and its effectiveness has been reported. In this case, several biologics were used as sJIA adult transition cases, but the disease control was poor. Symptom improvement was confirmed by administration of CAN, it is expected to be effective for sJIA adult transition cases and adult-onset Still's disease.

P2-232

Treatment and prognosis of 4 cases of Juvenile idiopathic arthritis (JIA) with cervical spondyloarthritis

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Conflict of interest: None

The most common cervical spinal changes related to Juvenile idiopathic arthritis (JIA) are fusion of cervical joint, atlantoaxial subluxation, atlantoaxial rotatory fixation, etc. Most reports indicate that TNF inhibitors have the efficacy for these conditions. We report treatment and prognosis of 4 cases of JIA with spondyloarthritis. Case 1: 42 year old female with history of JIA and ulcerative colitis presented with chronic neck pain, back pain and numbness of extremities. Vertebral fusion, atlantoaxial dislocation, and cervical spondylotic myelopathy were observed. 34 years after onset, Golimumab was initiated. Case 2: 16 year old male had HLA-B27 positive enthesitis related arthritis (ERA) with atlantoaxial sub-

luxation. 4 years after onset, he started Adalimumab (ADA) and has been on remission. Case 3: 3 year old female had seropositive polyarticular JIA with cervical rotatory fixation. 2 years after onset, ADA was initiated and she has been on remission. Case 4: 10 year old female had ERA with atlantoaxial rotatory fixation. 3 months after onset, we gave ADA and the remission was achieved. Summary: Patients with delayed introduction of TNF inhibitors tended to have severe cervical complications. We should consider TNF inhibitors soon after diagnosis of spondyloarthritis.

P2-233

The situations and problems of juvenile idiopathic arthritis cases visited from China

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Conflict of interest: None

With the affluence of China and the spread of the internet, there is an increasing number of travelers visiting Japanese medical institutions. As for pediatric rheumatology, an international consensus on medical strategy has yet to be reached in Asia. [Objective] We examined the situations and problems of juvenile idiopathic arthritis (JIA) cases visited from China. [Methods] The Chinese children who visited our institute from January to September 2019 were enrolled. Their clinical information were retrospectively reviewed. [Results] All six cases were JIA (five oligoarticular and one systemic). Most of them were previously visited University or children's hospitals in China. Upon the diagnosis of synovitis, joint ultrasonography was never applied. As for treatment, contraindicated medications for pediatric use in Japan were frequently used. The dosage and usage of methotrexate and biological agents were inappropriate. All cases requested a prescription in Japan because they believe that medications produced in China were of low purity. Their medical care was not seemed to be based on unified guidelines. [Conclusions] It is suspected that many other JIA cases are receiving inappropriate medical care in China. We need to standardize medical care in Asian pediatric rheumatology.

P2-235

Clinical features of children with enthesitis

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Conflict of interest: None

[Introduction] Children with enthesitis are included into enthesitis-related arthritis (ERA), psoriatic arthritis or unclassifiable juvenile idiopathic arthritis (uJIA). Although some of those have been repoted to be child-food-onset cases of adult spondyloarthritis, they are difficult to diagnose early, have low remission rates, and their prognosis is still unclear. [Object and Methods] We included children clinically diagnosed or suspected of enthesitis, who under 16 years old and referred to our department between February 2016 and November 2019. [Results] 16 patients, 9 were males. age of onset and at visit were 9.5 (3-14) and 11.0 (6-16) years old. Chief complaints were polyarthralgia, hip pain, general pain and others. 14 had enthesis tenderness, including Achilles tendon, plantar fascia. 10 had sacroiliac tenderness and 9 showed sacroiliac arthritis in MRI. Initial diagnosis was 3 ERAs, 8 suspected ERAs and 5 uJIA. Treatment were NSAIDs, salazosulfapyridine, methotrexate, prednisolone, adalimumab and baricitinib. 3 are in drug-free remissions, 4 in remissions under medication and 9 in non-remissions. [Conclusions] Appropriate management of enthesitis requires early diagnosis. Final diagnosis and prognosis will be discussed.

P2-238

Four cases of NXP-2 antibody positive juvenile dermatomyositis

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Conflict of interest: None

[Case 1] A 6-year-old boy presented with rash and muscle weakness. Combined with macrophage activation syndrome (MAS), glucocorticoid (GC), intravenous immunoglobulin (IVIG), mycophenolate mofetil (MMF), methotrexate (MTX) treatment led to remission. [Case 2] An 11-year-old girl presented with rash, myalgia and muscle weakness. Remission was achieved with GC and MTX. [Case 3] A 2-year-old boy presented with rash, muscle weakness, and dysarthria. GC and IVIG treatment were undergo. MAS was combined, followed by intravenous cyclophosphamide (IVCY). There was aspiration during the course. After discharge, relapse was observed repeatedly. [Case 4] A 5-year-old boy presented with rash, myalgia and muscle weakness, and dysarthria. He was treated with GC and IVCY, and remissioned with plasma exchange and IVIG. During the course, aspiration pneumonia was repeated. After discharge, the patient relapsed repeatedly. [Discussion] NXP-2 has been reported that muscle weakness is strong, remission rate is low 2 years after the start of treatment. This case also showed significant muscle weakness, and in the case with dysarthria, also caused respiratory disorder. There were two cases of MAS. In cases of NXP-2 antibody positivity, aggressive treatment were considered necessary.

P2-240

Ultrasonography of salivary glands in children with primary Sjogren's syndrome

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Conflict of interest: None

Objective: We examined the characteristics of ultrasonography of salivary glands in children with primary Sjogren's syndrome. Method: Twenty pediatric patients (male 3, female 17, aged 12.8±3.5 yrs.) with primary Sjogren's syndrome that underwent ultrasonography of both parotid and submandibular salivary glands from August 2012 to September 2019 were enrolled. Disease characteristic findings were recorded and their frequencies were calculated. Results: Multiple hypoechoic areas in salivary glands and hyperechoic spots were revealed in 80% and 35% (16/20, 7/20 cases), respectively. Increased Doppler signal was found in 20% (4/20 cases). Of the cases showing multiple hypoechoic areas, 50% were in both parotid and submandibular glands, 37.5% in the parotid gland, and 12.5% in the submandibular gland. Conclusion: In primary Sjogren's syndrome in children, characteristic ultrasonography findings of salivary glands were observed at a high rate. Detection rate could increase by examining both parotid and submandibular glands.

P2-241

A 13 years-old-boy with haploinsufficiency of A20 showing clinical features of SLE

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Conflict of interest: None

[Background] Haploinsufficiency of A20 (HA20) was initially identified as early onset Behçet-like phenotype. However, the other phenotypes like SLE with it are also reported. We reported a boy of SLE with an abscess of the gluteus maximus muscle at the 63th annual meeting of JCR. As the boy has been made a final diagnosis as HA20, we report a newly getting findings again. [Case report] A 13 years-old-boy was admitted with pyrexia and diarrhea. His mother has Sjögren syndrome. He was made a diagnosis as SLE, and occurred with an abscess of the gluteus maximus muscle. He was treated by an antimicrobial agent and a drain. His conditions improve by treatment for SLE. Because of his unimproved hypogammaglobulinemia and his mother's past history, we performed further ex-

aminations to rule out primary immunodeficiency (PID). Thus, we made him as HA20 because of *TNFAIP3* gene mutation. [Conclusions] If patients show unexpected features of SLE and/or have family history of autoimmune diseases, it needs to rule out monogenic SLE as several PIDs, and take a notice of PIDs for avoiding unnecessary immunosuppressants. [Acknowledgement] We thank Dr. Kohsuke Imai (the Department of Pediatrics and Developmental Biology, Tokyo Medical and Dental University) for his valuable advice and suggestions.

P2-242

A case of pediatric systemic lupus erythematosus effectively treated with belimumab for coagulopathy associated with increased disease activity

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Conflict of interest: None

[Case] 12 years old girl. Past history: Absence seizure since she was 6 years old. Family history: Elder brother has epilepsy. History of present illness: She developed SLE at 9 years old (lupus nephritis class 2). She received 3 courses of methylprednisolone pulse therapy and was in remission. There was possibility of the antiphospholipid antibody syndrome because of the positive lupus anticoagulant and anti-CL-β2GPI, although she had no thrombosis or thrombocytopenia. Therefore, she was treated with prednisolone (PSL), tacrolimus (Tac) and aspirin. When the dose of PSL was reduced to 0.4 mg/kg/day, decreased complement, increased anti-dsDNA antibody, and blood FDP and D-dimer were increased. Although Tac was changed to azathioprine, the effect was insufficient. So, it was changed to mycophenolate mofetil (MMF) and hydroxychloroquine was added. The blood test was improved, and PSL was reduced to 0.16 mg/kg/day. When she was 12 years old, FDP, D-dimer and anti-dsDNA antibody levels were elevated. We started belimumab treatment, blood tests quickly normalized after 3 doses, and PSL was successfully reduced. [Conclusions] Belimumab might be effective in coagulation abnormalities associated with disease activity in pediatric SLE.

P2-243

An autopsy case of suspected TAFRO syndrome with acute course systemic edema

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Conflict of interest: None

A 62-year-old female was admitted to the hospital with complaints of fatigue, systemic edema. Increased inflammatory response and increased hepatobiliary enzymes was seen. Thrombocytopenia, acute renal failure, and pleural effusion were observed. PSL was started after lymph node biopsy and bone marrow biopsy. At the day20, hemodialysis and ventilator management were initiated. Based on systemic edema, thrombocytopenia, high inflammatory response, mild hepatosplenomegaly, progressive nephropathy, and result from lymph node biopsy, TAFRO syndrome was diagnosed. The treatment was continued under the condition of ventilator and hemodialysis, and the steroids, plasma exchange, CyA, TCZ, and RTX were used as medication. However, no improvement was observed, and the patient died on day55. During the course, a persistent increase in hepatobiliary enzymes and a transient increase in amylase were observed. Histopathology revealed cholestasis in the bile duct, acute pancreatitis, cirrhosis of the liver, renal tubular necrosis, and interstitial fibrosis. It is important to diagnose TAFRO syndrome to exclude differential diagnosis. Although the symptom and clinical course of the case shows TAFRO syndrome, none of the histopathological result showed the evidence of TAFRO syndrome.

P2-244

The effectiveness of short-term steroid can be effective of Fibromyalgia

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Conflict of interest: None

Objects: To investigate the effective ness of short-acting steroids for pain of Fibromyalgia. Methods: In 20 cases diagnosed with Fibromyalgia, when hydrocortisone sodium succinate 250mg +Neurotropin 2A was administered. The degree of pain can be more improved when using hydrocortisone sodiem 250mg using the scale. Results: In 16 of 20 cases, significant improvement of pain was obserbed when hydrocortisone sodium succinate 250mg +Neurotropin 2A was adminisstered, compare to using Neurotoropin 2A alone was adoministered. In 2 cases, the improvement of pain was more effective using Neurotoropin 2A only. Conclusion: In 16 cases out of 20, the degree of improvement of pain was clearly more effective than using Neurotoropin 2A only. The effectiveness of short-acting steroids can be due to factors such as cytokine involved in pathogenesis of Fibromyalgia.

P2-245

A case of seronegative systemic sclerosis diagnosed by the onset of intestinal pseudo-obstruction as the first obvious symptom during the course of rheumatoid arthritis

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Conflict of interest: None

[Case] A 60-year-old woman with a 14-year history of rheumatoid arthritis (RA) felt palpitation. She was pointed out to have pericardial effusion. She was treated with 30 mg/day of prednisolone. However, pericardial effusion worsened, and pericardial drainage was needed. Pericardial effusion was exudative but infection and malignancy were denied. After pericardial effusion was controlled, abdominal pain and vomiting suddenly appeared. Intestinal pseudo-obstruction (IPO) was diagnosed. She was transferred to our hospital. She had never noticed Raynaud's phenomenon nor telangiectasia, but thickness of skin was detected on her dorsal hand, forearm, and abdomen. Antinuclear antibody, anti-Scl-70 antibody, anti-RNA polymerase III antibody and anti-centromere antibody were all negative. Abdominal CT images showed pneumatosis cystoides intestinalis (PCI), and abdominal skin biopsy showed increased collagen fibers and decreased cutaneous adnexal density. She was diagnosed having systemic sclerosis (SSc). The IPO was considered to associate to SSc. [Discussion] This case lacked typical skin manifestations and autoantibodies, thus having SSc was missed until she developed IPO and PCI. To report this case is important in considering the course and pathogenesis of SSc.

P2-246

A case of porokeratosis complicated with Adult-onset Still's disease

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Conflict of interest: None

Porokeratosis is a rare disease characterized by association with genetics, ultraviolet radiation and immunosuppression. We report a case of porokeratosis complicated with Adult-onset Still's disease. A case is a 69 years old female who had had brownish rash on her face and four extremities since her 40s. She presented to our dermatologist because of itchy erythematous patches on the brownish rash one week after her first pylorus eradication. Topical corticosteroid and antihistamine-1 were initiated which led to worsening of the rash. The biopsy of the skin from the erythematous patch revealed typical characteristic of porokeratosis and necrosis and liquefaction degeneration which could be seen in AOSD. She was referred to our department because of fever, arthralgia, and high LDH level. We diagnosed her as AOSD from classification criterion by Yamaguchi et al (1992). Prednisolone 5 mg was initiated which improved the erythematous rash, but arthralgia and hyperferritinemia were persistent. Prednisolone 40 mg led to remission and no relapse of AOSD or porokeratosis has occurred while we tapered dose of prednisolone at 1.5 mg. Porokeratosis is thought to be associated with immunosuppression, so we should be

careful when we treat a patient with autoimmune disease with porokeratosis.

P2-247

Unusual organ involvement in sarcoidosis: sarcoid myopathy and peritoneal sacroidosis

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Conflict of interest: Yes

[Case] 64 y. o female [Chief complaint] muscle weakness [History of present illness] 7 years earlier, the patient was treated with methotrexate for polyarthritis with positive rheumatoid factor, but discontinued the medication due to liver dysfunction. 3 months earlier, periorbital swelling with proximal muscle weakness and abdominal pain developed. CT scan showed misty mesentery with moderate ascites. MRI of the right arm revealed diffuse high STIR signals of muscles. Laboratory data showed normal creatin kinase, elevated aldolase and CA125 levels (15.3 U/L, 270.1 U/ml, respectively). Exploratory laparoscopy showed multiple white nodules in the round ligament of the liver, greater omentum, and peritoneum. The right triceps and peritoneal biopsy showed noncaseating granulomas with multinucleated giant cells, which is consistent with sarcoidosis. Oral prednisolone 20mg daily and methotrexate failed to improve abdominal pain, and the patient complained of blurry vision. Opthalmologic examination was consistent with uveitis due to sarcoidosis. Infliximab improved visual symptoms and abdominal pain. [Discussion] Muscle and peritoneal biopsy provided diagnostic clues for sarcoidosis with myopathy and peritoneal involvement, when hilar adenopathy was absent.

P2-248

Castleman disease complicated with Connective tissue disease: two cases and review

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Conflict of interest: None

We report two cases of Castleman's disease (CD) complicated with connective tissue disease (CTD). **Case 1:** 63-year-old man, who had a 13-year history of rheumatoid arthritis (RA) and maintained remission, developed thrombocytopenia, pleural effusion, hepatosplenomegaly, lymphadenopathy, and proteinuria. Biopsied specimen of lymph node revealed the diagnosis of multicentric CD. Therapeutic efficacy of high-dose prednisolone (PSL) was insufficient; subsequently, tocilizumab (TCZ) was administered, achieving in remission. **Case 2:** 34-year-old woman indicated fever, arthritis, skin rash, pleural effusion, and lymphadenopathy since 6 months. She was diagnosed with Sjögren's syndrome; in addition, histology of lymph node lead to the diagnosis of multicentric CD. She was treated with high-dose PSL, whereas additional administration of TCZ was required because of relapse in lymphadenopathy and arthritis, consequently resulting in the achievement of remission. **Consideration:** Given our report as well as some previous cases, majority of patients with CD, who were concomitantly diagnosed with CTD or in remission phase of underlying CTD, demonstrated refractory to PSL monotherapy, suggesting that additional administration of TCZ may be required for improving prognosis.

P2-249

Refractory relapsing polychondritis successfully treated with adalimumab

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Conflict of interest: None

Relapsing polychondritis (RP) is a rare immune-mediated disease that is associated with inflammation in cartilaginous tissue throughout the body. The retrospective study showed the efficacy of biologics to treat patients with RP who were resistant to non-biologic DMARDs. A 28-year-old Japanese woman presented with a worsening of hearing the loss on the right side during combination therapy with tocilizumab. Biopsy of auricular cartilage revealed auricular chondritis, she was diagnosed with RP at the age of twenty-three. Her hearing loss on the left side and auricular chondritis were gradually exacerbated despite multiple conventional immunosuppressive therapies with glucocorticoids in combination with azathioprine, or infliximab with methotrexate, or tocilizumab with methotrexate. After switching from tocilizumab to adalimumab, her hearing loss on the right side and audiometry were improved.

P2-250

An Early Eosinophilic Fasciitis requiring differentiation from Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: None

[Case report] A 47 year-old man presented with bilateral lower leg edema and back pain. His past history was adult-onset asthma for 10 years. On examination, there were bilateral non-pitting edema with tenderness and sensory dullness. Laboratory studies showed peripheral eosinophilia and elevated C-reactive protein and erythrocyte sedimentation rate. Working diagnosis was EF, but eosinophilic granulomatosis with polyangiitis (EGPA) was differential diagnosis. Lower leg Magnetic Resonance Imaging (MRI) revealed increased signal intensity within superficial and deep fascial layers of gastrocnemius muscle. Skin to muscle biopsy showed diffuse inflammatory infiltrates within the fascia, composed lymphocytes and eosinophils. We diagnosed with EF and administered prednisone 60mg per day. His symptoms promptly resolved within a few days. [Discussion] Previous study reported that 79% of EF patients were initially misdiagnosed and another study showed a poor outcome was associated with a diagnosis time delay. To our knowledge, there is no report on the relationship between EF and adult-onset asthma. In our case, MRI and biopsy were useful for early diagnosis.

P2-251

A case of adult Still's disease successfully treated with anti-IL-1 inhibition therapy

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Conflict of interest: None

There are few reports on anti-IL-1 inhibitor therapy for adult Still's disease (ASD) in Japan, but anti-IL-1 inhibitor therapy is also performed overseas. This time, we report a case of AOSD using anti-IL-1β antibody, canakinumab, that was very effective. The case was a 67-year-old woman. ASD was diagnosed based on fever, skin rash, increased neutrophils, liver dysfunction, hepatosplenomegaly, lymphadenopathy, Ferritin> 40,000 ng / ml, IL-18 303,000 pg / ml. Although glucocorticoid administration improved fever, high levels of CRP and Ferritin persisted. When Canakinumab 150mg was administered by subcutaneous injection twice at a 2-week interval, it quickly improved. Tocilizumab is also used for intractable cases of ASD, but sometimes macrophage activation syndrome cannot be controlled, and for severe cases it is better to have many treatment options. There are few clinical trials for rare intractable diseases, and even globally effective treatment cannot be performed. In rare intractable diseases, the accumulation of case reports may lead to the expansion of new indications for treatment, and the effectiveness of IL-1 inhibitor therapy for ASD is clear worldwide, but reports in Japan Since there is almost no, we will report this time.

P2-253

A case of pulumonary arterial hypertension (PAH) associated with Adult onset Still's disease (AOSD)

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Conflict of interest: None

4 years ago, A 20-year-old woman was diagnosed as AOSD by skin eruption, joint pain, neutrophil-dominated leukocyte elevation, sore throat, and negative test for RF/ACPA. She was treated with an immunosuppressant and a PSL. TCZ was started 4 years ago because of treatment resistance, but relapsed repeatedly, and TCZ subcutaneous injection (162mg/week) was introduced 6 months before hospitalization. From May20XX, she was hospitalized with fever and respiratory distress. Blood test showed an elevated CRP, Ferritin, LDH, and decreased Plt. She was diagnosed to AOSD relapse and hemophagocytic syndrome. On the other hand, TR-PG 74mmHg was detected by echocardiography, but chronic pulmonary artery thromboembolism was not detected by CT and pulmonary blood flow scintigraphy. Cardiac examination revealed mPAP 55mmHg and PCWP 7mmHg, and she was diagnosed to PAH associated with AOSD. Treatment with steroid pulse therapy, followed by Betamethasone 5mg/day, TAC 1.5mg/day, colchicine 0.5mg/day, and MTX 8mg/week. For PAH, symptomatic improvement was observed by introducing macitentan, riociguat, and tryptostinil. Although PAH associated with collagen disease have mixed tissue disease 5%, scleroderma 2.6%, systemic lupus erythematosus 0.9%, and myositis 0.6%. PAH in AOSD has been reported to correlate with AOSD activity.

P2-254

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), we reviewed PMR patients recently refered to our hospital. [Methods] forty seven patients (M/F=19/28) 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 72.4years. Five patients with malignancy, but no giant cell arteritis was observed. Clinical features include shoulder pain 100%, pelvic pain 68.1%, peripheral arthritis 68.1%, and swelling of hands due to TS 34%. Either BS or TS was demonstrated by US in 44.7%. Mean dose of prednisolone was 13.3mg/day at the start of therapy and was tapered to 3.1mg/day at the second year. Rate of GC-free patients in 2 years later was 31.9%, respectively. [Conclusions] Factors such as Hb, CRP and gender were involved in the course of PMR.

P2-255

Effectiveness of JAK inhibitor for treatment of Crohn's disease (CD) with refractory adult-onset Still's disease (AOSD): a Case Report

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Conflict of interest: None

[Case] A 49-year-old male suffered from adult-onset Still's disease in 2001. After the remission by administration of moderate dose of prednisolone (PSL), he relapsed in 2008. Afterwards, he had repeated relapses (fever, arthritis and rash) and gradually became refractory and he required a large amount of steroids in 2011 and 2014. From 2015, combined with cyclosporine (CyA), tocilizumab (TCZ) 162mg sc every 2 weeks was initiated. 2 months later, hematochezia was observed, he was diagnosis with small and large bowel, perianal Crohn's disease. Expect to the effects on AOSD and CD, CyA + TCZ was switched to azathioprine + adalimumab, but AOSD immediately relapsed and the endoscopy revealed active inflammation of CD. So CyA and ADA was switched to tofacitinib (TOF), and then to baricitinib (Bari) for arthritis, remission was obtained for both diseases. [Clinical significance] The complication of AOSD and CD are rare. Although there are many reports of effectiveness of TCZ for AOSD, in this case, CD might developed due to enhanced effects of other cytokines secondary to anti-IL-6 therapy. JAK inhibitor seemed to have a role in the treatment of diseases involving multiple cytokines, like CD and AOSD. We should take care of unexpected complications during anti-cytokine therapy.

P2-256

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. [Purpose] 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 shared epitope (SE) of HLA-DRB1 and the onset of arthritis. [Results] Among 230 ICI treated cases, 12 (5.2%) developed arthralgia that couldn't be explained by cancer. The mean period to onset was 181 days. Rheumatologists intervened in only 4 cases, and 3 of which were diagnosed as arthritis and relieved with oral steroid therapy. Among 12 cases, RF / ACPA was measured in 6 / 5 cases respectively, and all were negative. No one had the autoimmune diseases before started ICI. 7 out of 12 cases have SE, but there is no significant difference to control. [Conclusion] Since these events are rare, further study of the large cohort is necessary. Besides, it became clear as a future issue of how rheumatologists will intervene for appropriate diagnosis and treatment.

P2-257

Efficacy of adalimumab in treatment-refractory neurosarcoidosis: a case report

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Conflict of interest: None

A-22-year old man with a fever and headache for one month was admitted to neurology department in our hospital. The CSF test showed aseptic meningitis. He also had uveitis and bihilar lymphadenopathy without symptoms. A lymph biopsy showed noncaseating granulomata, so a diagnosis of sarcoidosis including meningitis was made. Prednisolone (PSL) 0.5mg/kg per day was started after methylprednisolone (mPSL) pulse therapy, which made symptoms improved partially, but a meningitis got worse 3 months after, then he visited to our department. We administered mPSL pulse therapy again and switched PSL to dexamethasone considering CSF penetration, and added methotrexate. For a while, he got better, but when we switched to PSL in order to decrease steroid, a relapse occurred. We administered adalimumab as treatment-refractory neurosarcoidosis and his symptoms improved after 6 weeks, so we decrease PSL and discontinue. His CSF result also continued improvement. The frequency for neurosarcoidosis is 5% in sarcoidosis patients, and half of them are symptomatic at newly diagnosis. Most cases are improved by steroid, but 27 and 9% needs second and third line therapy, respectively. Successful therapies

with anti-TNF alpha have been reported and our case is also support for effectiveness.

P2-258

A rare case of coexistence of autoimmune pulmonary alveolar proteinosis and Sjogren syndrome

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Conflict of interest: None

An 84-year-old man was referred to our clinic with dry cough lasting three months. Chest CT showed ground-glass opacities (GGOs), especially in both lower lung fields. Because of KL-6 elevation, positive anti-SS-A and SS-B antibodies, a positive Saxon test, and findings of salivary gland scintigraphy, Sjogren syndrome (SS)-related interstitial pneumonia was diagnosed. The administration of prednisolone (20 mg/day) was started. A follow-up chest CT performed 3 months later showed that the GGOs were significantly improved. Prednisolone was gradually tapered to 8 mg/day over 8 months, but a subsequent chest CT showed a new appearance of diffuse GGOs with subpleural sparing. Transbronchial lung biopsy revealed PAS-positive lipoproteinaceous deposition within the alveoli. Autoimmune pulmonary alveolar proteinosis (aPAP) was diagnosed by a positive serum anti-GM-CSF antibody result (115.7 μg/ml). Clinical significance: aPAP is a rare lung disorder characterized by an accumulation of abnormal protein within the alveoli. A few cases of coexistence of aPAP and the other autoimmune disorders were reported, but this is the first report of coexistence with SS. When encountering a patient with KL-6 elevation in diffuse lung diseases, aPAP should be considered as a differential diagnosis.

P2-259

A pulmonary complication prevalence rate for elderly-onset rheumatoid arthritis male is high

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Conflict of interest: None

[Objective] When using MTX and biologics in the treatment of rheumatoid arthritis, pulmonary complications are major issues. With the aging of the population, the aging of rheumatoid arthritis patients is also progressing, and the number of elderly rheumatoid arthritis patients with pulmonary complications is increasing. In elderly-onset rheumatoid arthritis (EORA), pulmonary complications are frequently observed, especially in male EORA. We examined whether male EORA had a higher frequency of pulmonary complications compared to juvenile-onset rheumatoid arthritis (YORA). [Methods] Rheumatoid arthritis patients were divided into YORA with onset under 65 and EORA with onset over 65. A patient was diagnosed with pulmonary complications when a radiologist diagnosed a pulmonary lesion in a radiological examination or when KL-6 was elevated at onset. [Results] In both men and women, EORA had significantly more pulmonary complications than YORA ($P < 0.05$). Male EORA had more pulmonary complications than female YORA ($P < 0.01$) and female EORA ($P < 0.01$). [Conclusions] Male EORA had frequent pulmonary complications at the onset of rheumatoid arthritis. In male EORA, it is important to consider pulmonary complications in tight control from early onset.

P2-261

Hypersensitivity pneumonitis in a patient with rheumatoid arthritis

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Conflict of interest: None

A 55-year-old woman receiving methotrexate and golimumab for rheumatoid arthritis admitted to our hospital due to fever, cough and dyspnea. Bilateral ground glass opacity was observed in chest computed tomography (CT). Bronchoalveolar lavage showed increased lymphocytes and CD4/CD8 ratio. Further medical interview revealed that she was a strawberry farmer and her respiratory symptoms get worse on every May. These findings led to a diagnosis of hypersensitivity pneumonitis. As her symptom was less severe, we carefully followed up without using corticosteroid or antibiotics. Her respiratory failure resolved on day 3. Chest CT on day 7 showed improvement of ground glass opacity. This case showed the importance of medical interview on diagnosing hypersensitivity pneumonitis.

P2-262

Clinical analysis of patients with connective tissue diseases related progressive fibrosing interstitial lung diseases

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Conflict of interest: None

[Background] Interstitial lung diseases (ILD) are common and intractable manifestations of connective tissue diseases (CTD) which define patients' prognosis. Although most patients receive immunosuppressive therapy, some of them are resistant to treatments and suffer from chronically progressive fibrosing ILD (PF-ILD). In the present study, we analyzed chronical characteristics of patients with CTD related PF-ILD. [Method] We retrospectively reviewed records of 19 CTD-ILD patients who met the criteria for progression of interstitial lung disease within the 24 months before the last visit: a relative decline in the FVC of at least 10% of the predicted value, a relative decline in the FVC of 5% to less than 10% of the predicted value and worsening of respiratory symptoms or an increased extent of fibrosis on high-resolution CT, or worsening of respiratory symptoms and an increased extent of fibrosis. [Results] The mean age of the 19 patients was 60 years (37-77 years), and 12 patients were female. Of the 19 patients, RA/SSc/PM/DM/MCTD/SS were 7/7/5/1/1/1. 14 patients showed fNSIP pattern and 4 patients showed UIP pattern in HRCT. Immunosuppressive agents included IVCY, TAC, AZA and median dose of PSL was 6.36 mg (0-15 mg). Median relative decline in the FVC was 13.5% (5.3-22%).

P2-263

Outcomes of connective tissue disease-related pulmonary arterial hypertension (CTD-APAH) -Analysis of 25 patients treated with selective pulmonary vasodilators

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Conflict of interest: None

[Objective] The prognosis of patients with pulmonary arterial hypertension has improved, but CTD-APAH is still considered poor prognosis. Therefore, we clarified the outcome of our CTD-APAH patients and aimed to extract mortality risk factors. [Methods] From Nov. 2014 to Sep. 2019, CTD-APAH cases treated with pulmonary vasodilator were extracted from medical records. Background factors at the start of treatment were compared between the death group and the survival group. [Results] The 25 CTD-APAH cases extracted were 19 surviving (mean observation period 68 weeks) and 6 dead (77 weeks) as of Oct. 31, 2019. When the above background factors were compared for both groups, the only significant mortality risk factors were elderly (p-value 0.035 t-test) and male (p-value 0.035 chi-square test). There was no significant difference in other background factors: primary disease (Lc-SSc or not), disease duration, comorbidities (gastrointestinal tract, heart, lung, liver, malignant tumor), autoantibodies, and circulatory dynamics. [Conclusions] Only the elderly and males were the prognostic factors for CTD-APAH. Additional case accumulation and analysis are needed to identify possible prognostic factors that can intervene in improving the outcome of this disease.

P2-264

Two cases of organizing pneumonia complicated with psoriasis

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Conflict of interest: None

Case 1: A 67-year-old man with a more than ten-year history of psoriasis visited our hospital because of multiple small nodular shadows in the lungs by chest computed tomography (CT). Transbronchial lung biopsy showed findings compatible with organizing pneumonia (OP). Oral prednisolone (PSL) at 35 mg/day was started. When PSL was tapered as the OP improved, OP flared up. PSL was restarted and ixekizumab was additionally started; this regimen has maintained good control of his OP and psoriasis. Case 2: A 36-year-old woman who was under the care of a dermatologist for psoriasis for one year visited our hospital. Her chief complaints were slight fever and dyspnea. Chest CT revealed multiple infiltrative shadows in bilateral lower lung fields. Antibiotic treatment brought no change; however, the abnormal shadows improved without therapy. We consider her clinical course as being consistent with OP. [Conclusion] Both patients had no other symptoms suggesting rheumatoid arthritis and collagen disease, although case 1 was positive for rheumatoid factor and case 2 for antinuclear antibody. They did not have any other new drug exposure and no sign of worsening psoriasis at the onset of OP. OP rarely develops in psoriasis patients without progression of psoriasis or concomitant drug use.

P2-265

A case of rheumatoid arthritis with central nervous system involvement and elevated anti-cyclic citrullinated peptide antibody in the cerebrospinal fluid

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Conflict of interest: None

We describe a case of a 61-year-old female with a history of RA in remission for 7 years, who presented with numbness, weakness in the left upper limb, dysarthria, and headache. Magnetic resonance imaging (MRI) of the brain showed the meningeal enhancement effect in the frontal, parietal, and temporal lobes. Cerebrospinal fluid (CSF) examination showed high titers of rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA), with a high ACPA-IgG index ((ACPA in CSF/IgG in CSF)/(ACPA in serum/IgG in serum)) (=2.7). She was diagnosed with rheumatoid meningitis (RM), and her symptoms promptly improved with oral prednisolone and intravenous infusion of cyclophosphamide. After treatment, the titers of RF and ACPA in the CSF declined, and MRI showed improvement in meningeal structure. Central nervous system (CNS) involvement including encephalopathy, encephalitis, leptomeningitis and pachymeningitis in rheumatoid arthritis (RA) is rare. This case, along with current literature, suggests that the level of ACPA in the CSF may be a useful marker to diagnose CNS involvement in RA and assess the effectiveness of CNS involvement in RA treatment.

P2-266

The calcineurin inhibitor nephropathy in the treatment of collagen disease at our institution

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Conflict of interest: None

Calcineurin inhibitors (CNI, tacrolimus: TAC, cyclosporine: CyA) are indispensable for the induction and maintenance of rheumatoid arthritis, vasculitis, myositis, etc. in the treatment of collagen disease. Because the contraindications for administration to pregnant women have also been eliminated, the use opportunities are likely to increase. On the other hand, CNI nephropathy is a well-known side effect. We investigated CNI use cases at the facility.

P2-267

Risk factors of renal dysfunction after tacrolimus treatment in patients with rheumatoid arthritis, systemic sclerosis, systemic lupus erythematosus, and dermatomyositis

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Conflict of interest: None

[Objective] The aim of this study was to assess risk factors of renal dysfunction after tacrolimus treatment in patients with rheumatoid arthritis (RA), systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and dermatomyositis (DM). [Methods] We retrospectively investigated renal function in patients with RA, SSc, SLE, and DM who were treated with tacrolimus at our hospital. [Results] Fifty-eight RA, 15 SLE, 8 SSc, and 5 DM patients were enrolled. The average age was 58.9 ± 19.3 years and average body weight was 54.2 ± 11.9 kg. Tacrolimus dose was significantly higher in DM patients (4.8 mg/day) than in another patients. Serum creatinine levels were significantly worthened 0.75 ± 0.26 mg/dl to 0.79 ± 0.26 mg/dl at 24 weeks and to 0.83 ± 0.31 mg/dl at 48 weeks (p=0.007 and p=0.016, respectively). eGFR were also significantly decreased 75.2 ± 24.1 ml/min/1.73m^2 to 68.3 ± 20.4 ml/min/1.73m^2 at 24 weeks and to 64.9 ± 21.3 ml/min/1.73m^2 at 48 weeks (p=0.002 and p=0.01, respectively). The proportion of patients with eGFR decreased by 20% or more at 24 weeks was 60% for DM and 0% for SLE. [Conclusions] TAC treatment significantly decreased eGFR, particularly in patients with DM.

P2-268

The evaluation of the time to chronic kidney disease and related factors in RA patients using the IORRA cohort

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Conflict of interest: None

[Objective] To investigate risk factors for chronic kidney disease (CKD) in RA patients without CKD using IORRA. [Methods] Subjects were RA patients without renal dysfunction who participated in the IORRA study between 2010 to 2012, whose two consecutive eGFR (ml/min/1.73m^2) indicated 60-89 (CKD grade G2). CKD was defined as eGFR<60 (CKD grade G3 or lower). The period until progression to CKD was evaluated by the Kaplan-Meier method. In addition, factors at baseline related to the period until the progression to CKD were evaluated by Cox regression. The observational period was 5 years. [Results] A total of 4,127 patients were analyzed. The patient background was as follows; female: 84.5%, mean age: 69.4 years, RA disease duration; 13.1 years, DAS28-ESR: 2.8, eGFR: 74.9, and concomitant with hypertension: 16.9%. During the observation period, 34.8% had progression to CKD. Multivariate analysis confirmed that elderly (/10 years) (HR: 4.0, [95%CI: 3.1-4.9]), hypertension (HR 1.1 [95%CI: 1.0-1.2]), higher DAS28 (/1 increase) (HR 1.5, [95%CI: 1.2-1.9]), taking corticosteroids (HR 1.1 [95%CI: 1.0-1.2]), and not taking MTX (HR 1.2 [95%CI: 1.1-1.3]) were significant factors associated with progression to CKD. [Conclusion] The risk factors of CKD in patients with RA patients were clarified.

P2-269

A case of sarcoidosis who was asymptomatic for a long course, but worsened as hypercalcemia

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Conflict of interest: None

[Case] A 79-year-old man who had multiple granular shadows in both lungs in 2007. He was treated as tuberculos but treatment was not effective. PET-CT done in 2008 demonstrated accumulation of FDG in bilateral hilar lymph nodes and lung nodules in 2008. Angiotensin converting enzyme (ACE) was 28.9 IU/L and transbronchial lung biopsy showed multiple non-caseating granulomas. He was diagnosed as having sarcoidosis. He was asymptomatic, thus followed without treatment. He felt extreme tiredness in July 2009. From the following data, Ca; 14.0 mg/dL, BUN; 41.5 mg/dL, Cre; 1.63 mg/dL, FECa; 4.0 %, 1,25-$(OH)_2$VitD; 224 ng/mL, PTH-intact; <1.1 pg/mL, PTHrP; 1.1 pmol/L, urinary β2 microglobulin; 14,809 mg/L, ACE; 28.6 U/L, lysozyme; 24.5 mg/mL, sIL-2R, 3,216 U/mL, and biopsy proven tubulointerstitial renal injury, we confirmed that hypercalcemia was due to sarcoidosis. He started taking prednisolone at 20 mg/day and his tiredness and hypercalcemia was resolved promptly. [Discussion] We recommend to keep paying attention to renal involvement due to sarcoidosis by checking serum Ca and ACE levels even if patients are asymptomatic for a long time.

P2-270

Development of sarcoidosis after switching Etanercept to Certolizumab-pegol for treatment with rheumatoid arthritis

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Conflict of interest: None

[Case] A 72-year-old woman. She was diagnosed with rheumatoid arthritis 13 years ago. She was treated with prednisolone (PSL), methotrexate and etanercept (ETN), but low to moderate disease activity remained. ETN was switched to certolizumab-pegol (CZP). After 2 years of therapy, she presented pain and swelling bilateral leg and erythema nodule. Skin biopsy revealed epithelioid cell granuloma and septal panniculitis. Uveitis was detected at the same time. CZP was discontinued, and she introduced to our hospital. The patient's lysozyme and sIL-2R level were elevated. Antibacterial drugs was not effective. Ziehl-Neelsen staining did not identify any acid-fast bacilli. She was diagnosed with sarcoidosis. Despite stopping CZP, granulomatous uveitis was gradually developed. After increasing the dose of PSL, she improved. [Discussion] While TNF inhibitors are therapeutic agents for sarcoidosis, it has been reported that sarcoidosis is induced from TNF inhibitors, especially with ETN. CZP-induced sarcoidosis has recently been reported. In this case, sarcoidosis developed after 2 years switching to CZP. The choice of biologics after developing TNF inhibitor-induced sarcoidosis is controversial. In this case, treatment with non-TNF biologics or Janus Kinase inhibitors may be considered.

P2-271

A case of rheumatoid arthritis treated with baricitinib in a paradoxical reaction and increased disease activity

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Conflict of interest: None

[Case] A 70-year-old female. In X-7 years, rheumatoid arthritis (RA) was diagnosed at other hospitals due to polyarthritis of the extremities of the extremities, high RF and ACPA. Treatment continued with methotrexate, bucillamine, and etanercept to maintain remission. Visited our hospital for X-4 years and withdrew from etanercept in May of X-3 due to maintenance of remission. X-1 Relapsed from around February 1 and combined with etanercept BS in January X. From March of the same year, eruptions appeared on elbows, knees, and heels. Diagnosis of psoriasis-like eruption as paradoxical reaciton by TNF-α inhibitor in dermatology, and started topical application of active vitamin D and steroids. Etanercept BS continued, but disease activity and skin rash continued. After changing from Etanercept BS to Balicitinib in July, various symptoms were improved and remission was achieved. [Discussion] A paradoxical reaction due to administration of a TNF-α inhibitor has been reported. However, this is a relatively rare complication and the pathology is unknown. In this case, TNF-α inhibitor was discontinued due to continued skin eruption, and valicitinib was used to improve the duration of Achilles tendonitis and other arthritis.

P2-272

A rare case of rheumatoid arthritis associated with Crowned Dens syndrome

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Conflict of interest: None

Recent epidemiologic studies suggest a positive association of rheumatoid arthritis (RA) and pseudogout, but reports of combined Crowned Dens syndrome (CDS) are rare. Scutellari et al reported that 11 cases were associated with RA based on CT images of 38 CDS patients who visited the hospital for neck pain during 2001-2004. Here we report a 78-year-old man who had a CDS with RA who had been in remission with etanercept. He visited our clinic because of neck pain that had occurred several days ago and his neck could not be turned. The body temperature was 37 ° C, but CT was checked because CDS was suspected due to positive jolt accentuation test and CRP 2.70 (previously 0.99). CT was a characteristic finding of CDS called calcification of the transverse ligament of the Atlas. Immediately, oral treatment with acetaminophen 2400 mg / day and PSL 10 mg / day for 3 days (and then 5 days for PSL 5 mg / day) was started, and the symptoms almost disappeared 2 weeks later. (CRP 0.49) Although this case initially appeared to be a symptom related to RA, CDS was suspected due to positive signs of cervical rotation disorder and meningeal irritation. If the above symptoms appear during treatment of elderly RA, suspicion of CDS and a cervical CT scan for definitive diagnosis are required.

P2-274

SLE cases with EV viremia tend to have a high incidence of severe psychiatric symptoms

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Conflict of interest: None

Neuropsychiatric systemic lupus erythematosus (NPSLE) is one of the refractory diseases. The pathogenesis and mechanism of NPSLE remains unclear, but environmental factors such as viral infection are considered to be involved in the development of SLE. Among viral infections, it is well known that Epstein-Barr virus (EBV) is involved in the development of rheumatoid arthritis and Sjogren's syndrome. Therefore, we examined whether EBV is associated with NPSLE. We retrospectively examined the diagnosis and symptoms in 385 patients who were received EBV-DNA quantitative blood test from January 2013 to October 2019. EBV-DNA was quantified by real-time PCR. Of 385 cases, 145 cases had the positive result for EBV-DNA. SLE was diagnosed in 28 cases. Among 28 SLE cases, neuropsychiatric symptoms were observed in 10 cases. The symptoms in 10 NPSLE cases included psychosis in 2 cases (7.1%) and acute confusional state in 4 cases (14.3%). In a meta-analysis reported in 2011, the incidence rates of psychosis and acute confusional state were 4.6% (95%CI: 2.4-8.8) and 3.4% (1.1-10.3), respectively. In our EBV-positive SLE patients, the incidence rates of severe neuropsychiatric symptoms were higher. It was suggested that EBV infection may be related to certain neuropsychiatric symptoms in SLE.

P2-275

Fitz-Hugh-Curtis syndrome associated with reactive arthritis caused by Ureaplasma parvum infection: A case report

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Conflict of interest: None

A 40-year-old woman presented with a 3-week history of fever, left ankle and right shoulder pain. Blood tests revealed elevated serum levels of C-reactive protein (CRP) and liver enzymes. Contrast-enhanced computed tomography revealed hepatic capsular enhancement. She denied abdominal pain, and physical examination revealed a nontender uterus and adnexa. Assay with Polymerase chain reaction (PCR) to detect *Neisseria gonorrhoeae* and *Chlamydia* in cervical specimens showed negative results. *Mycoplasma/Ureaplasma* PCR assays of urine specimens revealed positive results for *Ureaplasma parvum*. Fever and left ankle pain gradually improved along with reduction in serum CRP levels. Based on the patient's clinical course, physical findings, and various test results, we ruled out other arthritic conditions, such as rheumatoid arthritis. Finally, she was diagnosed with Fitz-Hugh-Curtis syndrome associated with reactive arthritis caused by *Ureaplasma parvum* infection. She was administered a single dose of azithromycin (1 g), which led to reduction in serum liver enzymes and improved perihepatitis.

P2-276

Successful treatment of severe necrotizing fasciitis of the right leg caused by Vibrio vulnificus in a patient with rheumatoid arthritis

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Conflict of interest: None

[Case] A 75-year-old man had been treated for rheumatoid arthritis (RA) and spondylarthritis. Low disease activity had been maintained with oral adalimumab, methotrexate, and betamethasone. A few days ago, he had fever and pain and swelling of the right lower leg without any trigger and visited another hospital, where he was diagnosed as having cellulitis of the right lower leg and received an intravenous antibiotic infusion. As no improvement was observed, he was referred and admitted to our hospital. The following morning, he fell into shock and was admitted to the intensive care unit (ICU), where he received mechanical ventilation and plasmapheresis. Although the right leg was not tensed, its skin appeared pale in color, and blisters developed. Fasciotomy and debridement were performed. *Vibrio vulnificus* was detected by culture of wound and blood specimens. The fascia was necrotic. Under the diagnosis of necrotizing fasciitis, intravenous antibiotic infusion was continued. As his general condition was gradually improved, he was discharged from the ICU. Continuous negative-pressure vacuum therapy and debridement were repeatedly applied to the skin soft tissue defects. Ultimately, the affected leg was preserved by skin grafting, and the patient was saved.

P2-277

A case of coxotuberculosis of a RA patient treated with corticosteroid and low-dose methotrexate (MTX)

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Conflict of interest: None

77 years old male who had left hip arthrodesis over 50 years ago received three years' treatment for RA. His treatment started with PSL and salazosulfapyridine and low dose MTX was added. Regular check-ups revealed elevation of β-D-glucan and emphysematous and fibrous changes of lungs on chest CT. Additional ST mixture kept him stable for a while. CRP elevated gradually without specific symptoms but general fatigue. CT scan of chest-abdomen only revealed infiltrative lesion of lower lobe of right lung and sputum culture was positive for Klebsiella oxytoca but negative for Mycobacterium even though interferon-gamma release assays were positive. After 2 months, he had left coxalgia. Imaging tests indicated fluid accumulation at the left thigh. Aspirated specimen was white and purulent and eventually proved Mycobacterium tuberculosis infection (Tbc) by culture and PCR. Four-antitubercular drugs were started and operation of drainage and removal screws followed. He is currently under four-drug chemotherapy. History of hip arthrodesis suggests possible infection of Tbc but it was difficult to confirm after over 50 years. Immunosuppressant therapy sometimes leads to opportunistic infections. Relapse or new infection, Tbc should always be kept in mind.

P2-278

Systemic lupus erythematosus and IgG4-related disease associated with Epstein-Barr virus infection

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Conflict of interest: None

A 66-year-old male was admitted to our hospital because of night sweat. The serum level of IgG4 was elevated at 418 mg/dl. And CT scan revealed systemic lymphadenopathy, retroperitoneal fibrosis, and parathoracic vertebral tumor lesion. These laboratory and imaging findings fulfilled a possible diagnosis of IgG4-related disease (IgG4-RD). Laboratory test reveled leukocytopenia, low complements (C3 32 mg/dl, C4 2 mg/dl), and positive for ANA (x1280, homo), anti ds-DNA antibody (100 IU/ml). Upon these finding, physical examinations revealed arthritis, and he was diagnosed with Systemic lupus erythematosus (SLE). Test for EBNA-IgG, EBVCA-IgG were positive, EBVCA-IgM was negative, PCR for EBV using whole blood showed high levels of viral DNA, and EBER positive cells in bone marrow and lymph node, which were indicative of chronic EBV infection. But in this case, EBV was detected in B cells, not in T or NK cells. Therefor, he did not fulfill the diagnostic criteria for chronic active EBV (CAEBV). Resent findings link dysregulation of EBV and autoimmune disease development. Herein, we present a rare case of SLE and IgG4-RD associated with Epstein-Barr virus infection.

P2-279

A case of atypical mycobacterial infection in a patient with malignant rheumatoid arthritis

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Conflict of interest: None

60 years old level man Malignant rheumatoid arthritis with the polyneuritis was diagnosed from X-14 year and received medical treatment, but it was resistant to various kinds of antirheumatic drugs and was poor in control, and the dosage of PSL10mg and sarirumab was performed. Nine a year X moon high heat, inappetence, diarrhea developed and became this course introduction hospitalization. The saft mass which there were swelling and pain on pressure in was seen in both level of Both wrists, both hands knuckle joint transformed it, and pain on pressure was seen, and both knee joints accepted the saft mass which there were swelling, pain on pressure in. There was the crimson mass of the walnut size, and there was a walnut size red mass to the left thigh, and a mass was seen in tibia region in the becoming poor chest. CRP14.06mg/dl, MMP-3 166.1ng/ml, Mycobacterium marinum was detected in a left knee joint part soft tissue. The lesion was not seen in a lung field. I started treatment in CAM800mg /day, MINO200mg/day, LVFX500mg/day. Consideration: A main infection organ of the NTM symptom was the lungs, but skin, saft, a bone, joint, the lymph node were reported, and it was thought with the condition of a patient that you should warn in the rheumatic treatment.

P2-280

A case of rheumatoid arthritis (RA) patient who developed remière syndrome

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Conflict of interest: None

Case: A 59-year-old female [chief complaint] fever, cervical rotation disorder, mouth opening disorder [medical history and course] A woman with RA was treated with MTX, TCZ, and TAC. NSAIDs were started at a local physician due to acute cervical range limitation 4 days before admission. One day before admission, the range of motion of anteroposterior bending was improved, so she was judged as crowned dens syndrome. Outpatient treatment was continued with NSAIDs. But, the next day, she was admitted to the our hospital because of swelling of the upper left eyelid, photophobia, stiff neck, and mouth opening disorder. *S. anginousus* was detected in cerebrospinal fluid culture and blood culture. Contrast CT showed thrombophlebitis in both internal jugular veins and left external jugular vein. The patient was diagnosed as *S. anginousus* remière syndrome, secondary meningitis. All DMARDs were discontinued and MEPM and VCM was started. [Clinical significance] Purulent thrombophlebitis is called Remi?re's syndrome. This is a disease that causes cervical rotation disorder, but is rarely included in the differential diagnosis because it is a rare disease. Since rheumatologists are accustomed to recalling crowned dens syndrome due to cervical rotation disorder, this case is easily misleaded.

P2-281

Immune reconstitution inflammatory syndrome developing as a progressive Pneumocystis jirovecii pneumonia in a patient with rheumatoid arthritis

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Conflict of interest: None

A 69-year-old woman with a history of rheumatoid arthritis was admitted to our hospital due to pancytopenia (the leukocyte count, 1,100/?L; the level of hemoglobin, 7.7 g/dL; and the platelet count, 3.8×10^4/ μ L) and an abnormal shadow on chest computed tomography (CT). She had been treated with methotrexate 6 mg weekly and actarit 100 mg daily. The serum C-reactive protein level was 35.85 mg/dL, and the eGFR was 24 mL/min/1.73m^2. Leucovorin was started for the pancytopenia. Chest CT revealed ground-glass opacity in the bilateral lungs and a consolidation in the left lower lobe. Antibiotic treatment was started for the clinical diagnosis of bacterial pneumonia. As the level of serum β-D-glucan was turned out to be 156 pg/mL, Pneumocystis jirovecii pneumonia (PCP) was also diagnosed; trimethoprim-sulfamethoxazole and prednisolone were administered. However, repeated chest CT showed further worsening of consolidations in the bilateral lungs, suggesting the exacerbation of PCP. Taken together with the recovery of the leukocyte count (24,200/μ L), immune reconstitution inflammatory syndrome (IRIS) was considered. Methylprednisolone pulse therapy was performed, and her general condition was improved. IRIS can occur not only in HIV patients but also in non-HIV immunosuppressed patients.

P2-282

Examination of 12 cases of nontuberculous mycobacterial disease associated with collagen disease in our hospital

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Conflict of interest: None

[Purpose] Nontuberculous mycobacterial disease is an infectious disease whose morbidity has increased in the elderly and immunocompromised patients in recent years. The clinical course of nontuberculous mycobacteriosis varies from individual patient to patient, and some patients do not require treatment and are stable, while others follow a refractory course. Treatment is based on isolated bacterial species, drug susceptibility testing, and disease severity, but usually requires multiple antibiotics for a long period of time and often experiences poor tolerance of the drug. [Methods] Twelve patients with collagen disease who returned for follow-up visit were complicated by nontuberculous mycobacteriosis. [Results] There were 2 cases of SLE and 10 cases of rheumatoid arthritis, 10 cases of women and 2 cases of men, and the median age was 72.5 years. Eight patients under treatment, four during non-treatment follow-up, 11 cases of pulmonary nontuberculous mycobacteriosis. [Conclusion] Nontuberculous mycobacterial disease is common in older adults, and it was possible to control infection in all patients by using multiple antibiotics, but exacerbated after enhanced immunosuppressive treatment Also admitted.

P2-283

The Comparative Efficacy of Pneumocystis Pneumonia (PCP) Prophylactic Regimens in Patients with Connective Tissue Diseases (CTDs) Receiving Prolonged High-dose Glucocorticoids (GCs)

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Conflict of interest: None

[Objective] Trimethoprim-sulfamethoxazole (TMP-SMX) is recommended as a first-line agent of PCP prophylaxis for those who receive prolonged high-dose GCs. Alternative agents can be used, but relative efficacies of them are unknown. [Methods] Adult CTDs patients who were treated with over 4 weeks of GCs (over 20mg/day prednisolone) in our hospital between 2013 and 2017 were included. The patients were categorized into three groups; TMP-SMX, alternative agents (atovaquone or aerosolized pentamidine), and no prophylaxis. One-year incidence rate of PCP among the three groups was compared using a cox proportional hazards model. [Results] A total of 480 patients were identified. Two hundred ninety-six patients received TMP-SMX while 115 received alternative agents (107 atovaquone and 8 aerosolized pentamidine). As compared with no prophylaxis, TMP-SMX and alternative agents significantly reduced the PCP incidence (TMP-SMX: adjusted HR=0.009, 95%CI 0.0005 to 0.15, $p<0.01$. Alternative agents: adjusted HR=0.034, 95%CI: 0.003-0.47, $p=0.01$.). [Conclusion] Not only TMP-SMX but alternative agents significantly reduced the PCP incidence in CTDs patients receiving prolonged high dose GCs.

P2-284

Side effects of trimethoprim-sulfamethoxazole prophylaxis for pneumocystis pneumonia in connective tissue disease patients in our center

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Conflict of interest: None

[Objective] To detect risk factors of side effects (SEs) of trimethoprim-sulphamethoxazole (TMP-STX) for prophylaxis against pneumocystis pneumonia (PCP), we reviewed the medical records of patients with connective tissue diseases (CTDs). [Methods] We retrospectively reviewed 246 patients receiving TMP-STX for prophylaxis from 2010 January to 2019 October. We analysed age, sex, autoantibodies, underlying diseases, dose of TMP-STX, SEs occurred in 3 months from the start of TMP-STX and detail of SEs. [Results] SEs occurred in 42 patients (17.0%). SEs developed frequently in patients with anti-RNP antibody, anti-Sm antibody and anti-SS-A antibody. Multivariate analysis demonstrated that anti-RNA positivity and anti-SS-A antibody positivity was risk factors of SEs. Grade3/4 SEs occurred frequently in patients with MCTD, adult onset still's disease (AOSD), anti-RNP antibody and anti-Sm antibody. Incidence of AEs was considerably higher in patients treated with daily a week administration of a TMP-STX tablet, though the difference was not statistically significant. [Conclusions] Positivity for anti-RNP antibody and anti-SS-A antibody is a risk factor for SEs caused by TMP-STX. MCTD, AOSD, anti-RNP positivity, anti-Sm antibody and anti-SS-A antibody are risk factors for severe SEs.

P2-285

Search for genes associated with herpes simplex and herpes zoster infection in rheumatoid arthritis using biologics

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Conflict of interest: None

[Objective] Herpes simplex and herpes zoster are known as side effects of using biologics in rheumatoid arthritis (RA). These side effects may be caused by the effects of genetic factors. Therefore, identifying the causative gene is very important to evaluate the risk of these side effects. In this study, we searched for the causative gene using genome wide association study. [Methods] The subjects were 458 Japanese female patients of RA using biologics (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol, tocilizumab and abatacept). They were categorized into two groups: herpes group (n=82) and non-herpes group (n=376). 302,814 SNPs were used in this study. Case-control study was carried out between herpes and non-herpes group using Chi-Squared test in Recessive Model. [Results] The SNP (rs10774580, $p = 10^{-6.1}$) on *OASL* (2'-5'-oligoadenylate synthetase like) gene was found among SNPs with comparative lower P value. Odds ratio for the minor allele was 6.9 (95%CI 2.9-16.4). [Conclusions] It has been reported that DNA virus such as herpes virus becomes able to replicate because ectopic expression of OASL inhibit interferon induction. Thus, rs10774580 on *OASL* may be involved in herpes simplex and herpes zoster infection in RA.

P2-286

Paternal exposure to low-dose methotrexate: A systematic review and meta-analysis

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Conflict of interest: None

[Objective] The labeling of methotrexate (MTX) states that the partners of men taking MTX for rheumatoid arthritis (RA) should avoid pregnancy during its administration and for <3 months after its termination. This study aimed to examine whether paternal MTX increases the congenital major malformation in infants. [Method] We conducted a systematic review about paternal MTX for RA and congenital malformations in infants. [Results] Reviewing 157 reports resulted in 2 papers remaining. One was a prospective study in Germany, showing the risk of congenital malformation did not increase (OR: 1.02, 95% CI: 0.05-7.0) by comparing 113 pregnancies with men using MTX during conception periods and 412 pregnancies without exposure to teratogenic substances. Another was a study using the Danish National Registry, showing the risk of congenital malformation did not increase (adjusted OR: 1.01 (0.73-2.71)) by comparing 127 infants whose fathers used MTX within 90 days before pregnancy and 849,549 infants whose fathers did not use MTX. A metaanalysis also revealed no increase of risk (OR: 0.94 (0.38-2.33)). [Discussion] The paternal use of MTX seems to be acceptable even though the pregnancy is planned if the use is indispensable.

P2-287

Effectiveness and pregnancy outcomes of certolizumab pegol for Woman of Childbearing Age (WoCBA) of rheumatoid arthritis

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Conflict of interest: None

[Objectives] We reported shortening of time to pregnancy for the cases in which Woman of Childbearing Age (WoCBA) of rheumatoid arthritis (RA) had continued TNF inhibitors at the conception. In this study, we investigate the effectiveness and pregnancy outcomes in the cases of certolizumab pegols (CZP) which were introduced for WoCBA. [Methods] We examined 22 WoCBA for whom CZP were initiated from January 2014 to October 2019. We analyzed RA disease activity, continuation rate, time to pregnancy, and pregnancy outcomes. [Results] 80% of all cases were biologic naïve, and 64% did not use methotrexate, while 24% discontinued before the initiation of CZP. DAS28-CRP had improved at fourth weeks regardless of the past history of biologics or the combination of methotrexate, and 70% of all cases achieved remission. 10 patients (13 pregnancies) conceived, and the mean time to pregnancy was 6.7±5.2 months. Their pregnancy outcomes are 4 cases (30.8%) of spontaneous abortions, 1 case (7.7%) of preterm birth, 2 cases (15.4%) of low birth weight newborns, and 1 case (7.7%) of light-for-date newborn. [Conclusion] As the treatment strategy for WoCBA of RA, early introduction of CZP resulted in the control of disease activity and shortening of time to pregnancy.

P2-288

The disease course of pregnant rheumatoid arthritis patients with discontinuation of etanercept at the positive pregnancy test

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Conflict of interest: None

[Objective] There is a scarcity of reports about the association of discontinuing tumor necrosis factor inhibitors in early pregnancy with disease flare during pregnancy. The aim of this study was to investigate the disease course in women with rheumatoid arthritis (RA) with the discontinuation of etanercept (ETN) at the positive pregnancy test. [Methods] 11 RA patients were received ETN before pregnancy and discontinued ETN in early pregnancy. Then ETN was restarted at postpartum. Disease activity was assessed by DAS28-CRP at before pregnancy, during pregnancy and postpartum. [Results] Among 11 pregnant patients, increased disease activity during pregnancy occurred in 53.8% of patients. Before pregnancy, disease activity was low or remission in 84.6% of patients, but the proportion of low or remission disease activity was decreased postpartum (61.5%). [Conclusions] After stopping ETN in early pregnancy, disease activity increased during pregnancy. All patients were immediately received ETN therapy at postpartum, but the proportion of the low or remission disease activity was decreased compared with that of before pregnancy.

P2-290

To prevent progression of joint damage for RA patients who tried to conceive, we should use bDMARDs

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Conflict of interest: None

[Objective] When RA patients attempt to get pregnant, we often turn down the strength of treatment. In this period, joint damage would progress. But no detailed report has been made about the relationship between this period and joint damage. So we examined risk factors of progressing joint damage during this period. [Methods] We assigned 22 patients (the mean age was 33.0±4.9 years, the mean disease duration was 7.8±5.3 years). We investigated their drug, disease activity (DAS28 CRP), and joint damage (mTSS). We identified the factors which affect progression of joint damage. [Results] 11 patients (50%) got pregnant. The mean fol-

low-up period was 3.5 years. During this period, mTSS was significantly got worse ($p<0.05$, Wilcoxon signed rank test). Only the age at a patient started trying to conceive was affected the prolongation of the time until patients got pregnant. In nonpregnancy group, using rate of bDMARDs was higher. In proportional hazards regression analysis using progression of joint damage as event, we found that using bDMARDs was the only inhibiting factor (HR; 0.216 95%CI 0.045-1.037, p=0.056). [Conclusions] Using bDMARDs didn't raise the rate of pregnancy. But to prevent joint damage, we should not hesitate to use bDMARDs.

P2-291

The current treatment of WoCBA (Women of Child-Bearing Age) with rheumatoid arthritis

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Conflict of interest: None

[Background] The recent rheumatoid arthritis consists of progress of the treatment with the illness that achievement of remission is possible, and I put it to the patient of the young age onset, and pregnancy delivery comes to be thought about practically, but there is the necessary thing, and discontinuation is often limited in treatment depending on a use drug. [purpose] I intended for the patient of the woman younger than 40 years among rheumatoid arthritis patients during our House going to hospital medical treatment and investigated the present conditions of the marriage, the presence of the child, presence of current desire to bear children, contents of the treatment, a disease background. [object, method] The woman during our House going to hospital medical treatment younger than 40 years was 17 people. The onset average age was 5.6+-3.4 age during 28.6+-5.7 years old, the mean contraction of a disease period. Nine first medical examination married people the bachelorhood eight people (three people marry all over the going to hospital progress). Seven people were the onset after the delivery experience.

P2-292

The Study of the relationship between intrauterine exposure to immunosuppressive agents and allergic diseases in offspring

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Conflict of interest: None

Objective: Some immunosuppressant (IS) are allowed in autoimmune diseases during pregnancy. But there're few reports on the long-term effects on children. It's been reported using IS after organ transplantation may increase allergy in infants, so it's thought allergy may be increase in children by intrauterine exposure to IS. To clarify, we conducted this study. Methods: A case-control study using chart review and self-filled questionnaire (International Study of Asthma and Allergies in Childhood) was conducted on women with autoimmune disease and their children managed at our facility during 2002-2018. They're divided for two groups with or without intrauterine exposure to IS, and statistically examined the prevalence of allergic symptoms in children. Results: Answers were collected about 85 children. Ever rash (OR 3.93, 95%CI 1.18-13.03, p= 0.03) and Current rash (OR 3.50, 95%CI 1.04-11.81, p= 0.04) were increased significantly in exposed group. The prevalence of asthma, rhinitis, and food allergy weren't significantly difference between two groups. Conclusions: This study suggests atopic dermatitis may increase in children with intrauterine exposure to IS, but it's hard to conclude because of limitations such as the number of cases and memory bias. Further studies are required.

P2-293

A study of postnatal immunity in infants who exposed to Etanercept (ENT) or Certolizumab pegol (CZP) during pregnancy

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Conflict of interest: None

[Objective] Recently there are many cases used biologics (bio) during pregnancy. In 2010, one child whose mother used IFX throughout pregnancy died due to disseminated BCG after receiving BCG at 3 months. Since then, it is prefer for infants whose exposed bio during pregnancy to avoid from live attenuated vaccines until the drug disappears from infant. We already know that ETN/CZP are low placental transfer, so theoretically they have little effect on the infant's immunity. However there is no research to prove this. We try to clarify the effects on immunity of infants exposed ENT/CZP during pregnancy. [Methods] Lymphocyte and serum immunoglobulin (Ig) on day5 were compared between exposed infants (BIO; ENT5, CZP1) and non-exposed infants (CONTROL; 9). In the BIO, the lymphocyte subset at 1 month was examined. [Results] There was no difference between them about leukocyte, lymphocyte, lymphocyte subset (CD3+, CD4+, CD8+, CD16+/CD56+, CD19+), and serum Ig levels on day5. Also, there was no abnormality of lymphocyte subset and no clinical infectious signs in the BIO at 1 month. [Conclusion] Low placental transfer biologics such as ETN/CZP may not lead to immunosuppressive condition that could cause serious infections. It will be necessary to evaluate various functions of acquired immunity.

P2-294

Adverse pregnancy outcomes which could be affected by low dose glucocorticoid

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Conflict of interest: None

[Objectives] It is revealed that high dose glucocorticoid is a high risk for preterm birth, low birth weight, premature rupture of membrane (PROM), hypertensive disorder. We investigate the dose of glucocorticoid which influences on these adverse pregnancy outcomes. [Methods] We examined 181 pregnancies (131 patients) complicated with connective tissue disease (CTD) from April 2006 to October 2019. We analyzed the association between preterm birth, light-for-date (LFD), PROM, hypertensive disorder and glucocorticoid use or its dose during pregnancy. [Results] Glucocorticoid was administered in 106 cases (58.6%), and mean prednisolone dose was 4.3±5.3mg per day. The cases of preterm birth had higher rate of glucocorticoid use, and higher dose of glucocorticoid significantly (P=0.03, <0.01), and logistic regression analysis showed the cut-off value as 7.5mg per day. The cases which delivered LFD newborns, hypertensive disorder, preterm PROM had higher dose of glucocorticoid (P=0.02, <0.05, 0.03), and cut-off value was 6.7, 8.8, 2.0mg per day. [Conclusion] Glucocorticoid is often used for CTD patients during pregnancy, however, it is a risk for preterm birth, LFD, PROM. Our study revealed that relative low dose glucocorticoid could cause these adverse pregnancy outcomes.

P2-295

Pregnancy Outcomes in Patients with Systemic Lupus Erythematosus (SLE) with or without Lupus Nephritis (LN)

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ate School of Medicine

Conflict of interest: None

[Objective] To compare pregnancy outcomes in SLE patients with or without history of LN (renal SLE vs. non-renal SLE). [Methods] We retrospectively examined 111 pregnancies in 71 SLE patients who treated in our department from January 1996 to March 2018. [Results] SLE was complicated at conception in 98 pregnancies in 58 patients and SLE was newly developed during pregnancy or after delivery in 13 patients. Among 98 pregnancies with SLE at conception, median age at delivery and serum creatinine at conception were not significantly different between renal SLE and non-renal SLE. Pregnancy outcomes were not different: natural abortion 6, induced abortion 6, stillbirth 1, delivery 31 among 44 pregnancies in renal SLE and natural abortion 7, induced abortion 1, stillbirth 0, delivery 31 among 54 pregnancies in non-renal SLE. Preterm birth was observed in 11 (35%) and 9 (21%) in renal SLE and non-renal SLE, respectively (P=0.179). Low birth weight was observed in 16 (52%) and 13 (29%) in renal SLE and non-renal SLE (P=0.098). [Conclusions] There was not significant difference in pregnancy outcomes in SLE patients with or without history of LN. In addition, in SLE patients, frequency of preterm birth and low birth weight was high, regardless of the existence of history of LN.

P2-296

Pregnancy Outcome of SLE Patients at our Hospital

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The University of Tokyo Hospital

Conflict of interest: None

[Objective] Pregnancies in systemic lupus erythematosus (SLE) patients are often associated with adverse outcomes. To investigate pregnancy outcomes in Japanese SLE patients, a retrospective chart review was performed. [Methods] Medical records of SLE patients who had visited our hospital between April 2014 and March 2019 were reviewed. Pregnancies managed at our hospital were analyzed. Patients who chose to have abortions were excluded. [Results] There were 15 pregnancies in 12 women. There was 1 woman with secondary anti-phospholipid antibody syndrome. 2 women were positive for lupus anticoagulant but had no history of thrombosis. In 14 pregnancies (93%), the patients were taking steroids with an average dosage of 6.9±1.9mg prednisolone. In 7 pregnancies (40%), the patients were taking immunosuppressants. There was 1 miscarriage (7%) before 12 weeks and 1 fetal loss (7%) between 12 weeks and 22 weeks. There were no deliveries or fetal losses between 22 weeks and 36 weeks. Of the 13 live births, 5 (38%) babies were less than 2500g. 1 pregnancy (7%) was associated with hypertensive disorders of pregnancy, and 3 pregnancies (19%) were associated with SLE flares. [Conclusions] SLE pregnancies often result in babies with low birth weight and are often associated with SLE flares.

P2-298

Current status of pregnancy and childbirth in patients with rheumatoid arthritis and systemic lupus erythematosus

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Conflict of interest: None

[Background] There are still many cases of RA or SLE in young women, in which case pregnancy and childbirth are serious problems. [Methods]: The subjects were RA patients who visited our department as of October, 2019, and SLE patients who had a history of visiting our department from April 2014 to October 2019, we investigated the number of pregnancy and childbirth in the 16 years. Next, we investigated the age of the mother, the number of weeks of childbirth, the weight of the newborn in cases delivered at our hospital. [Results] RA cases have an average of 1.36 pregnancy / year and an average of 1.11 birth / year, SLE cases have a 1.76 pregnancy and a 1.16 birth of year. Compared to RA cases, SLE cases had a lower rate from pregnancy to childbirth. Birth weight was significantly lower in the SLE group compared to the RA group. RA was often untreated at the time of pregnancy and childbirth, but SLE, steroids were administered at the time of delivery of all cases, and immunosuppressants were used in a few cases when pregnancy became apparent. Neither RA nor SLE had death related to childbirth. [Conclusions] The low birth rate of both RA and SLE requires treatment at a younger age to reduce disease activity, and early collaboration with obstetrics and gynecology would be desirable.

P2-299

A case of rheumatoid arthritis treated with etanercept through pregnancy, childbirth and childcare

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Conflict of interest: None

[Purpose] We report on an RA case that were observed from pregnancy to childbirth, childcare using etanercept (ETN). [Case] She, a 34-year-old woman, gave birth to her first child when she was 30 years old. Later, symptoms of joint inflammation appeared, RA was diagnosed, methotrexate (MTX) was taken, and tocilizumab (TCZ) was introduced for the presence of symptoms. A remarkable effect was obtained, and the administration was suspended for 6 months. Later, when the joint pain recurred, Certolizumab Pegol (CZP) was used because the second child wanted to become pregnant. CZP was effective, but the effect diminished from the third month. Then, it switched to ETN. ETN was followed by administration of 25 mg once a week. Celecoxib and prednisolone were used in combination for pain. Pregnancy was confirmed about 6 months after the start of ETN. Childbirth was normal vaginal delivery, and there was no problem for both mother and newborn. Although colostrum was fed, artificial milk was used from 1 month after giving birth. The newborn was given a live vaccine 3 months after delivery, but there was no problem. [Discussion] BIOs such as CZP and ETN were considered not to adversely affect pregnancy, childbirth and childcare.

P2-300

A case of transient arthralgia and myalgia during postpartum

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Conflict of interest: None

A 31-year-old woman has suffered from spontaneous intracranial hypotension since 18-year-old. She gradually had complained polyarthralgia and myalgia around shoulder, elbow and knee after her first delivery from about 2 months before the first visit to our hospital. There is no sign of arthritis and muscle grasp pain. CK 59 IU/ml, CRP 0.45 mg/dl, RF, ACPA and ANA were negative, fT4 2.09 ng/ml (0.7-1.48), TSH <0.01 ng/ml, thyroglobulin 71.5 ng/ml, Anti-TPO Ab 109 IU/ml, Anti-TgAb 457 IU/ml, TRAb <0.3 IU/L, cortisol 0.24 μg/dL (6.24-18), ACTH 18.9 pg/ml. We diagnosed with postpartum thyroiditis and transient adrenal insufficiency. We injected her with hydrocortisone sodium succinate and prescribed hydrocortisone and bisoprolol fumarate for tachycardia. We changed to prednisolone because hydrocortisone was not effective. Her symptom gradually disappeared and prednisolone was gradually reduced in 2 months, and her thyroid function and adrenal function were also normalized. Postpartum thyroiditis presents with transient toxicosis (tachycardia, palpitation, heat, etc) for 2-4 months after delivery, and then relieves spontaneously. If arthralgia and muscle myalgia were strong during postpartum as in this case, it was considered necessary to search for adrenal function.

P2-301

A case of the multicentric reticulohistiocytosis that experienced delivery

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Conflict of interest: None

[Introcuction] We reported efficacy of amino bisphosphonate, but the

safety for the pregnancy is not established, and there are a few delivery reports of the MRH case. [Case] A 37 years old woman developed finger arthralgia in X-9 year and was diagnosed as MRH by a biopsy of the eruption. After starting intravenous administration of alendronate 10 mg/once a month in X-8 year, eruption and arthralgia was improved, and it was continued until X-4 year. The first pregnancy was detected in X-2 year but she had a stillbirth because of HELLPS in 29 weeks. The abnormality was absent by the genetic screening. She became pregnant again in X year, and as for the MRH, eruption, arthralgia were remission. Because of imminent abortion and IUGR on 37 weeks 4th, she delivered girls weighing 1,930g by a cesarean section. It was low weight, but the abnormality of the skeletal system was absent. [Discussion] In this case past administration of massive dose of alendronate did not cause any abnormality of a skeletal system and an immune system of the baby. Therefore the amino bisphosphonate administration to women of the childbearing age (WoCBA) could be considered. Also, as for condition of the MRH having been improved during pregnancy, the effect of the immune tolerance in pregnancy was suggested.

P2-302

Canakinumab throughout pregnancy with TNF-receptor associated periodic syndrome

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Conflict of interest: None

[Introduction] TNF receptor-associated periodic syndrome (TRAPS) is the autoinflammatory syndrome caused by TNFRSF1A mutation. 2 pregnant cases with TRAPS were reported, but canakinumab use throughout pregnancy is not reported. We experienced TRAPS patient who had a flare after the discontinuation of canakinumab during 1st trimester and resumed canakinumab throughout pregnancy. [Case] 32-year old woman. She started to suffer from periodic abdominal pain, arthralgia, cutaneous erythema and fever lasting over 7 days at the age of 19. These symptoms recurred 1-2 times per month. At the age of 26, TNFRSF1A gene examination showed Thr90Ile hetero mutation. With canakinumab, her symptoms improved. At the age of 30, she became pregnant and canakinumab was discontinued at gestational age (GA) 2w0d. However, fever and abdominal pain recurred. Canakinumab was resumed at GA 14w2d and continued until GA 35w1d. She had premature rupture of membrane at GA 40w0d and delivered the baby at GA 40w2d. These was no remarkable postpartum event and the baby had no apparent anomaly. The child development did not have any remarkable problem and no severe infection during the 1st year. [Conclusion] Canakinumab may be a reasonable treatment option during the pregnancy with TRAPS.

P2-303

An elderly woman with granulomatosis with polyangiitis who relapsed after pregnancy with an egg donation

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Conflict of interest: None

[Case] A 62-year-old Chinese woman. Sore throat from 7 years ago and fever from 6 years ago repeated. Introduced to our department 5 years ago for arthralgia. Serum CRP and ANCA are negative. Since pharyngeal mucosa biopsy showed no evidence of vasculitis and symptomatic treatment was ineffective, localized granulomatosis with polyangiitis (GPA) was suspected and she started taking steroids. After that, the symptoms improved. She stopped taking steroids 3 years ago. Multiple nodular shadows appeared in both lungs on chest CT one year ago. After that, she returned to China and she became pregnant by donating eggs in China. Then, fever, joint pain, nasal discharge and sore throat relapsed. Steroid resumption and discontinuation (self-interruption) are repeated. Since her symptoms worsened, She returned to Japan and visited our department again. The patient had a fever of 40 degrees and polyarthritis. Chest CT showed no multiple nodules in both lungs. She was diagnosed with GPA. Marked improvement was observed by high dose steroid. [Clinical significance] GPA has been reported to get worse by pregnancy. Egg donation pregnancy may contribute to a new onset or exacerbation of autoimmune disease because the state of immune tolerance is different from normal pregnancy.

P2-304

The efficacy of hydroxychloroquine in pregnancy outcome with antiphospholipid antibodies syndrome associated with systemic lupus erythematosus

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Conflict of interest: None

A 36-year-old woman. She was diagnosed as systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome (APS) because of pleurisy, hypocomplementemia, cytopenia, positive antinuclear antibodies, anti-dsDNA antibodies, anti-Sm antibodies, anti-RNP antibodies, lupus anticoagulant, anti-cardiolipin IgG antibodies. She was initiated with high-dose prednisolone (PSL). In her first pregnancy, she developed intrauterine fetal death (IUFD) at gestational age for 22 weeks despite of treatment with low dose aspirin (LDA). Tacrolimus (TAC) was added at postpartum. In her second pregnancy, She was treated with standard therapy, LDA and intravenous unfractionated heparin (UFH). Although She delivered 498g girl (Apgar 1/3) by caesarean section at gestational age for 24 weeks because of HELLP syndrome. In her third pregnancy, she developed IUFD at gestational age for 16 weeks despite of standard therapy and intravenous immunoglobulin (IVIG). HCQ was additionally administered for SLE and APS. In her fourth pregnancy, She was treated with PSL 8mg and TAC 4mg for SLE, standard therapy, IVIG and HCQ for APS. She delivered 2618g boy (Apgar 9/10) by caesarean section at gestational age for 35 weeks. From this case, HCQ was considered to be effective for refractory APS.

P2-305

Use of hydroxychloroquine before conception for a woman who had a previous child with cutaneous manifestation of neonatal lupus

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Conflict of interest: None

A 31-year old woman who was found to have anti-SSA antibodies when her previous child was diagnosed with cutaneous neonatal lupus (NL) visited us for a consultation of prevention of NL in the subsequent pregnancy. She had photo sensitivity, Raynaud phenomenon and fatigue. We started hydroxychloroquine (HCQ) 300 mg/day during the preconception period, and increased the dose to 400mg/day at 8 weeks gestation and continued throughout pregnancy. Cardiac NL did not occur, however, cutaneous NL recurred one month after birth. Cutaneous NL is not uncommon (5-16%) in mothers with anti-SSA antibodies and tended to be overlooked. When the previous child had cutaneous NL, 23.1% subsequent child develops cutaneous NL and 12.8% develops cardiac NL. Thus, it is important to examine mother's anti-SSA antibody when the fetus develops characteristic skin rash. When the previous child had cardiac NL, the subsequent child had increased risk of cardiac NL up to 15-18%. The recent clinical trial (PATCH) showed that HCQ 400mg/day reduced the risk of cardiac NL to 7.4% and a prospective multi-center study (J-PATCH,

jRCTs031180312) is undergoing in Japan. Similar approach might be applicable even if the previous fetus had cutaneous NL.

P2-306

Life event of pediatric rheumatic patients. Questionnaires survey on educational background, job, marriage and pregnancy

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Conflict of interest: None

[Objective] To clarify the life event like educational background, job, marriage, and pregnancy of pediatric rheumatic patients. [Method] Questionnaires were sent for patients over the age of 20 who developed rheumatic diseases in childhood and who were hospitalized or visited multiple times to our facility after obtaining approval by our ethics committee. The results were compared with national surveys of the same age (shown in parentheses). [Results] Responses for 91 of the 249 people mailed were examined. The collection rate was 37%, and the average age was 27.7 years. The advancement rate was 86% (99%) for high school, 44% (58%) for university and colleges, and 37% (16%) for Vocational school. 41% (15%) worked as medical staffs. 36% (33%) were married and 26% (28%) were pregnant. Of the 16 pregnant women, 13 were being treated before pregnancy, and 10 changed their treatment. [Conclusion] Many patients have found employment in the medical welfare field that was familiar in their childhood. Marriage and pregnancy experience was comparable with the same aged population. The experiences in their childhood may became valuable information for children with on-going treatment for rheumatic diseases.

P2-307

A case of juvenile idiopathic arthritis that worked on improving adherence during pregnancy

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Conflict of interest: None

[Case] A 19-year-old woman who was diagnosed with juvenile idiopathic arthritis (polyarticular type) due to fever and polyarthritis that lasted for more than 6 weeks at age 12. Although the treatment response with methotrexate (MTX) was good, arthritis often recurs due to withdrawal, and bone erosion is gradually progressing. Since the 11th week of pregnancy was found in December 201X, she visited our department. As for MTX, she has been stopped since 8 weeks ago, and it was judged that relapse. Prednisolone (PSL) 15 mg was started from the 12th week of pregnancy, and Certolizumab pegol (CZP) was started from the 16th week of pregnancy. Arthritis was stable, and 2997 g of boys with 39 weeks of gestation were delivered by normal vaginal delivery under the use of CZP + PSL 7.5 mg. There was insufficient knowledge about the symptoms that must be consulted and how to deal with poor health It has been found. Provided information on patient illness, financial support, and postpartum support. After giving birth, she can also describe her thoughts on treatment content and parenting breastfeeding, and it can be said that good oral adherence can be maintained in parallel with childcare. [Conclusion] We report a case of improvement in adherence after pregnancy and childbirth.

P2-308

Two cases of arthritis associated with hyperuricemia and suspected to be related to enthesitis by HR-pQCT image

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Conflict of interest: None

[Objective] The mechanism of urate crystal deposision in the joints is unclear. We report interesting findings from HR-pQCT observation of inflammatory joints in patients with hyperuricemia. [Case 1] 30s male had repeated pain in the ankle, fingers joints and wrist joints from 3 years ago. UA value was 11.3mg/dl. In joint US findings, double contour signs were observed at the MTP joint and multiple finger joints. In HR-pQCT, bone formation was observed at the Achilles tendon as well as bone erosion of the tarsal bones, and pencil in cup deformity was observed in the right 5th PIP joint with tophus. [Case 2] 40s male had repeated pain in MTP, ankle and knee joints since 10 years ago. UA value was 12.1mg / dl. In joint US findings, the inflammation was observed in the left and right quadriceps tendons and the left and right patella ligaments and the left 1st MTP joint. HR-pQCT showed bone formation at the Achilles tendon, plantar fascia, and talus neck. [Conclusion and clinical significances] Arthritis with hyperuricemia was associated with enthesitis, bone formation, and pencil in cup deformity suspected of peripheral spondyloarthritis. IL-17 has been reported to be involved in gouty arthritis, It was suggested that enthesitis may be involved in the pathogenesis of gouty arthritis.

P2-309

Three cases of crystal induced arthritis with difficulty for differential diagnosis from bone and soft tissue tumor

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Conflict of interest: None

Crystal-induced arthritis is not difficult to diagnose. Three cases were reported that lacked typical symptoms and blood biochemical findings had a very similar image to a bone and soft tissue tumor. Case 1: 62 Y.O. F, C.C. : index finger soft tissue nodule P.I. : A nodule appeared around the DIP joint from about 1 year ago. The mass had a shadow slightly thinner than bone on X-ray. The excised surface showed with white granules and suspected histologically chondroid tumor. As a crystal with birefringence was proved, and tophaceous pseudogout was diagnosed. Case 2 58 Y.O. M, C.C. : right ring finger DIP joint mass P.I. : 3 years ago, a mass appeared near the DIP joint. On X-ray, the bones around DIP joint were resolved. The open curettage found the small white crystals of lesion were long-angled crystals without birefringence, and it was diagnosed as pseudogout arthritis. Case 3: Y.O. M, C.C. : pain and swelling of the left great toe C.C. : he had redness, swelling, local heat in his IP joint from few days ago. An osteoid osteoma was suspected. Histologically, gout nodules was diagnosed. Uric acid levels should be measured even if tit is not common sites. If bone and soft tissue tumors in the periphery of the limbs are suspected, crystal-induced arthritis must be differentiated without symptom.

P2-310

Pseudogout in our hospital

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Conflict of interest: Yes

[Objective] To diagnose CPPDs and find best treatment by analize our practice of CPPDs in our hospital [Methods] In hospital patients after 2018 in our facurluty, who doctor suspect CPPDs [Results] 1 of 4th was Pyogenic arthritis,1 of 4th was pyogenic spondylitis, 2 of 4th were CPPDs. 1 og 2nd CPPDs was relapse after once gotten remissioned. [Conclusions] When we see a patient with fever and arthrytis, we must rule out pyogen, but if the patient is with CPPDs, she/he shoud be treated with rest and NSAIDs and corhitin, or glucocorticoids. Sooner rheumatologists or Orthopeditians diagnosis, may sonner discharge of hosipital and better outcome.

P2-311

Fractalkine/CX3CR1 axis in peripheral CD14++CD16+ monocytes contributes to disease development of patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] Fractalkine (FKN) and its receptor, CX3CR1 are involved in chemotaxis of immune cells. Our previous data showed that the $CX3CR1^{+}/CD14^{++}CD16^{+}$ ratio was remarkably decreased in SLE active patients. In this study, we investigated the possible involvement of FKN/CX3CR1 axis in immunological abnormalities and clinical features of SLE. [Methods] The $CX3CR1^{+}/CD14^{++}CD16^{+}$ ratio in patients with SLE active (SLEDAI: >10, n = 32), SLE inactive (SLEDAI: <10, n = 27) and healthy controls (HC, n = 34) was analyzed by FACS. The serum level of FKN was measured by SOMAscan^{R}assay. The serological data of the patients was collected by clinical records. [Results] The $CX3CR1^{+}/CD14^{++}CD16^{+}$ ratio of SLE patients was negatively and positively correlated with the SLEDAI score and serum level of C3, respectively. Serum level of FKN was significantly higher in SLE active patients than SLE inactive and HC. Moreover, the serum FKN level of the patients was positively and negatively correlated with SLEDAI score and C3, respectively. Notably, the $CX3CR1^{+}/CD14^{++}CD16^{+}$ ratio was negatively and significantly correlated with serum FKN level of the patients. [Conclusions] Our results imply that FKN/CX3CR1 axis is involved in acceleration of migration of $CD14^{++}CD16^{+}$ monocytes to organs in SLE.

P2-312

Efficacy of omega-3 fatty acid ethyl for rheumatic disease

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Conflict of interest: None

[Object] Inuit has less inflammatory diseases such as rheumatoid arthritis and ulcerative colitis than Westerners, and the anti-inflammatory action of polyunsaturated fatty acids abunudant in marine products has attracted attention. Omega-3 fatty acid ethyl contains not only eicosapentaenoic acid (EPA) but also docosahexaenoic acid (DHA). [Methods] 10 patients with rheumatic diseases who had Raynaud symptom and who took ethyl eicosapentate but were not effective were changed to ethyl omega-3 fatty acids to investigate its efficacy. [Results] Of the 9 cases that could be changed. 8 cases showed improvement in peripheral circulatory disturbance. DHA increased significantly and the EPA/AA ratio was 0.83, which was not lower than the Japanese average (0.58 to 0.74). [Conclusions] A lower EPA/AA ratio is a risk factor for coronary events. If the EPA/AA ratio is 0.404 or higher, the onset of events is significantly reduced. High DHA/AA ratio does not reduce coronary events, but DHA has anti-inflammatory effects similar to EPA. It is considered that the effect of DHA was added to EPA by changing from ethyl eicosapentate to omega-3 fatty acid ethyl. Changing to omega-3 fatty acid ethyl is useful in cases where ethyl eicosapentate is ineffective.

P2-313

Association between macrophage cell death and hyperferritinemia in adult-onset Still's disease

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Conflict of interest: None

[Objects] Hyperferritinemia is frequently used as a biomarker of various autoimmune diseases, but its cause and mechanism remain unknown. We here carried out experiments to investigate the cause of hyperferritinemia in adult-onset Still's disease (AOSD). [Methods] $CD14^{+}$human monocytes from healthy controls (HC; n=46) and AOSD (n=35) were differentiated to M1 macrophage (Mφ) and M2 Mφ by GM-CSF or M-CSF stimulation, respectively. The cell counts were compared on day 9, and cell viability was assayed over time. Ferritin concentration in the culture supernatant (SN) was measured by ELISA. The AOSD patients with active disease was defined as Pouchot score ≧4. [Results] Unexpectedly, IL-1b, IL-6, and TNF-a levels were significantly lower in the SN from Mφ stimulated with LPS. Decreased number of M1 and M2 Mφ were observed after 9-day culture [HC vs AOSD, M1: 420.9 vs 162.6 ($p<0.0001$), M2: 260.1 vs 133.4 ($p=0.0069$)]. Viability of Mφ was decreased in AOSD active phase, but was normalized after the remission. Serum ferritin levels negatively correlated with numbers of survived Mφ after 9-day culture. Ferritin in SN from M1Mφ was significantly elevated compared with HC and inactive AOSD. [Conclusion] Our data showed that hyperferritinemia might be caused by cell lysis of M1Mφ in active AOSD.

P2-314

Exacerbation and suppression of inflammatory arthritis via regulation of CD80 in RA mouse model, D1BC mouse

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Conflict of interest: Yes

[Object] D1BC mouse is established as a novel arthritis model, which expresses murine B7.1 in chondrocytes and synovial cells. D1BC mouse is high susceptible for arthritogenic antigen, We investigated whether anti-CTLA-4 antibody (4F10) and abatacept affect exacerbation and suppression of arthritis symptoms via CD80, respectively. [Methods] D1BC mice induced chronic inflammatory arthritis by low dose of bovine Col2 (0.02mg/mouse). Anti CTLA4 antibody and abatacept were injected intra-peritoneally and monitored by clinical score. Histopathological examination and FACS analysis were performed. [Results] Because 4F10 blocks CTLA4 signaling, it activates T cells. Injection of 4F10 exacerbated inflammatory arthritis. Abatacept, which inhibits T cell activation by blocking CD28 pathway via binding to B7.1 molecule, suppressed inflammatory arthritis. Next, we investigated whether immuno-suppression is observed in lymph node by administration of abatacept. Immunohistochemical staining of lymphoid cells revealed no obvert phenotype. It was the same results in FACS analysis. [Conclusions] Immune activation and suppression could be regulated through control of co-stimulatory signaling alone. Administration of abatacept ameliorates inflammatory arthritis without an obvert immune suppression.

P2-315

Studies on the production of cytokines from $CXCR5^{-}ICOS^{hi}PD\text{-}1^{hi}$ CD4 T cell as autoantibody-inducing CD4 T (*ai*CD4 T) cell which induces SLE

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Conflict of interest: None

[Object] Autoantibody-inducing CD4 T (*ai*CD4 T) cell is indispensable for our 'self-organized criticality theory' that induces SLE. We previously showed that *ai*CD4 T cell contains $CXCR5^{-}ICOS^{hi}PD\text{-}1^{hi}$ population in addition to follicular helper T (Tfh) cell. Here we examine the production of cytokines from these CD4 T cells. [Methods] BALB/c mice were repeatedly immunized with OVA, and SLE was induced. Splenic $CXCR5^{+}PD\text{-}1^{hi}$ Tfh cell, $CXCR5^{-}PD\text{-}1^{hi}$ CD4 T cell and $CXCR5^{-}PD\text{-}1^{-}$ CD4 T

cell were stimulated with anti-CD3 and anti-CD28 antibodies, and cytokines in the culture supernatant were detected by using ELISA. [Results] The production of IL-6, IL-21 and TGFβ1 from Tfh and $CXCR5^{-}PD\text{-}1^{hi}$ CD4 T cells was significantly increased as compared to that from $CXCR5^{-}PD\text{-}1^{-}$ CD4 T cell. On the other hand, those of IL-2 and TNFα were significantly decreased. The production of IFNγ and GM-CSF from $CXCR5^{-}PD\text{-}1^{hi}$ CD4 T cell was also significantly decreased. As compared to Tfh cells, $CXCR5^{-}PD\text{-}1^{hi}$ CD4 T cells produced significantly higher amounts of IL-21 and lower amounts of IL-6 and GM-CSF. [Conclusions] IL-21-producing $CXCR5^{-}ICOS^{hi}PD\text{-}1^{hi}$ CD4 T cell may be responsible for helping B cell to induce autoantibody and driving CD8 T cell to cause lupus tissue injury.

P2-316

Ultra-fine morphological analysis of rheumatoid arthritis synovial tissue

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is an autoimmune disease based on abnormal immune responses, suggesting a close relationship between dendritic cells, lymphocytes, and plasma cells. In this study, we analyzed RA synovial tissue morphologically using an electron microscope. [Methods] Synovial tissues collected from RA patients undergoing synovectomy were prepared for this study. Ultra-fine morphological analysis was performed using an electron microscopy, 3D features, and tomography. To examine the characteristics of RA synovial tissue, enzyme electron microscopy and immunohistological staining were performed. [Results] In RA synovial tissues, many synovial dendritic cells with long slender axis were observed by electron microscopy. Synovial dendritic cells showed a nursing phenomenon with adjacent plasma cells and cell-to-cell contacts were observed. Immunohistological staining revealed that most synovial dendritic cells were positive for HLA-DR and CD14, and some cells were positive for CD68. Some CD14 positive cells were positive for vimentin. [Conclusions] Synovial dendritic cells found in RA synovial tissue might be responsible for chronicity of inflammation and might be greatly involved in the pathogenesis of RA.

P2-317

Immunophenotyping research of patient with anti- IL-6 autoantibody using the analysis with mass cytometer CyTOF

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Conflict of interest: Yes

[Object] A 16-year old healthy man developed acute necrotizing appendicitis. Peritonitis with intraabdominal abscess were repeated despite of antibiotics and surgical treatments. During the peritonitis, CRP and IL-6 level hardly increased. Even in the elevation of neutrophils to 29,800/ml, CRP only increased to 2.5 mg/dl. The purpose of this study is to clarify the pathology of this patient. [Methods] ELISA and FACS were utilized for detection of autoantibody or phosphorylation of STAT3 in peripheral blood mononuclear cells (PBMCs), respectively. Cytometry by time-of-flight (CyTOF) was utilized for estimation of immunophenotyping. [Results] The production of IL-6 and phosphorylation of STAT3 was normal in this patient. ELISA or IL-6 reporter assay showed that his serum contained anti-IL-6 autoantibody and neutralized IL-6 activity. CyTOF analysis revealed that the proportion of $CD45RO^{+}$ effector $CD4^{+}$ T cells and $Ki67^{+}$ activated $CD14^{+}$ monocytes did not increase under peritonitis in this patient. After treatment of peritonitis, his basal level of Th2, Th17, Treg, and Tfh in $CD4^{+}$ T cells were low compared with healthy donors. [Conclusions] Our findings indicated that anti-IL-6 autoantibody impaired activation of monocytes or $CD4^{+}$ T cells, resulting in persistent peritonitis with abscess.

P2-318

IL-6 induces the resistance for apoptosis-induction via mitochondrial pathway in synovial cells

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Conflict of interest: None

[Object] Interleukin-6 (IL-6) is responsible for the pathogenesis of rheumatoid arthritis (RA), however, the detailed mechanism how it effects on synovial hyperplasia remains unclear. We have reported the relation between the growth activity of RA fibroblast-like synoviocytes (RA-FLS) and clock genes. In this study, we explored the effect of IL-6 on dexamethasone (DEX)-induced apoptosis of RA-FLS. [Methods] Synovial cells were treated with or without DEX (10,100,300,500 μM: 24 hr) and examined cellular viabilities by WST-8. Synovial cells were treated with or without IL-6/sIL-6R (100 ng/ml) and DEX (100 μM) for 24 hr to examine cellular viabilities by WST-8, expressions of Caspase-3/Caspase-8/ Cytochrome c/PARP by western blotting and *Hlf*/*Tef*/*Dbp*/*Bik* by qPCR. [Results] DEX decreased cell viabilities dose-dependently, which was disturbed by IL-6/sIL-6R. IL-6/sIL-6R inhibited the release of Cytochrome c and the cleavages of Caspase3/PARP, but not Caspase8. Also, the expressions of circadian transcriptional factor *Hlf* and pro-apoptotic factor *Bik* were suppressed. by IL-6/sIL-6R. [Conclusions] Results suggested that IL-6 regulates mitochondrial pathway and induces the resistance for apoptosis via clock genes in RA-FLS.

P2-319

Clock controlled gene Tef regulates proliferation of RA-FLS under stimulation of IL-6 and TNF-alpha

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Conflict of interest: None

[Object] We reported that expressions of clock genes in leukocytes of RA patients were significantly different from healthy controls and those expressions were correlated with the disease activity. However, the detailed relation between the pathogenesis of RA, cytokines 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, Hlf or Tef* siRNAs, RA-FLS were stimulated with or without IL-6/sIL-6R (100ng/ml) or TNF-α (10ng/ml) to examine the cell viabilities by WST-8 assay. Total protein was extracted from RA-FLS to analyze the expression of Cyclin D, a cell cycle regulator, by western blot. [Results] Under the suppression of *Tef* in RA-FLS, stimulation of IL-6/sIL-6R and TNF-α significantly increased the cellular viabilities and expressions of Cyclin D. [Conclusions] The results suggested that Tef upregulated Cyclin D expression by IL-6/sIL-6R and TNF-α, subsequently induced proliferation of RA-FLS.

P2-322

The analysis for the inhibition of angiogenesis by JAK inhibitor

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Conflict of interest: None

[Object] 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 and tube formation were analyzed by counting assay and tube formation assay, respectively. [Results] The proliferation activity increased by VEGF was suppressed by TOF and PEF, but was not by BAR. The tube formation activity increased by VEGF was suppressed by TOF and PEF, but was not by BAR. VEGF induces the angiogenesis through JAK3. This study demonstrated that TOF and PEF, which has the relatively high affinity to JAK3, suppressed the angiogenesis of HUVECs stimulated by VEGF. [Conclusions] Our results indicated that JAK inhibitors might suppress the angiogenesis of RA through the inhibition of JAK3.

P2-323

Histopathological Changes of Synovial Tissue in Rheumatoid Arthritis Patients Treated with TNF inhibitors

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by hyperplasia of synovial tissues. Tumor necrosis factor inhibitors (TNFi) have been shown to act on inflammatory cells and form the discoid fibrosis in the sublining layers. In this study, we showed the histological changes around discoid fibrosis in RA synovium treated with TNFi. [Methods] Synovial tissues were obtained from 30 RA patients including 6 patients treated with TNFi. The sections were stained by HE, TdT-mediated dUTP nick end labeling (TUNEL) and the immunohistochemical staining with antibody of CD86, CD163, CD3 and CD20. [Results] The discoid fibrosis on the sections stained with HE and the apoptosis of lining cells around the discoid fibrosis on the sections with TUNEL staining were both found in synovial tissue treated with TNFi. Immunohistochemical staining revealed that the number of CD 86 and CD 163 positive cells were increased and that that of CD3 or CD20 positive cells were decreased in ining layer in synovial tissue treated with TNFi. [Conclusions] This study showed the apoptosis of lining cells derived from macrophages resulted in the discoid fibrosis. These findings indicated TNFi might induce apoptosis of macrophage leading to the suppression of RA synovitis

P2-324

A study of the role of IL-29 in rheumatoid arthritis

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Conflict of interest: None

[Object] One of the cytokines produced by immunocompetent cells, interleukin (IL) -10 is known to show high levels in the serum of patients with rheumatoid arthritis (RA), and IL-29 has the characteristics of IL-10. We found that IL-29 is high in RA serum and synovial fluid, that it is expressed in monocytic cells in the synovial tissue, and that TNF-α stimulates migration and adhesion in peripheral blood mononuclear cells (PBMC). In this study, we investigated the identification of other cells producing IL-29 in RA and how they are regulated. [Methods] RA synovial fibroblasts (FLS), human umbilical vein endothelial cells (HUVEC), human monocytic cells (THP-1), THP-1 with phorbol 12-myristate 13-acetate (PMA) (THP-1 + PMA) was stimulated with polyinosinic-polycytidylic acid (poly (I: C)), lipopolysaccharide (LPS), and interferon α (IFNα). IL-29 was measured by enzyme-linked immunosorbent assay (ELISA). [Results] IL-29 production was observed 24 hours after FLS stimulation with IFNα and Poly (I: C) ($p = 0.007$). IL-29 production was observed 4 hours after HUVEC stimulation with Poly (I: C) and LPS, respectively ($p = 0.016$, $p = 0.003$). [Conclusions] It was suggested that IL-29 was involved in RA by stimulation with poly (I: C), LPS, and IFNα.

P2-325

The effect of Mat2a inhibition for systemic lupus erythematosus model mice

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Conflict of interest: None

[Object] B cell and T cell are activated and differentiate with the expression of key transcription factors and those downstream genes induced by cytokines and stimulations. Such inducible gene expression is often regulated by epigenomic alterations including methylation of DNA and histone. Various kinds of methyltransferases transfer methyl group to substrates. H3K4me3 is increased at the regulatory regions of activation-related genes during lymphoid cell activation. An inhibition of Mat2a, a catalytic enzyme of SAM synthesis, can comprehensively repress methylation compared to that of specific methyltransferases. We have shown Mat2a inhibition represses B cell activation and proliferation, so examined whether inhibition of Mat2a improves the disease activity of systemic lupus erythematosus (SLE). [Methods] 14-week-old female mice were intraperitoneally injected PBS or Mat2a inhibitor cycloleucine (CLEU); four times once a week and analyzed in five days after last injection (n=5). [Results] Splenomegaly, lymphadenopathy, the titer of serum anti-ds DNA antibody and renal histopathology were improved by CLEU, however, CLEU-treated mice became thinner and inactive and showed tremor. [Conclusions] Mat2a inhibition by CLEU improved SLE disease activity but showed a strong side-effect.

P3-001

Examination of ultrasonographic (US) findings of peripheral joint lesions confirmed bone erosion and bone formation of finger joints by HR-pQCT

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Conflict of interest: None

[Objective] Bone formation and erosion is a characteristic finding of peripheral joint lesions of spondyloarthritis (SpA lesions). We investigated US findings of finger that were confirmed SpA lesions using by HR-pQCT. And the change of US findings by administration of anti-IL-17A antibody was examined. [Methods] 15 patients were confirmed SpA lesions by 3D and 2D images of HR-pQCT. Enthesitis of the nail bed, extensor tendinitis, joint synovitis were examined by US. [Results] SpA lesions were 43 DIP / IP joints and13 PIP joints. In these 56 joints, ths enthesitis of nail bed was observed in 60%, which was significantly higher than 42% in unchanged joints ($p = 0.0403$), and extensor tendinitis was observed in 53%, which

was significantly higher than 31% in unchanged joints (p = 0.0136). Synovitis was found in 17 joints but was not clearly associated with joint lesions. Secukinumab was administered to 4 cases of SpA, and US findings at 6 weeks after the start of administration showed improvement of enthesitis and extensor tendinitis in 3 cases. [Conclusions] The finger joint lesion with bone formation and erosion confirmed by HR-pQCT was significantly associated with enthesitis and extensor tendinitis. Secukinumab administration was useful for improving enthesitis and tendinitis.

P3-002

Diagnostic predictability of antisynthetase syndrome by chest HRCT

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Conflict of interest: None

[Objective] To statistically verify the working hypothesis that antisynthetase syndrome can be diagnosed from chest high-resolution computed tomography (HRCT) findings. [Methods] As of the end of October 2019, we enrolled 63 patients with collagen rheumatic diseases with interstitial lung disease (CTD-ILD). The associations between diseases and chest HRCT findings were analyzed retrospectively. [Results] The subpleural atoll sign of chest HRCT were found in 12 cases, 10 of which had antisynthetase syndrome. In the cases without antisynthetase syndrome, the subpleural atoll sign was observed only in 2/47 cases. The positive predictive value of the subpleural atoll sign for antisynthetase syndrome was 0.83, and the subpleural atoll sign was specific to antisynthetase syndrome (specificity 0.96, p=0.0000). [Conclusions] The subpleural atoll sign of chest HRCT predicts the diagnosis of antisynthetase syndrome. Anti-ARS antibodies should be examined even if the subpleural atoll sign is observed without any sign of dermatitis or myositis. Furthermore, the subpleural atoll sign may improve the diagnostic efficiency of antisynthetase syndrome since the MESCUP anti-ARS test cannot detect anti-OJ antibodies.

P3-003

Usefulness of lung ultrasound (LUS) in connective tissue disease-associated Interstitial lung disease (CTD-ILD)

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Conflict of interest: None

[Objective] To evaluate usefulness of B-line score (BS) by LUS and a correlation between Warrick score (WS) by HRCT and BS In CTD-ILD. [Methods] In this cross-sectional study, 22 hospitalized patients with new-onset CTD, including myositis in 9, rheumatoid arthritis in 6, scleroderma in 2, vasculitis in 2, lupus in 1, MCTD in 1, and adult still's disease in 1, who simultaneously performed HRCT and LUS are recruited. BS was evaluated at 50 and 14 lung intercostal spaces (LIS), respectively, according to a previous manner. We analyzed a correlation between BS at 50 LIS and BS at 14 LSI, and that between BS at 14 LIS and WS. We also compared BSs between an ILD subset (n=13) and a non-ILD subset (n=9). [Results] BS at 14 LIS was significantly correlated with BS at 50 LIS ($r=0.97$, $P<0.01$). BS at 14 LIS also had a significant correlation with WS ($r=0.85$, $P<0.01$). BS at 14 LIS is significantly higher in the ILD subset than in the non-ILD subset (median 38 versus 4, $P<0.01$). In the ILD subset, BS at 14 LIS tended to be inversely correlated with diffusing capacity for carbon monoxide ($r=-0.63$, $P=0.06$). [Conclusions] LUS is a potent useful tool for evaluation of ILD as well as HRCT in patients with CTD.

P3-004

A retrospective study of utilities of whole body diffusion-weighted MRI in the field of rheumatic disease

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Conflict of interest: None

[Objective] To identify utilities of whole body diffusion-weighted MRI in the field of rheumatic disease. [Methods] 20 cases of rheumatic disease, FUO and miscellaneous symptoms were examined with whole body diffusion-weighted MRI. 20 patients were enrolled into 3 groups: Group A: n=11 (average: 70 years old, CRP: 7.9mg/dl) patients with suspected PMR and RS3PE syndrome. Group B: n=6 (average: 73 years old, CRP: 7.4mg/dl) patients with FUO. Group C: n=3 (average: 63 years old, CRP: 1.3 mg/dl) miscellaneous patients (with RA and multiple tumors, with clubbed finger and with severe back pain). [Results] In group A, no malignancy was observed and false positive for suspected bone metastasis in one case was indicated. In group B, remarkable lymph node swelling was observed in 2 cases. Colon cancer was detected in one case. In group C, bone metastasis of cancer was observed in one case. In two cases with MTX LPD and Kikuchi's disease, whole body diffusion-weighted MRI was sensitive to detect lymph node swelling. [Conclusion] Whole body diffusion-weighted MRI was highly effective for detection of lymph node swelling and sensitive for detection of cancer. Further studies of the utilities of whole body diffusion-weighted MRI will be needed

P3-005

Comparative analysis of low-field magnetic resonance imaging in patients with rheumatoid arthritis who achieved clinical remission by treatment with abatacept or infliximab

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Conflict of interest: None

[Objective] To clarify the change in findings by low-field MRI (compacTscan; cMRI) in RA patients who achieved clinical remission (CR) by treatment with biologics (Bio). [Methods] RA patients, who achieved and maintained DAS28-CRP remission by iv abatacept (ABT) or infliximab (IFX), were enrolled. We compared 1) background and clinical course, 2) cMRI findings when CR was achieved, and 3) change in cMRI findings after CR, between ABT and IFX treated group, retrospectively. [Results] 1) Between ABT (17 cases) and IFX (29 cases), age, sex, disease duration, and DAS28-CRP were comparable at the start of Bio. MTX use (ABT 58.8% vs IFX 100%, P=0.004) and first Bio (64.7% vs 93.1%, P=0.008) were significantly more frequent in IFX. 2) When CR was achieved, the frequency of bone marrow edema (BME) (ABT 41.2% vs IFX 24.1%) and synovitis (88.2% vs 82.7%) was comparable. 3) The observation period after CR was similar between ABT (11.8 ± 3.2 month) and IFX (13.2 ± 6.5). The proportion of patients who showed increased bone erosion score was significantly higher (ABT 11.8% vs IFX 41.4%, P=0.04), while that of new BME was significantly lower (7.6% vs 0.0%, P=0.04) in IFX. [Conclusions] After achieving CR, cMRI showed residual inflammation, and subsequent changes differed between ABT and IFX.

P3-006

DWIBS (Diffusion weighted whole-body imaging with background body signal suppression) is helpful in the diagnosis and follow-up of LVV (Giant Cell Arteritis and Takayasu Arteritis): two case reports

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Conflict of interest: None

Early diagnosis and treatment are required in Large vessel vasculitis (LVV) including giant cell arteritis (GCA) and Takayasu arteritis (TAK). However, LVV is a disease whose diagnosis is difficult to make because there are neither specific signs nor diagnostic laboratory findings in early stage. Very recently, two intriguing case reports were presented which sug-

gest a possibility of that DWIBS might be valuable imaging modality for diagnosis and follow-up of LVV. Here, we also report two cases of LVV involving descending aorta which were revealed by DWIBS. Case 1; A 74-year-old woman was diagnosed with TAK. DWIBS showed signal enhancement at descending aorta inflammation. Case 2; A 68-year-old man was diagnosed with GCA. DWIBS showed signal enhancement at descending aorta inflammation. In both cases, we could clearly confirm improvement the signal enhancement around the aortic salls detected by DWIBS after treatment. We consider that DWIBS is useful in the diagnosis and evaluation disease activity in LVV. In addition, there is a possibility that DWIBS may be an alternative to FDP-PET CT with no radiation exposure, and much lower cost.

P3-007

MRI characteristics of RA in which joint destruction progresses despite the use of biologics

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Conflict of interest: None

[Subjects] Three RA patients in whom joint destruction progressed (group A), as confirmed by X-p, along with 7 patients in whom destruction did not progress (group B) following the use of biologics. [Method] Take MRIs prior to using biologics (baseline) and one year following the use of biologics. We gave scores on bone erosion, joint space narrowing (JSN), bone edema, synovitis, and tenosynovitis. [Results] Bone erosion and JSN both deteriorated from baseline in 3 patients in group A, with a bone erosion score of 29.7 from 10.0 as well as a JSN score of 26.0 from 18.7. Moreover, in group A, bone edema deteriorated from baseline in one patient but improved in 2 patients, with bone edema score of 14.7 from 19.3. Synovitis also deteriorated in one patient but improved in 2 patients, with synovitis score of 6.7 from 9.3. Tenosynovitis improved from baseline in 3 patients in group A, with a score of 6.0 from 13.7. [Discussion] Although bone edema is predictive factor of joint destruction, baseline score for bone edema in this study was high in two of 3 patients in group A. Moreover, baseline scores for JSN and tenosynovitis in group A were also higher than group B, potentially indicating that JSN and tenosynovitis can also be considered to be predictive factors of joint destruction.

P3-008

Changes in magnetic resonance imaging findings in patients with rheumatoid arthritis using tocilizumab for eight years or longer

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Conflict of interest: None

[Objective] We encountered three patients with RA who used TCZ for eight years or longer. We examined the MRI findings of these patients. Case1: 63y. o female, disease duration: 17.8 years, stage 1, class 1 Case2: 75y. o F, : 16.6 Ys, 1, 1 Case3: 86y. o F, : 19.1 Ys, 4, 1 [Methods] MRI using gadolinium contrast was performed at the start of treatment with TCZ, after 4-5 years of TCZ use, and after 7-8 years of TCZ use. The updated rheumatoid arthritis MRI scoring system was used to score bone erosion (250 points), joint space narrowing (88), bone marrow edema (75), synovitis (24), and tendon sheath synovitis (42). [Results] Case1: bone erosion 13→11→12, joint space narrowing0→0→0, bone marrow edema 30→2→2, synovitis 4→5→3, tendon sheath synovitis 6→3→1, DAS28-ESR 4.19→2.00→1.79, and CDAI 3.5→0.9→2. Case2: 15→16→20, 0→0→0, 41→4→8, 19→7→14, 9→0→24 4.88→1.96→4.68, 23.2→1.3→19.5. Case3: 66→63→66, 62→62→62, 36→13→15, 8→4→4, 16→12→9, 4.52→1.58→1.14, 12.0→0.9→3.3. [Conclusions] Even with long-term TCZ use, all three patients showed no progression of bone erosion and joint space narrowing. There was almost no progression of bone erosion once bone marrow edema improved. Bone marrow edema, synovitis, and tendon sheath synovitis scores presented with the almost the same changes as DAS28 and CDAI scores, even with long-term TCZ use.

P3-009

The utility of FDG-PET/CT for evaluation of disease activity and localization in patients with polyarteritis nodosa

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Conflict of interest: None

[Objective] To investigate the utility of FDG-PET/CT for evaluation of disease activity and localization in polyarteritis nodosa (PAN). [Methods] Nine active PAN patients who underwent FDG-PET/CT at our hospital between April 2009 and October 2019 were studied. [Results] PET/CT revealed FDG uptake in six of nine patients. FDG accumulation was noted in the brachial, femoral, popliteal arteries of two patients, and in the posterior tibial arteries of three. PET/CT findings were positive in all four patients with systemic PAN and in two of five patients with cutaneous PAN, in whom potential systemic vasculitis was also identified. The PAN PET/CT findings and clinical findings did not differ significantly. In patients in whom the PET/CT findings were positive and negative, the CRP levels were 9.24 ± 8.16 and 5.44 ± 4.36 mg/dL (means ±SDs, p>0.99) respectively; the ESR were 80.0 ± 19.0 and 57.3 ± 47.5 mm/h (mean ± SDs, p=0.63). Thus, although the differences were not significant, the inflammatory marker levels tended to be higher in the PET/CT-positive group. [Conclusions] FDG-PET/CT is useful for evaluating and localizing PAN disease activity. Especially in cutaneous PAN patients, PET/CT detects potential systemic vasculitis, which facilitates clinical decision-making.

P3-010

A case of polymyalgia rheumatica in which FDG-PET/CT was useful

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Conflict of interest: None

[Case] 56 years old, female. [Chief complaint] Proximal limb pain [Present illness] She became aware of systemic muscle pain in August 20XX. Although she had been followed up, there was no improvement. So she was referred to our hospital in October the Yth, and was admitted to the hospital. blood tests showed CRP: 1.76 mg/dl, ESR: 38 mm/hr, and QFT positivity. RF and anti CCP antibody is negative. Joint ultrasonography showed tendon sheath synovial thickening of the long biceps tendon, but negative power Doppler. For the differential diagnosis between polymyalgia rheumatica (PMR), and other diseases FDG-PET/CT was performed. FDG accumulation image, observed in the vicinity of the humerus, sciatic nodule, femoral trochanters, spinal spinous processes, and hip joints, was consistent with PMR. Her pain improved after prescribing PSL 15mg/day. [Discussion] Differential diagnosis of PMR and other inflammatory diseases is often difficult. In particular, differentiation from old-onset rheumatoid arthritis is often a problem. Even if the results of joint echo and other clinilal tests do not support the diagnosis of PMR, FDG-PET/CT findings can contribute to the diagnosis.

P3-011

Usefulness of Gallium-67 scintigraphy for diagnosis and treatment of polymyalgia rheumatica

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) has a feature of bursitis in shoulder, trochanter of humerus (TOH), and vertebral spinous processes (VSP), easily detected with FDG-PET/CT. We evaluate usefulness of Gal-

lium-67 scintigraphy (Ga scan) for diagnosis and treatment of PMR. [Methods] 112 patients with polyarthritis were examined with Ga scan from April 2012 to September 2019. Excluding other diseases, we retrospectively studied 30 patients who met PMR classification criteria (2012ACR/EULAR), treated with prednisolone (PSL) more than 1 year. [Results] The values are median (min-max). At baseline, age 76 (55-86) years old, female 20 cases, CRP 5.45 (1.12-14.92) mg/dl, ESR 91 (53-120) mm/hr, MMP-3 195.2 (61.5-2970) ng/ml, RF positive 1 case, ACPA positive 1case. 4 cases met RA classification criteria (2010ACR/EULAR). Ga scan showed increased uptake in shoulder (30 cases), TOH (30 cases), and VSP (24 cases). Before treatment, 3 cases used PSL5mg/day, 1 case used MTX8mg/week. Initial doses of PSL were 15 (5-20) mg/day. At 1 year after, CRP values significantly decreased to 0.09 (0.02-1.9) mg/dl (p<0.0001), PSL dose was significantly decreased to 5 (3-8) mg/day (p<0.0001). In all case, the diagnosis did not change after 1year. 5 cases had relapse, 2 cases complicated RA. [Conclusions] These results suggest.

P3-012

Evaluation of Direction of Probe in Ultrasound Sonography of Second and Fifth Metacarpal Phalangeal Joints in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] Ultrasound sonography (US) is important in examination of rheumatoid arthritis (RA). Although decreasing of examination joints can save time, risk of missing pulse Doppler (PD) or bone erosion (ERO) should be considered. This study evaluated direction of probe in US examination on 2nd and 5th MCP joints in RA patients. [Methods] 102 RA patients in whom US were performed from July in 2018-August in 2019 were used in this study. Detection rates of PD and ERO in 2nd and 5th MCP joints were compared. [Results] Patients' characteristics: 81 female and 21 male. Mean age was 64.9 years old. RA duration was 8.8 years. Mean DAS28-CRP was 3.2. Mean mHAQ was 0.42. Detection rates of PD: Positive in 21.6% at 2nd MCP and 11.5% at 5th MCP from the sagittal view. Positive in 22.5% at 2nd MTP and 10.8% at 5th MCP from the side view. Detection of ERO: Positive in 3.4% at 2nd MTP and 0% at 5th MCP from the sagittal view. Positive in 7.3% at 2nd MCP and 2.9% at 5th MTP from the side view. [Conclusions] Although there were not so much differences in detection rates of PD between the sagittal view and the side view, there were differences in detection rates of ERO between the sagittal view and the side view.

P3-013

Evolution of Joint Echo examination Management system (JEM)

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Conflict of interest: None

[Objective] In order to cope with increasing joint ultrasonography (JUS) examination, we developed an efficient input interface for Joint Echo examination Management system (JEM). [Methods] We developed an efficient input interface for JEM with HDC Co., Ltd. (Sapporo City). We unified joint findings comments that had been input freely, and made it possible to input them with a button. [Results] 1) The number of joint ultrasonography examination has been increased (2,567 in 2013 to 4,363 in 2018) in our hospital, and we were able to cope with them by improving JEM input system. Even with conventional JEM, it was possible to easily enter gray scale and power Doppler ultrasound grading, evidence of bone erosion and tendonitis with a button. We unified other joint findings comments that had been input freely, and made it possible to input them with a button. The examiner was able to operate JEM with one hand. 3) The examination time was shortened by improving input interface of JEM. [Conclusions] A new interface of JEM enables efficient joint ultrasonography examination.

P3-014

The frequency of the ECU tendonitis in RA clinical practice

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Conflict of interest: None

[Objective] We investigated the frequency of the ECU tendonitis in RA clinical practice. [Methods] We conducted a retrospective survey of US records of the RA patients who received US examination of hand joint from Jan 2019 to June 2019. We were compared with ECU tendonitis (ECU group) and non-ECU tendonitis group (non-ECU group) for the frequency, background factors, and disease activity. [Results] 234 patients were evaluated. ECU group 42 cases (ECU alone 10 cases), non-ECU group was 192 cases (119 cases with wrist), the frequency of ECU tendonitis was 17.9%. The ECU group, age 64.6±2.3 years, duration of RA 12.2±1.7 years, MTX 73.8%, dosage of MTX 8.4±5 mg / week, bDMARDs 19.0%, SDAI 13.4±0.6, DAS28-ESR 3.9±0.2. SJC, DAS28, and RF was a significant difference between the ECU group and the non-ECU group (Wilcoxon signed rank sum test: p<0.01). Similarly, SJC, DAS28, SDAI and RF was a significant difference between the ECU group and the non-ECU group with wrist. Patient general VAS and mHAQ was a difference between ECU alone group and ECU group (p<0.01). In the ECU group with the wrist, there was a tendency of higher disease activity. [Conclusions] The ECU tendonitis was relatively frequent in RA clinical practice.

P3-015

Global examination using ultrasound in the shoulder joint -Comparison in Rheumatoid arthritis, Polymyalgia rheumatica, Frozen shoulder-

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Conflict of interest: None

[Purpose] Using US, we examined the details of the examination sites in several locations in rheumatoid arthritis (RA), rheumatoid polymyalgia (PMR), and Frozen shoulder (FS), which are similar diseases of the shoulder joint. [Methods] The subjects were RA16 shoulder, PMR18 shoulder, FS19 shoulder, and control19 shoulder. Evaluation items were Doppler area by US power Doppler method, grading by Grayscale method, peek systolic velocity (PSV value) and resistance Index (RI value) of the anterior circumflex humeral artery. The Doppler area and the grayscale method are observed at the biceps groove (BG), rotator interval (RI), subacromial bursa (SAB), subdeltoid bursa (SDB), glenohumeral joint for posteriol. For statistics, multiple comparison test and chi-square test were used. [Results] The difference between RA and PMR was significantly higher in BG in PMR and lower in RI value in RA. In the grayscale method, RA and PMR were examined, and grades were significantly higher in all regions of RA. [Conclusion] When comparing RA and PMR, the grayscale method can be used, and the power Doppler method can be discriminated by observing the BG region and confirming the resistance Index of the anterior circumflex humeral artery.

P3-016

Consideration of the significance of blood flow signals (PD) of joint echoes in patients with rheumatoid arthritis (RA) who have neither physical findings nor subjective symptoms in the ACR68/66 joints, compared with the laboratory data and patient background

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Conflict of interest: None

Objective: We focused on RA patients in remission, and examined the relationship between their clinical backgrounds and PD sonography. Methods: 204 RA patients were examined with ultrasound on 32 joints and four tendons; both wrist, PIP, MCP and MTP joints, and flexor and extensor tendons of the fingers. Laboratory data and backgrounds were statistically analyzed on PD signals. Results: Positive PD signals were observed in 47.5% patients, 2.8 ± 1.8 joints per each patient. The mostly observed PD positive sites were right 2nd MCP, right wrist, left 2nd MCP and left wrist joint, in decreasing order. When restricted to the site with grade 3 PD, right extensor tendon was the most common site, followed by left extensor tendon. PD signals weren't significantly correlated to clinical backgrounds; age, RF, ACPA, disease duration, CRP, DAS28-ESR and MMP3. Conclusions: Nearly half of the RA patients without physical findings or subjective symptoms had PD signals, and most frequent sites were both wrist and 2nd MCP joints: if restricted to the sites with grade 3, both extensor tendons were mostly observed. PD signals weren't correlated to clinical backgrounds significantly. Therefore, joint sonography proved to be a very effective tool even in RA patients without physical joint findings.

P3-017

Usefulness of joint ultrasonography about the predictive factor of elderly-onset rheumatoid arthritis (EORA) with polymyalgia rheumatica (PMR)

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is similar to Elderly-onset rheumatoid arthritis (EORA) in the symptoms (the onset and progress) and a serologic change, and there are many cases having difficulty in differentiation. To analyze the predictive factor of the complication of EORA in PMR. [Methods] 47 patients were enrolled. The synovitis evaluated gray scale (GS) and power doppler (PD) with 24 both hands joints and both shoulder joints. I analyzed age, sex, the serologic characteristics (CRP, ESR, CCP, RF, MMP-3), GS, PD and dose of steroid statistically. [Results] 1. 14 cases complicated with EORA (29.8%). 2. In PMR group (N=33) and PMR+EORA group (N=14), I recognized significant difference in plural factors such as RF, RF-positive rate, CCP, CCP-positive rate, dose of steroid by the single variable analysis. By the multivariate logistic analysis, independent factors included ACPA-positive rate and PD≧2 of both hand and finger joints for significant difference. [Conclusions] When I recognized ACPA-positive or PD≧2 of both hand and finger joints, the possibility of the EORA complication was suggested at the time of PMR diagnosis. The usefulness of joint ultrasonography for both hand and finger was suggested for the purpose of distinguishing EORA complication.

P3-018

A case of lumbar interspinous bursitis in polymyalgia rheumatica detected by US

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Conflict of interest: None

<Case report>A 68-year-old woman presented with a 6-months history of fever, joint pain, and lower back pain. She was diagnosed as polymyalgia rheumatica (PMR) and treated with prednisolone (PSL) 15mg/day. About 4-months after the initiation of treatment (under PSL 7.5mg/day), fever and worsening of lower back pain were observed. Fluid in the lumbar interspinous bursae was revealed by enhanced CT, MRI, US, and PET. Specimen from CT guided needle biopsy was consistent with bursitis. She was diagnosed with lumbar interspinous bursitis associated with PMR. By increasing PSL to 20mg/day, the symptoms and the findings of MRI and US were improved. <Discussion>Interspinous bursitis is frequently found in patients with PMR. We experienced a case of PMR with lumbar interspinous bursitis detected by some imaging examinations and also proved pathologically. Further studies are needed to determine whether lumbar interspinous bursitis is specific for PMR and reflect to its activity. However we consider that US is useful modality in diagnosis with PMR differentiated from other diseases such as SpA, and in monitoring. <Conclusion> Active lumbar interspinous bursitis in PMR was detected by CT, MRI, US, PET and pathological examination. US is useful for evaluation and monitoring of bursitis in PMR.

P3-019

Ultrasonographic findings in patients with cancer who developed arthritis symptoms during treatment with the immune checkpoint inhibitor

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Conflict of interest: None

[Objective] In recent years, it has become possible to use immune checkpoint inhibitors (ICI) to treat cancer, but immune-related adverse events (irAE) have been reported. We have experienced various ultrasonographic findings in patients with cancer who developed arthritis symptoms during treatment of the ICI. [Methods] Ultrasound examination was performed in total six patients with cancer treated by ICI. 1: A 57-year-old man with lung cancer, 2: A 61-year-old woman with lung cancer, 3: A 77-year-old man with bladder cancer, 4: A 65-year-old man with bladder cancer, 5: A 60-year-old man with bladder cancer, 6: A 83-year-old man with bladder cancer. [Results] Ultrasound findings showed not only synovial proliferation in the joint but also tenosynovitis and enthesitis were found in various joint, tendon and enthesis in patients with cancer treated by ICI. In some patients, ultrasound findings look like spondyloarthtritis such as psoriatic arthritis. [Conclusions] Various inflammatory findings were detected by ultrasound in patients treated immune checkpoint inhibitor. It is very important to understand that irAE due to immune checkpoint inhibitors develop not only synovitis like rheumatoid arthritis but also tenosynovitis and enthesitis. We will show the representative images.

P3-020

Ultrasound findings during the use of immune checkpoint inhibitors

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Conflict of interest: None

[Objective] The classes and the number used of immune checkpoint inhibitors (ICIs) have increased in recent years. Since ICIs activate the immune system, immune-related adverse events (irAEs) sometimes occur during use. The incidence of arthritis, one of these irAEs, is low, there are few reports of its clinical features and evaluations with joint ultrasound (US) findings. We examined US findings in patients who had joint swelling and pain during the use of ICIs. [Methods] The subjects were 8 patients examined in our department for joint swelling and pain during ICIs use between January 2014 and August 2019. The US findings in those cases were compared. [Results] The ICIs was nivolumab, pembrolizumab, and durvalumab. US findings were synovial thickening alone in 2 patients, moderate synovitis in 3 patients, tenosynovitis in 1 patient, and moderately active synovitis with tenosynovitis in 2 patients. In the 2 patients with synovial thickening alone, the symptoms improved with discontinuation of the ICIs. [Conclusions] When joint symptoms appear during the use of ICIs, US findings are not consistent. This study suggests the possibility that, in cases when synovitis is not demonstrated with US, joint symptoms will improve only with discontinuation of the ICIs.

P3-021

The relationship between serum infliximab levels and ultrasonographic findings in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We examined the infliximab concentration, disease activity and ultrasonographic findings in patients with rheumatoid arthritis (RA) treated infliximab. [Methods] Thirty-five patients underwent Remicheck Q® were investigated for their association with disease activity and ultrasonographic findings. [Results] Of 35 cases, Remicheck Q was positive in 25 cases and negative in 10 cases. In order of Remicheck Q positive and negative, DAS28-CRP was 2.3±0.7 and 2.5±0.4, CRP was 0.2±0.3 and 0.2±0.3 mg/dl, MMP-3 was 70.3±30.2 and 99.4±101.4 ng/ml, there were no difference between the groups. However, RF was higher in the positive group (271.3 ± 340.0 and 96.9 ± 65.4 IU/mL). There was no significant difference between the two groups in the ultrasonographic findings. In patients with negative Remicheck Q and power Doppler positive active synovitis, improvement of power Doppler signal was observed after increasing the dose of infliximab. [Conclusions] Although some patients had low disease activity with negative Remicheck Q, some patients remained active synovitis even with negative Remicheck Q. Therefore, a more detailed disease activity evaluation becomes possible by combining the infliximab concentration measurement and ultrasound examination.

P3-022

Usefulness of synovitis evaluation in rheumatoid arthritis by combined use of ultrasonography and thermography: Two case reports

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Conflict of interest: None

[Background] In rheumatoid arthritis (RA), thermal sense (TS) of joints suggests the presence of synovitis. Power Doppler ultrasonography (PDUS) is used for the evaluation of RA. Thermography (TG) is a non-contact and non-invasive test for skin temperature (ST) measurement. However, there are few reports comparing TG and PDUS in synovitis in RA. [Objective] We evaluate synovitis by performing TG and PDUS. [Case 1] A 75-year-old female. She was treated with PSL and TAC. She had DAS28: 3.73 and TS of left hand. In TG, ST of the left wrist joint (38.8 °C) was higher than the right same side (31.5 °C). PDUS showed GS3 / PD3 synovitis in the left wrist joint, but no synovitis in the right same side. [Case 2] A 49-year-old female. She was treated with MTX and ADA. She had DAS28: 2.29, but complained of TS, swelling and stiffness of right hand. In TG, the right 3rd finger MP joint ST (34.1 °C) was higher than the left same side (31.1 °C). PDUS showed GS3 / PD2 synovitis in the right 3rd finger MP joint, but no synovitis in the left same side. [Discussion and Conclusion] Synovitis due to PDUS had a high ST by TG. TS of joints is useful for the evaluation of synovitis, but is based on subjective symptoms and evaluation. TG in combination with PDUS may allow more objective evaluation of synovitis.

P3-023

The efficacy of sonography for treatment decision by RA patients themselves: 2 cases report

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Conflict of interest: None

[Objective] We report two cases in which joint echo was useful for decision-making in the treatment of RA patients. [Case 1] 50 years old, female. Stage 4, class 2. Disease duration was 23 years. CRP 0.20, ESR 29mm / H. RF 284, anti-CCP antibody 58.0, MMP-3 39. mHAQ 7/24, SDAI 15.2. She was treated with MTX 8mg/W. The MP joint was swollen and dislocated. MP joint reconstruction and drug treatment enhancement were proposed. The patient and family decided to enhance drug treatment because of visualized active synovitis by sonography. [Case 2] 85 years old, female. Stage 1, class 2. She was suffered from a polyarthralgia with hip joint onset and treated with PSL 10mg in a diagnosis of rheumatic polymyalgia at a nearby clinic. CRP 3.68, ESR 98mm / H. RF 5, anti-CCP antibody <2.0, MMP-3 918.4. mHAQ 8/24, SDAI 30.68. We proposed DMARDs treatment as seronegative elderly onset rheumatoid arthritis. However, her family denied because of anxiety about side effect. Sonography showed PD grade 2 synovitis. They decided to start MTX treatment. [Conclusion] If blood exam data are within the standard range, patients might hardly change their treatment. Sonographic images were able to visualize active synovitis in an easy-to-understand manner and facilitated patient decision making.

P3-024

Changes in magnetic resonance imaging findings of wrist joint rheumatoid arthritis related to painless osteitis

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Conflict of interest: None

Introduction Silent synovitis was first reported in the 2013 European League Against Rheumatism Congress and recognized as non-symptomatic synovitis. RA-related painless osteitis of the wrist diagnosed using magnetic resonance imaging (MRI) became common. Objective We aimed to evaluate bilateral painless osteitis using MRI in patients who received biologic treatment before and after pregnancy. Subjects and methods Fourteen patients (mean age at birth: 32.9 years [range, 22-39 years]) became pregnant after biologic treatment, including one para 3 and one para 2. Biologic treatment was restarted postpartum for RA relapse in all the patients. Pre-pregnancy and post-delivery wrist MRI findings were compared. Results All the patients were right-handed. The mean time from the first to the last MRI was 9.5 years (range, 5-15 years). The MRI findings showed that the disease progressed respectively in the right and left hands in 9 and 3 patients, was unchanged in 5 and 10, and improved in 0 and 1. Discussion None of the patients had wrist pain during follow-up. In RA, osseous changes on MRI with no subjective pain indicate painless osteitis.

P3-025

Correlation of Self-Administered Foot Evaluation Questionnaire (SAFE-Q) and radiographic evaluation of feet and ankle joints for rheumatoid arthritis patients

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Conflict of interest: None

[Introduction] We investigated the correlation between SAFE-Q and X-ray evaluation of the feet and ankle joints of patients for rheumatoid arthritis (RA). [Subjects and Methods] Subjects were RA patients who visited our hospital from November 2018 to February 2019, and 73 people (male: 14 people, women: 59 people) were evaluated by X-ray of the feet and ankle joints. The age distribution was 36 to 84 y-o (average 64.2 y-o) and the duration of the disease was 1 to 53 years (average 13.6 years). The correlation between five subscale score of SAFE-Q, 1) Pain and Pain-Related, 2) Physical Function and Daily Living, 3) Social Functioning, 4) Shoe-Related, 5) General Health and Well-Being, and X-ray evaluation (Larsen Grade: LG 0 ~ 5) of feet or ankle Joints were investigated. [Results] 3) Social Function, 4) Shoe-Related and 5) General Health and Well-Being were significantly different between LG 0 and 5, LG 1 and 5,

LG 0 and 5, respectively. SAFE-Q and the X-ray of the ankle joints were not significantly different. [Conclusions] In RA treatment, it is most important to prevent the progression of joints destruction. Surgery on the progressively destructed joints will be possible to improve the ADL and shoe-related problems and general health and well-being.

P3-027

Image evaluation after total hip arthroplasty using artificial intelligence

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Conflict of interest: None

[Objective] The purpose of this study is to evaluate radiolucent line (RL) after total hip arthroplasty (THA) using a convolutional neural network (CNN), which is a deep learning technique, and to examine its diagnostic ability. [Methods] Two hip surgeons who are certified specialists of the Japanese Orthopedic Association studied 100 hip joints for each group diagnosed as having or not having RL with regard to frontal X-ray images of hip joints in patients who have passed more than one year after THA. The framework implemented the classification model as CNN using TensorFlow. Images of 20 cases different from those used for learning were used to verify the CNN classifier, and sensitivity, specificity, and accuracy were obtained. In both learning and diagnostic evaluation, the implant was unified into a Zweymüller stem. [Results] The diagnostic ability of the CNN classifier about RL in this study was 50% sensitivity, 100% specificity, and 75% accuracy. [Conclusions] Although the diagnostic ability of THA postoperatively using artificial intelligence was good specificity, there was a problem in terms of sensitivity. Although RL based on X-ray images may have a small amount of features, further improvement in diagnostic ability is expected by increasing the number of cases in the future.

P3-028

Diffusion-weighted Whole-body Imaging with Background Body Signal Suppression (DWIBS) as a Novel Imaging Modality for Disease Activity Assessment in sarcoidosis of bone

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Conflict of interest: None

Bone sarcoidosis is a relatively rare condition seen in 1% to 13% of patients. Most bone lesions are found in appendicular bones, and it is even rarer to affect axial bones. To evaluate bone lesions, scintigraphy and FDG-PET have been used, which pose problems including radiation exposure and a high cost. We report a case of bone sarcoidosis with multiple spinal lesions in which DWIBS was useful for disease evaluation. The case was a 76-year-old man. He had been diagnosed with pulmonary sarcoidosis in 2 years before and followed up without any treatment. From 10 months before, his blood tests had showed elevated ALP, γ-GTP. There was neither abdominal pain nor bone pain. On physical examination, he was afebrile and had no abdominal tenderness. MRCP showed diffuse stenosis of the intrahepatic bile duct and multiple spinal lesions. FDG-PET revealed skull, pelvis, and femur involvement. Bone biopsy was positive for non-caseating granulomas and he was diagnosed with bone sarcoidosis. He was treated with prednisolone, methotrexate, minocycline, and alendronate because of the high risk of pathological fractures. The disease was evaluated with DWIBS, which was inexpensive and non-radiation modality. All lesions had improved, and prednisolone was gradually reduced.

P3-029

Investigation of serum markers associated with abatacept (ABT) treatment in bio-naive patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] Examination of serum markers related to ABT treatment in RA patients [Methods, results] 1. Anti-CD3 antibody is coated on the plate, and peripheral blood mononuclear cells were cultured in the presence of ABT (500 μg / ml). Cytokines in the supernatant (TNF-α, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-13, IL-17A, IL-17F, IL-21, IL -22, IFN-γ) was measured by ELISA (Biolegend). ABT significantly suppressed IFN-γ production. 2. Anti-CD3-stimulated supernatant (10%) was cultured with synovial cell culture system in the presence of ABT. Twenty-three types of cytokines, chemokines (TNF-α, IL-1b, IL-1RA, IL-4, IL-6, IL-8, IL-10, IL-12p40, IL-23, IFN-γ, Arginase, CCL (2, 3, 4, 5, 11, 17, 20), CXCL (1, 5, 9, 10, 11) was measured by ELISA, and only CXCL10 production was suppressed by ABT. 3. Twenty-five RA patients who received initial ABT intravenous therapy at Higashi-hiroshima Memorial Hospital was divided into low disease activity (LDA) group (n=13) and non-LDA group (n=12) according to whether LDA was achieved after 6 months. Serum IL-2, IL-4, IL-6, IL-10, IL-,17A, TNF-α, IFN-γ, and CXCL10 were measured by ELISA, and CXCL10 was significantly decreased only in the LDA group after 6 months. [Conclusions] CXCL10 may be a therapeutic response marker for ABT.

P3-031

Functional impairment evaluated by the Locomo25 in rheumatoid arthritis

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Conflict of interest: None

[Objective] Locomo25 is a new index developed for the early detection of locomotive syndrome. In RA, joint impairment causes the appearance of problems affecting motor organs as a whole, as well as progressive functional impairment. As functional impairment progresses, it causes increasing immobility, which raises the risk of osteoporosis. Locomo25 was used to investigate functional impairment and its association with RA disease activity and osteoporosis indicators. [Methods] The subjects were 105 patients. The associations between the Locomo25 score and disease activity indices, bone mineral density, and bone turnover markers were investigated. [Results] Locomo25 grade was 1 in 24 (22.9%), and 2 in 44 (41.9%). Locomo25 grade was significantly associated with Steinbrocker class. DAS28-ESR and HAQ increased as locomotive syndrome progressed. Bone resorption markers and a bone quality marker **decreased** significantly as locomotive syndrome progressed. [Conclusions] The Locomo25 score was useful for evaluating functional impairment in RA. Elevated bone resorption and deteriorating bone quality were associated

with progressive functional impairment, suggesting that RA patients with advanced locomotive syndrome may be at risk of increasingly severe osteoporosis as a result of immobility.

P3-032

Rheumatoid arthritis (RA) with pulmonary mycobacterium avium complex diseases

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Conflict of interest: None

Intoroduction: Recently, the numbers of patients with pulmonary mycobacterium avium complex diseases have been increased in Japan, especially in patients with rheumatoid arthritis (RA) under immunosuppressive therapy. We examined factors influencing the prognosis of pulmonary NTM diseases complicated with RA patients. Methods: e retrospectively reviewed 50 RA patients who were diagnosed or suspected with NTM infections at Tokai University Hospital between 2006 and 2018. We analyzed age, biochemical markers, RA disease activity, drug therapy for RA, antimicrobial agents and radiographic findings as prognostic factors. Results: All patients were female and the mean age was 68.9 years. Isolated species of NTM was as follows; M. avium 76%, M. intracellulare 22%, and M abscessus 2%. The corse of soCT findings were classified into 3 groups; progression (8 cases), unchange 26 cases), and improvement (16 cases) by the CT findings. Immunosuppressive therapy was reduced in 38 patients. Advanced age, poor control of RA activity, extensive lesions with cavity formation and hypoalbuminemia were poor prognostic factors. Conclusion: In pulmonary NTM diseases complicated with RA patients, reduction of the immunosuppressive therapy is important with the control of RA disease activity.

P3-033

Chronic kidney disease affects the drug survival rate of biological disease-modifying anti-rheumatic drugs and Janus kinase inhibitors without methotrexate in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study is to clarify the relationship between the comorbidity of chronic kidney disease and the efficacy of biologics and Janus kinase (JAK) inhibitors without methotrexate in elderly patients with rheumatoid arthritis. [Methods] This is a retrospective cohort study performed in our hospital between July 2009 and September 2019. The study population comprised patients aged 75 years or older who were newly initiated with biologics and JAK inhibitors without concomitant methotrexate use. We investigated the drug survival of biologics and JAK inhibitors between the normal renal function group (estimated glomerular filtration rate: eGFR≧60 ml/minutes) and the chronic kidney disease group (eGFR<60ml/minutes). [Results] Fifty-nine patients in the normal renal function group and seventy in the CKD group were analyzed. The median drug survival was 44 months in the normal renal function as compared with 25 months in the CKD group (p=0.0493). Using a Cox proportional hazard regression model, the hazard ratio of CKD was 1.78 (95% confidence interval 1.03-3.09, p=0.039). [Conclusions] Chronic kidney disease is an independent risk factor that affects the drug survival rate of biologics and JAK inhibitors without methotrexate in elderly patients with rheumatoid arthritis.

P3-034

Usefulness of Remicheck® in the treatment of infliximab in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To clarify the usefulness of Remicheck Q® in the treatment of infliximab (IFX) in patients with rheumatoid arthritis (RA). [Methods] Thrity-four patients (2 males and 32 female) treated with IFX were examined. We compared the DAS28ESR and the dose and duration of IFX between the group of Remicheck Q® decision positive (group P) and that of negative (group N). [Results] Twenty-four (76%) of 26 patients belong to group P. In group P, 16 (62%) of 26 achieved clinical remission. In group N, 4 (50%) of 8 patients achieved clinical remission. One of 4 (25%) in regular dose [3mg/kg/8weeks] group and 3 of 9 (33%) in high dose/shortened period for administration group are negative. In 13 cases of the effect insufficiency for IFX, 4 of 13 (31%) were negative, and all cases were improved by dose escalation. In the 8 cases expressed positive, 4 were improved by dose escalation, 2 were improved in natural course, 2 were changed to other agents, and 1 continued IFX for other reason. In 5 cases at the time of the fourth IFX therapy, 2 of 5 (20%) were negative, and all cases were improved by dose escalation. In the 3 cases expressed positive, 2 were improved by dose escalation and 1 was changed to other agents. [Conclusion] Remicheck® in the treatment of IFX in patients with RA is useful.

P3-035

Treatment response of Golimumab for rheumatoid arthritis is associated with initial disease activity and initial dose of Golimumab

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Conflict of interest: Yes

[Objective] To examine the background factors that affect the treatment response of 100 patients who received Golimumab in patients with rheumatoid arthritis (RA). [Methods] 100 patients who started golimumab espesially started for 50mg assessed by Cox regression analysis using age, sex, disease duration, HAQ, TJC, SJC, gVAS, eVAS, CRP, DAS28-CRP, MTX, PSL, bio history, ACPA, RF. [Results] 70 Golimumab started at 100 mg and 30 started at 50 mg. Only baseline DAS28-CRP (Cut-off value: 3.7, AUC; 0.81) was extracted as a factor that continued to be effective after administration of 50 mg. In particular, in patients with baseline DAS28-CRP of 3.7 or higher (n = 52), the 3-year effective continuation rate was significantly different (log-rank, p). <0.001). In the 100 mg starting group, there was no difference in effective continuation rate with or without MTX (log-rank, p = 0.47). [Conclusions] The effective retention rate of Golimumab was found to be the largest factor in the use of Golimumab for baseline disease activity. In particular, the results of the study that started with 50 mg are consistent with the previous report (Clin Rheumatol. 2018; 37: 1417-1420.), and it is possible to start with 100 mg in Japan. Therefore, it seems important to set the dose for baseline disease activity.

P3-036

Patient-reported outcome in the patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Purpose of this study was to investigate the relationship between PRO and clinical features in patients with RA. [Methods] Subjects were 458 RA patients who were self-assessed using a questionnaire with morning stiffness, fatigue, and joint pain. We investigated the relationship between PRO and patient background, serum biomarkers, mHAQ, disease activity, and comorbidities. Spearman's rank correlation coefficient was used for statistical analysis. [Results] The patient background was an age of 66.6 years, 339 women (74%), and disease duration of 13 years. MTX and biologics were used 400 (87%) patients and 145 (33%)

patients respectively. Factors that significantly correlated with PRO were as follows, (1) Morning stiffness: class (r=0.31), TJ (r=0.38), SJ (r=0.21), PG-VAS (r=0.52), Dr-VAS (r=0.49), mHAQ (r=0.51), DAS28-CRP (r=0.44) (2) Fatigue: stage (r=0.26), class (r=0.27), lung disease (r=0.22), TJ (r=0.27), PG-VASr=0.43), Dr-VAS (r=0.41), mHAQ (r=0.45), DAS28-CRP (r=0.35) (3) Joint pain: stage (r=0.26), class (r=0.30), TJ (r=0.42), SJ (r=0.23), PG-VAS (r=0.62), Dr-VAS (r=0.58), mHAQ (r=0.52), DAS28-CRP (r=0.51). [Conclusions] It was suggested that various factors correlate with PRO. If these correlation factors are high, stiffness, fatigue, and joint pain may be worse, so it should be paid attention.

P3-038

Onset to treatment period of Rheumatoid Arthritis didn't affect the index of ability of daily life: A retrospective single center cohort

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Conflict of interest: None

Background: Disease duration has been reported to be a poor prognostic factor in patients with rheumatoid arthritis (RA). However, many studies defined disease duration as duration of therapy. Though, the onset to treatment period is assumed to affect the prognosis of RA patients, no study has shown whether that is true or not. Purpose: To clarify the onset to treatment period affects index of activities of daily living (ADL). Methods: We identified 79 patients who were started therapy for RA in our department between 2016 and 2017. We defined the onset of RA as the time patients recognized joint symptoms. Disease duration of 6 months or more was defined as group A, and less than that was defined as group B. We measured the index of ADL using the modified HAQ (mHAQ) score at baseline and one year after starting treatment. The Mann-Whitney U test was used for analysis. Results: The mHAQ score at baseline wasn't different from between two groups (Group A: 0.44±0.66, Group B: 0.54±0.58, p=0.20). There were also no difference between two groups of the mHAQ score at one year after starting treatment (Group A: 0.35±0.59, Group B: 0.43±0.74 (p=0.90)). Conclusion: This study shows that the onset to treatment time didn't affect the index of ADL at one year after initiation of RA treatment.

P3-039

A study of Abatacept efficacy with non-concomitant use of MTX against elderly-onset rheumatoid arthritis

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Conflict of interest: None

[Objective] Abatacept (ABT) is widely used for elderly-onset rheumatoid arthritis (EORA) due to its safety. Since elderly patients have a number of complications, many of them may possibly have a difficulty to use methotrexate (MTX) in their case. We examined a factor to improve ABT duration in case of non-concomitant use of MTX. [Methods] Among those patients who were over 75 and newly initiated ABT at our institution during a period from July 2009 to September 2019, we conducted a survey retrospectively by selecting 39 patient cases with non-concomitant use of MTX. [Results] Those patients indicated Average age 80.2 years old, Disease duration 7.1 years, and C-Reactive Protein (CRP) 0.82 mg/dL. There were 30 cases for female (77%), 14 cases for using conventional synthetic DMARDs (csDMARDs) at the start of ABT administration. In the analysis of ABT duration, we found that concomitant use of csDMARDs (P=0.045) and CRP < 0.3 mg/dL (P=0.008) contributed to the duration. In multivariate analysis, we also found that a CRP level is an independent factor (HR=1.45, P=0.016) involved in ABT duration. [Conclusions] For the patients who used ABT with non-concomitant use of MTX, it was suggested that a low CRP level and use of csDMARDs at the start of ABT administration contributed to ABT duration.

P3-040

Biological agent therapy in elderly rheumatoid arthritis, elderly onset and adult onset

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Conflict of interest: None

[Objective] Elderly rheumatoid arthritis patients are increasing. Not only life expectancy is improving, but also the age at onset is increasing. We investigate biologic agent therapy of rheumatoid arthritis in the elderly between elderly-onset RA (EORA) and adult-onset RA (AORA). [Methods] Records of relevant patients with RA were collected from the Tsurumai Biologic Communication Registry, wherein the department of Nagoya University and 20 affiliated hospitals in Japan are enrolled. A total of 873 biologics-naïve and age 65 and older patients were recruited from January 2004 to December 2014. We studied the choice of the biologic agent and drug continuation rates. [Results] TNF inhibitors are used most (EORA: 72.7% AORA: 80.8%). 2-years drug continuation rates due to all reasons are EORA: 50.6%, AORA: 48.1%. [Conclusions] There were no significant changes in drug continuation rates between EORA and AORA.

P3-041

Effects of Biological Disease-Modifying Anti-Rheumatic Drug Treatment on Physical Activity, Muscle Power, Agility and Inhibition of Fall in Patients with Rheumatoid Arthritis -Two Years Follow up-

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Conflict of interest: Yes

[Objective] This study investigated the efficacy of bDMARDs on physical function and fall risk in RA patients. [Methods] Periodic evaluation of physical function has been performed in RA patient who initiated their first bDMARDs treatment. 24 cases were completed for 2 years. Evaluation of physical function included evaluation of muscle power (grasping power [GP] and knee extension power [KEP]), agility (Time up and go test [TUG] and 10m walking time [10mW]) and questionnaire using portable fall risk index and the 25-question geriatric locomotive function scale (locomo25) at baseline and 1-3-6-12-24months. [Results] Baseline patients characteristics: mean age 60.8 yo, RA duration 12.3 y. SDAI and CRP were significantly improved on and after one month. GP and KEP significantly improved on and after 3 months and 6 months, respectively. TUG and 10mW significantly improved on and after 3 months and 6 months, respectively. Locomo25 significantly improved on and from 1 month. Portable fall risk index significantly improved on and after 12 months. [Conclusion] The changes from baseline and one month were more drastic in composite measure or biomarker of inflammation, followed by improvement of muscle power and agility. Inhibition of fall were achieved 12 months after bDMARDs initiation.

P3-042

Cost and effectiveness analysis of DMARDs therapy (annual report from Ninja 2018)-The cost-effectiveness of DMARDs improved again-

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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 2002-2018 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 500,000 yen / patient in 2018, 5,000 yen higher than the cost in 2017. The rate of the cost of biologics was 70.4 % and decreased in 4 years. However, the usage rates of JAK inhibitors increased to about 7%. 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. [Conclusions] The NHI price revision leaded to the stop of increase of the DMARDs' cost in 2014. And it continued without the price revision in 2015. 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.

P3-044

Treatment options and short-term results for early rheumatoid arthritis in clinical practice

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Conflict of interest: Yes

[Objective] To investigate the drug treatment choice and short-term treatment outcome for early rheumatoid arthritis (RA) in clinical practice. [Methods] Subjects were able to follow-up up to 6 months after the start of treatment among 185 patients enrolled in the multicenter collaborative early RA cohort (NICER-J) from June 2018 to October 2019 There were 108 cases. We examined the patient background at the start of treatment and the course up to 6 months after the start of treatment. [Results] The patient background at the start of treatment was mean age 60 years, female 67.0%, mean period 14 days from RA diagnosis to treatment intervention, anti-CCP antibody positive 80.4%, smoking history 46.7%. The change from the start of treatment → 3 months after the start → 6 months after the start, MTX usage rate: 79.4% → 81.3% → 81.3%, MTX dose: 7.1mg / week → 9.2mg / week → 9.3mg / week, molecule Target drug use rate: 0 %→ 5.6% → 10.2%, disease activity (DAS28-CRP): 4.26 → 2.74 → 2.27, DAS remission: 3% → 44% → 68%, HAQ: 0.67 → 0.31 → 0.26, HAQ remission: 55% → 65% → 75%. [Conclusion] After the diagnosis of RA, a good therapeutic effect was obtained in a short time by promptly taking appropriate treatment mainly with MTX. This research is funded by Eli Lilly Japan as a doctor-led study.

P3-045

Treatment status of elderly RA patients over 75 years old in our clinic

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Conflict of interest: None

[Purpose] In recent years, aging of RA patients has been reported, RA patients going to our clinic, the proportion of elderly people is high at 53.8% over 65 years old and 24.9% over 75 years old. This time, we report on the treatment status of elderly RA patients. [Subjects and Methods] The subjects were 62 elderly RA patients (12 men, 40 women) who were 75 years of age or older during treatment, with an average age of 79.4 years and an RA duration of 14.3 years. We investigated the time of RA onset, RA pharmacotherapy currently in use, and the status of treatment for osteoporosis. [Results] Elderly onset RA with onset age of 65 years or older accounted for 66.1%, 41 cases. Antirheumatic drugs were used in 34 patients with MTX, 32 patients with salazosulfapyridine, 3 patients with bucillamine, and 2 patients with iguratimod, and 21 patients with steroids. Biologics were used in 14 cases (golimumab 6, etanercept 2, adalimumab 2, abatacept 4), and 12 JAK inhibitors (tofacitinib 6 and baricitinib 6). At present, osteoporosis has been treated in 38 cases. [Conclusion] The patient satisfaction was high by using biologics or JAK inhibitors from a relatively early stage without increasing the dose of MTX for the treatment of elderly RA patients.

P3-046

A case of rheumatoid arthritis that developed at the age of 90

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Conflict of interest: None

A case of rheumatoid arthritis that developed at the age of 90 [Purpose] Rheumatoid arthritis (RA) cases are becoming older, and elderly onset RA cases also appear to be increasing. We have experienced an opportunity to treat an RA case that have developed beyond the age of 90. [Case] A 90-year-old woman visited our hospital with the two weeks complaining of swelling of the right wrist joint, pain, and stiffness of the fingers. She has not experienced any symptoms of joint inflammation before. Plain X-ray images showed no obvious joint disorders in the wrist and finger joints. Joint echo showed abundant blood flow signals in the right wrist joint. Laboratory findings were CRP (mg/dl) 1.42, RF (IU/ml) 61, anti-CCP antibody 47.7 IU/ml, ANA 80 times, ESR (mm/h) 106, and MMP3 (ng/ml) 248.6. The patient was diagnosed with RA and started drug therapy with bucillamine (BUC) 100 mg/day. After BUC administration, clinical symptoms showed improvement, and after 5 months later, the swelling, pain, and stiffness of the fingers disappeared, and the laboratory findings improved well with CRP 0.19, RF 33, MMP3 76.8, and ESR 37. [Discussion] Elderly cases frequently have cognitive dysfunction and complications, but should be treated with antirheumatic drugs if possible.

P3-047

Effects of acetaminophen on the kidney functions of patients with non-traumatic orthopedic disease treated with long-term nonsteroidal anti-inflammatory drug therapy

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Conflict of interest: None

[Objective] To investigate the kidney functions of patients with non-traumatic orthopedic disease who had been using NSAIDs for a long time and examined the possibility of switching to acetoainophen (AAP). [Methods] The subjects were 122 patients who had been using NSAIDs for at least 3 months. After checking their background characteristics, we measured their kidney functions and VAS scores, and then switched them from NSAIDs to AAP. One year after the switch, we remeasured their kidney functions and VAS scores, and investigated whether they could continue using AAP and whether they had used NSAIDs. [Results] The patient's mean age was 77 years, and their mean duration of NSAID use was 48 months. The mean VAS was 41.3 mm and mean eGFR was 66.4 mL/min/1.73 m2. After the switch, 67 patients had continuously used only AAP without NSAIDs. Fourteen patients had used NSAIDs for rescue purposes, 9 patients reused NSAIDs. Overall, the mean VAS was not change, but the mean eGFR was significantly decline as compared with before the switch. Of those who continued to use AAP without any NSAIDs, who did not change the mean VAS scores, but exhibited not a significant decline in mean eGFR. [Conclusions] Halting NSAIDs and switching to AAP could help maintain kidney functions, without pain exacerbation.

P3-048

Retrospective sturdy of rheumatoid arthritis complicated by lymphoproliferative disease

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is occasionally associated with lymphoproliferative diseases (LPD). We investigate clinical profiles of RA patients with LPD, focusing on treatment. [Methods] We retrospectively reviewed medical records of RA patients in our hospital who had developed LPD between April 2009 and October 2019. [Results] Nine patients (2 men and 7 women) were enrolled in this study (mean onset age of RA and LPD: 62.0 and 65.2 years, respectively, mean interval between RA and LPD onsets: 7.9 years). Methotrexate (MTX) was given to 6 patients with a mean dose of 6.6 mg/week at the onset of LPD. Pathological diagnoses of LPD consisted of diffuse large B-cell lymphoma in 6 patients, Hodgkin lymphoma in 2 and marginal B cell lymphoma in 1. All of the patients received chemotherapy for LPD in addition to cessation of MTX. Six patients achieved complete remission, 2 were being treated with chemotherapy and 1 died. Disease modifying anti-rheumatic drugs (DMARDs) used after treatment of LPD were MTX in 2 patients, salazosulfapyridine in 4, iguratimod in 1, bucillamine in 4, prednisolone in 2 and tocilizumab in 1. [Conclusions] RA often remains active still after treatment of associated LPD, requiring some DMARDs, including biologics, to control the disease activity.

P3-049

Treatment of 85 years old or older patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Rheumatoid arthritis patients are aging. Elderly cases may have reduced organ reserve and cognitive function, which may make it difficult to select drugs. We investigated the treatment and clinical course of patients older than 85 years. [Methods] We investigated the background, treatment details, and 3-year treatment responsiveness of 31 patients (2.6%) over 85 years old among 1199 RA patients currently in the hospital, and Compare with 78 cases (non-aged group) aged 40 to 59 years from the same population. [Results] In the elderly RA group, the renal function declined predominantly compared to the non-aged group. The average DAS28-CRP (DAS) and mHAQ in the elderly RA group were significantly higher than those in the non-aged group. Conventional synthetic anti-rheumatic drugs (csDMARDs) were used in 83.9% of the elderly RA group, but MTX was used less frequently than the non-aged group, and MTX average usage was significantly lower. [Conclusions] In elderly RA cases, the amount and use rate of MTX was low, and in combination with csDMARDs and PSL, short-term disease activity reduction and physical function improvement were obtained, but there were also cases where biological preparations were required.

P3-050

Investigation of medication adherence (AD) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] Although the efficacy of oral DMARDs is closely related to AD, it is a concern that AD may decline as RA patients aging. Since the pharmacist in pharmacy mainly provides medication management for outpatients, it is difficult for the pharmacist at a hospital to understand AD. Therefore we conducted a survey with the pharmacist in pharmacy to clarify AD. [Methods] The pharmacist in pharmacy distributed AD survey to the patients. The AD survey used 4 items of the commonly used AD scale (MAS), and the questions were conducted in three stages according to the prior literature: “I don’t think so, I can’t say either, I strongly think” . We also examined patient background, AD level, and social support. [Results] 156 patients participated. The rate of patients answered “I don’t think so” for all four MAS items is 45% and included “I can’t say either” is 75%. The rate of pharmacists judged “no problem with AD” is 85%. 70% patients didn’t adjust the residual drug. About 70% patients replied a few drug at home. 85 % patient brought the medicine notebooks at each time. [Conclusions] About 1/4 RA patients were poor AD. The patients replied that pharmacists are an important (78%) as strong as doctors (82%) and families (76%). We need to examine the causes of AD failure and countermeasures.

P3-051

The study of senile patients with rheumatoid arthritis; rhe efficacy and the risk of infection

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Conflict of interest: None

[Objective] The aim of this study was to assess the effect and the risk of the therapy to achieve the goal of T2T in senile RA patients. [Methods] The patients with RA were divided into two groups: the senile group (age over 75 years old) and the control group (age under 75 years old). During treatment these patients, we set the therapeutic goal by C-DAI, then evaluate the efficacy and the risk of infection. [Results] 222 patients in the senile grop and 222 patients in the control group were registered. MTX usage rate, MTX dose, bDAMARDs or tsDMARDs usage rate were significntly lower in the group of senile compaired with in the control group ($p<0.05$). The remission rate was significantly lower in the senile group (31.1% vs 63.1%, $P<0.05$). The serious infection rate was significantly high in the senile group ($p<0.05$). Multivariate analysis showed that the usage of bDMARDs or tsDMARs was significant risk factors for serious infection in the senile group (Odds ratio 14.5, $p<0.05$). [Conclusions] In conclusive, the patients with senile RA were difficult to get remission because of difficulty of applying enough dose of MTX, bDMARDs and tsDMARDs. Combined use of Sulfa + Trimethoprim may leads to risk redution of serious infection.

P3-052

Association between Methotrexate Dose and Renal Impairment in patients with Rheumatoid Arthritis (RA)

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Conflict of interest: None

(Objective) The purpose of this study was to evaluate the association between MTX dose, changes in renal function and disease duration. (Method) This retrospective study enrolled 71 patients who were treated and who received MTX at the same dose for 2 years (from 6 to 12 mg/week). We examined the relationship between the MTX dose, the annual change in eGFR (ml/min/year), and the duration of disease. (Result) The annual decrease rate of eGFR in the group with MTX less than10 (n=61) was1.0±2.3, and the other group with more than10 (n=10) was2.1±1.9. Although the rate of decline was large, there was no significant difference ($P=0.156$). MTX dose decreased significantly with increasing disease duration ($P<0.05$). The MTX dose of CKD grade 3patients (n=11) was maintained at 6mg in all cases, and the annual decrease rate of eGFR was1.1±2.4. On the other hand, the average MTX dose of non-CKD grade3patients (60patients) was 9.0±1.9mg, and the annual decrease rate of eGFR was

1.5±1.6, and there was no significant difference between the two groups (P=0.605). (Conclusion) The group with MTX10 tended to increase the rate of renal function decline. The MTX dose decreased as the disease duration increased. Decreased renal function is one of the factors to reduce the MTX dose.

P3-053

Clinical feature of elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] Along with aging of the populations, the number of elderly RA patients is increasing. We investigated a clinical feature of elderly RA patients. [Methods] We compared patients over the age of 70 as of April 2017 with patients under the age of 70 for the characteristic. We also investigated complications and deaths that occurred between April 2017 and April 2019. [Results] There were 50 patients who were over 70. The disease duration was 12.5 years and the RF positive rate was 70.0%. It was Steinbrocker's class, the rate of MTX, PSL use, DAS 28 CRP that showed a significant difference compared with patients under the age of 70 in the patient characteristic. There was no difference in the dosage of MTX and the rate of biologics use. 5 year retention rate of biologics was 77%. Complications included 7 fractures, 6 lung diseases. There were 5 deaths. [Conclusions] We showed that the use rate of MTX was low, and relying on the use of steroid. The retention rate of biologics was good, which was thought to be due to selection of the patient. Complications included many fractures, suggesting the effects of steroid. In elderly patients, active treatment may not be possible as young, so adequate prevention is necessary when using steroid because fractures worsen the prognosis of life.

P3-054

Trends after one year of patients with rheumatoid arthritis over 65 years old with chronic kidney disease: AORA registry 2016

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Conflict of interest: None

[Objective] Evaluate the trends one year after in patients with rheumatoid arthritis (RA) 65 years of age or older who had chronic kidney disease (CKD) in 2016 using AORA registry data. [Methods] Cases with a creatinine-based estimated glomerular filtration rate (eGFR) of less than 60 were considered CKD cases. We compared the cases of CKD patients over 65 who obtained eGFR in 2016 and 2017. [Results] In 2016, there were 337 cases with an eGFR of less than 60. Among them, 245 cases obtained eGFR in 2017. The number of cases with improved disease stage was 187, of which 18 were improved by more than 3 stages. With the improvement of renal function, the use of methotrexate (MTX) increased from 2 to 14 cases, and the use of steroids decreased from 13 to 9 cases. There were 14 cases of worsening disease stage. As renal function deteriorated, the use of MTX decreased from 10 to 3 and the use of steroids increased from 7 to 12. [Conclusions] There are many drugs used for the treatment of RA that need to be adjusted according to renal function and drugs that cause kidney damage. In this study, we found many cases of improved stage even in the elderly CKD patients. It is considered that RA can be controlled by adjusting the administration drug according to renal function as the stage improves.

P3-055

Risk of herpes zoster in patients with rheumatoid arthritis treated

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Conflict of interest: Yes

[Objective] RA is frequently treated with PSL and BIO, herpes zoster develops as a complication and the frequency is compared with non-RA patients. There are few reports on recurrence based on treatment changes after the onset. [Methods] Age at the time of diagnosis of shingles during RA treatment at multicenter for 5 years from April 2011 to March 2015, PSL use rate amount, BIO use rate breakdown used, RA treatment after onset The presence or absence of drug withdrawal and recurrence rate were investigated. [Results] As of March 31, 2015, there were 1351 patients who were continuing our RA treatment, and 40 of them developed shingles. The mean observation period is 42.87 months, all women, the mean age of onset patients is 68.96 years, and PSL is used in 18 cases with an average of 3.71 mg, 7 BIO cases: IFX 1 case, ADA 2 cases, TCZ 2 cases, ETN 1 case, ABT 1 case used, 2 cases change treatment after shingles onset. There were 2 cases of treatment changes after shingles and 0 cases of recurrence. [Conclusions] There was no clear difference from previously reported literature. However, sufficient information was not available at our hospital regarding recurrence, and there were many cases where there was no change in treatment, but there were no cases of recurrence.

P3-058

Clinical short-term results of interchangeability from etanercept originator to etanercept biosimilar in patients with RA

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Conflict of interest: None

[Objective] To evaluate efficacy and safety of interchangeability from etanercept originator to etanercept biosimilar in patients with RA [Methods] 69 RA patients received subcutaneous etanercept originator medicated by presenter at Spring, 2019. We researched the efficacy and safety in patients with the interchangeability from etanercept originator to etanercept biosimilar by efficacy measurements included Simple Disease Activity Index (SDAI) and Adverse events (AE). Patient profile is average of age,19.7years old, duration RA,19.7years, The rate of combination therapy with MTX57.1%, MTX average dose 7.94mg/week, The dose of ETN-BS, 50mg weekly 73%, below 25mg weekly 27%. [Results] SDAI was 5.5±4.5 (baseline) 5.5±4.4 (8-12w). Patient pain VAS was 19.9±20.0 (baseline) 20.5±20.0mm (8-12w). 83 years old, elderly RA, male is administrated by sepsis at 1month after interchangeability, but AE was none led to discontinuation like serious infectious disease. [Conclusions] Interchangeability from etanercept originator to etanercept biosimilar in patients with RA was good clinical course.

P3-059

The screening and the monitoring of the hepatitis B virus infection in immunosuppressive therapy at our hospital

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Conflict of interest: None

[Objective] Hepatitis B virus (HBV) reactivation became the problem treated in immunosuppressive therapy (IST). We conducted some investigations about HBV infection in IST of this hospital and examined it. [Methods] We examined HBs antigen (HBs-Ag), HBs antibody (HBs-Ab), HBc antibody (HBc-Ab), quantity of HBV-DNA and treatment history about 801 patients with IST at this hospital by October, 2019 from May, 2015. [Results] The average age was 64.5±14.6 years old. The HBs antigen was positive in 10 cases. Of these, as for 3 cases, HBV-DNA was detected. 8 cases included vaccine intake history, and other 197 patients were with positive one of HBs antibody/HBc antibody. It was used for PSL 86 (4.8±3.1 mg/day), MTX 126 (7.0±2.4 mg/week), and bioDMARDs 44 cases. HBV-DNA threw 7 cases on detection during an observation period. Hepatologist examined all the cases that HBs antigen-positive case and

HBV-DNA were detected. 8patients took entecavir. Hepatitis developed in nobody. [Conclusions] By the RA treatment of the HBV history infected person, the practice in conformity with guidelines is important. In the case that HBV reactivated, we can continue IST by treating with hepatologist without hepatitis developing.

P3-060

Experiences of malignant lymphoma in patients with rheumatoid arhtirits treated with abatacept

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Conflict of interest: None

Objective: We experienced cases of malignant lymphoma and lymphosites prorifaration diseases using abatacept in patiens with rheumatoid arthritis. Method: Five cases were malignant lymphoma (4cases without methotrexate) and 3 cases (1 case without methotrexate) were lymphosites prorifaration diseases. We checked out these cases. Results: All were 60 years of age or old, stage 1: 1, stage 2: 3, and stage 3: 1. Disease duration were from 9 months to 16 years. Conclusion: Although the onset of malignant lymphoma has not yet been clarified, it is necessary to carefully observe the patient's use of abatacept, which is said to be highly safe.

P3-061

Utility and safety of tocilizumab in Rheumatoid arthritis comorbid with Mycobacterium avium Complex: A case report

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Conflict of interest: None

Case report The patient was 72-year-old, male. He was diagnosed with Rheumatoid arthritis (RA) at age 50 when he presented with bilateral MCP, PIP and shoulder synovitis. He was started on prednisolone (PSL) and Methotrexate (MTX). 3 years before fiist visit, he developed diffuse large B cell lymphoma. Discontinuance of MTX and chemotherapy led to complete remisson. After that, moderate disease activity persisted despite treated with bucillamine and PSL. Therefore he was introduced our hospital to induct molecularly-targeted therapy. We started Tocilizumab (TCZ) injection. 2 months after initiated TCZ, he presented shortness of breath. Chest computed tomography showed infiltration with cavity at right upper lung lobe. Microbiological test revieled the positivity for sputum Mycobacterium smear, Gaffky scale 3, and positive for M. intracellulare in nucleic acid identification and culture specimen. He was treated with Clarithromycin (CAM), Ethambutol (EB) and Rifampicin (RFP), respiratory symptom was gradually improved. We continued TCZ to avoid the occurrence of Immune Reconstitution Syndrome. Clinical Significance To our knowledge, this is the first case of successful management of Mycobacterium intracellulare pneumoniae with oral CAM, EB and RFP without discontinuation of TCZ.

P3-062

Analysis of factors that block treatment enhancement in rheumatoid arthritis

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Conflict of interest: None

[Objective] Rheumatoid arthritis treatment should achieve clinical remission, which can be difficult due to individual risk factors. We report factors blocking treatment enhancement in outpatients. [Methods] Factors blocking treatment enhancement among DAS28-ESR, HAQ, eGFR, and administered drugs were analyzed in 534 outpatients (103 males, 431 females, average 64.1 years, 17-91 years) at our hospital, May 1-Sept 30, 2019. [Results] Blocking factors were malignant tumor complications, respiratory infections, interstitial pneumonia, kidney damage, liver damage, pregnancy, economic factors, and aging. Respiratory infections, liver damage, interstitial pneumonia, and economic factors had strong effects, with economic factors showing the greatest effect. Lower priced drugs (MTX and PSL) tended to be higher in patients with economic factors. [Conclusions] Various risk factors can be addressed by combined use of biologics, JAK inhibitors, and csDMARDs. The availability of biologics and immunosuppressive agents has improved joint prognosis in patients who wish to give birth. Remission rates in patients with interstitial pneumonia, liver disorders, and kidney disorders were low. This was likely because use of basic MTX was difficult in these patients, so biological drugs should be considered.

P3-063

The Clinical Problems of RA in Elderly Patients

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Conflict of interest: None

<Objective>To identify the clinical problems of RA treatments in elderly patients. <Methods>Retrospective study of 11 patients aged over 85 years old in recent one year (Mean average age 88.5, female 9, male2). Discussed items were as followed; Onset time (EORA or not), ACPA/RF, Past history (Disease), Usage of PSL, DMARD and Biologics (Bio). Clinical complications. <Results> 6 patients were suggested as EORA.3patients revealed Possibility of ACPA/CCP. Most patients had some disases. MTX were prescribed 4 patients. Bio were used for 5 patients. No complications occured in this series. <Conclusions>According to proper selection, in elderly patients of RA, DMARDs or Bio could be used safely.

P3-064

A case of iatrogenic immunodeficiency-related lymphoproliferative disease with a sinus mass and multiple nodular shadows that differentiated from polyangiogenic granulomatosis

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Conflict of interest: None

Case: 69 years old, female. Course: She got diagnosis of RA in 18 years before. She had used tocilizumab and etanercept, but due to infection, she was finally treated with a small amount of steroid and methotrexate (MTX) 4 mg/week. She got pneumonia and was admitted and got rapidly progressing nasal congestion. CT showed a paranasal sinus mass, nasal septal perforation, and multiple nodules of both lungs. Pathological specimens from the paranasal sinus showed suspicious of granulomatosis with polyangiitis or T-cell lymphomas. In hospital, MTX was stopped and sinus mass and lung nodules were improved. Due to the re-evaluation of pathology, infiltration T and B cells and a large number of EBER positive cells were revealed. Based on pathological findings and the course improved only by stop of MTX, we diagnosed sinus and pulmonary lesions due to iatrogenic immunodeficiency-related lymphoproliferative disease following MTX administration. Discussion: The iatrogenic immunodeficiency-related lymphoproliferative disorder has various pathological findings and presents in various places. This is an educational and important case that initially required differentiation from multiple granulomatosis with polyangiitis by both clinical findings and histopathology.

P3-065

Efficacy of ultrasonography-guided articular injection by out-of-plane needle approach for small and ankle joint symptoms in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] We investigated the efficacy of ultrasonography (US)-guided articular injection by out-ot-plane needle approach for small joint, such as finger, toe, and wrist, and ankle joint symptoms in patients with rheumatoid arthritis (RA). [Object and methods] Forty-six swollen and/or tender joints in 29 RA patients were injected with corticosteroid by US-guided articular injection by out-of-plane needle approach. Sterilized echo-jelly was not used and the needle was punctured avoiding the jelly. After one month, disappearance rate of joint symptome and complication were evaluated. [Results] The changes in the swollen joint (SJ) and tender joint (TJ) counts before and after articular injection (before→after) and disappearance rates (parentheses) were shown here: 8 PIP joints: SJ 8→1 (88%), TJ 6→1 (83%), 7 MCP joints: SJ 7→1 (86%), TJ 2→1 (50%), 16 wrists: SJ 16→9 (44%), TJ 8→2 (75%), 12 ankles: SJ 6→4 (33%), TJ 9→3 (67%), 3 MTP joints: SJ 0, TJ 3→2 (33%). The overall disappearance rate of swollen and/or tender joints was 80% (46→37 joints). There were no complications such as bleeding, neuropathy, and tendon injury. [Conclusions] US-guided articular injection by out-of-plane needle approach was simple and effective method to improve joint symptom in RA patient without complications.

P3-066

Usefulness of drug-specific check sheets and pharmacist interventions in the introduction of biologics and JAK inhibitors at the JR Hiroshima Hospital Rheumatology Department of Internal Medicine

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Conflict of interest: None

[Objective] At the medical corporation JR Hiroshima Hospital (hereinafter referred to as “Rheumatoid”), a pharmacist intervenes a screening using a drug-specific check sheet (prepared in March 2019) at the time of introduction of a biologic and a JAK inhibitor. We investigated the implementation of safe drug therapy without leakage. [Methods] The subjects were patients who received biologics and JAK inhibitors in rheumatoid internal medicine for 5 years from April 2014 to October 2019. Based on the medical records, we examined retrospectively whether there were any missing test items before and after using the drug-specific check sheet prepared by our hospital. [Results] The use of check sheets for each drug led to the prevention of leakage of drug-specific precautions, and was considered effective for safe drug therapy. [Conclusions] Accurate screening has become possible for all patients. Discussing the items to be described at the time of check sheet creation at the conference will lead to alerting doctors and helping them become aware. When necessary, a special conference is held and opinions are exchanged for seamless cooperation and collaboration within the team. Became possible. This effort has improved inspection data checking.

P3-067

Equol improved menopausal arthropathy after excluding rheumatoid arthritis

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Conflict of interest: None

[Objective] Arthropathy is a partial symptom of menopause disorder, and hormone replacement therapy (HRT) is known to be effective. However, HRT has some adverse events and is difficult for rheumatologists to handle. Equol is a metabolite of soy isoflavone, a supplement, but has a estrogen-like action. We investigated the effect of equol in female patients with arthropathy excluded RA. [Methods] Equol was taken at 10 mg daily. We compared the Disability of the Arm, Shoulder and Hand (DASH) questionnaire and Simplified Menopausal Index (SMI) 3 months before equol start. [Results] 90% of 224 patients were female, and 87% were not RA. After explaining equol, patients suspected of having arthropathy as a partial symptom of menopause, 58 people purchased equol and 11 responded to a voluntary questionnaire three months later. The DASH score was improved by 33% and the SMI was improved by 42%, both of which showed a significant difference. There were no adverse events. [Conclusions] In female patients with arthropathy excluded RA, equol significantly improved arthropathy as well as menopausal symptoms. Equol, a supplement (food), is easy to handle and is considered to be useful as an improvement for female patients with arthropathy.

P3-068

Efficacy of tofacitinib for the patients with rheumatoid arthritis for two years

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Conflict of interest: None

[Objective] The aim of this study was to investigate therapeutic effects of Tofa for the patients with RA. [Method] 10 patients with RA who were administered Tofa were selected from ZAO registry, our local biologic registry. We evaluated CRP, ESR, DAS-CRP, DAS-ESR, MTX dose (mg/week) and PSL dose (mg/day) before and 6 months, 1 year, and 2 years after starting Tofa. [Result] Receiving Tofa after 1st biologics (BIO) were 2 cases, 2nd BIO were 2 cases, 3rd BIO was 1 case. The mean score of DAS-ESR was 5.1, 4.0, 3.8 and 3.7, and of DAS-CRP was 4.4, 2.9, 2.9 and 2.8. The mean value of ESR (mm/hr) was 45.8, 38.7, 37.5 and 25.9, and of CRP (mg/dl) was 2.7, 0.4, 0.4 and 0.4. The mean number of tenderness joints was 7.1, 2.9, 2.3 and 3.0, and of swelling joints was 4.3, 2.1, 2.5 and 2.4. The mean dose of MTX (mg/week) was 10.2, 10.2, 9.8 and 9.0, and of PSL (mg/dl) was 2.6, 1.4, 1.4 and 1.2. The tenderness joints, Patient VAS, Drs VAS, DAS-ESR, DAS-CRP and dose of PSL in two years after starting Tofa were less decreased significantly compared to them of starting Tofa ($p< 0.05$). [Discussion] Tofa has been improved disease activity of RA, even in switching case from BIO, and reduced dose of PSL gradually. [Conclusion] Tofa may be one of therapeutically effective drugs for RA.

P3-069

Relationship between response to TNF inhibitors and efficacy of JAK inhibitors

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Conflict of interest: None

[Objective] Precision Medicine for biologics and JAK inhibitors is not clear. JAK inhibitors do not directly inhibit TNF. Therefore, JAK inhibitors may be effective when TNF inhibitors are ineffective. we examined whether treatment response to TNF inhibitors is related to the effectiveness of JAK inhibitors. inhibitors. [Methods] We evaluated 17 patients who used JAK inhibitors after TNF inhibitors in RA patients who visited our hospital. Treatment response to TNF inhibitors was evaluated using the EULAR response. We divided 17 RA patients into 2 groups, 9 in Good / Moderate group and 8 in Non response group. Then, the efficacy of JAK inhibitors in both groups was evaluated using ΔDAS-28CRP. [Results] Baseline DAS28-CRP was 3.24 ± 1.31 in the Good or Moderate group and 3.68 ± 0.90 in the Non response group. ΔDAS28-CRP at Week 24 was -0.78 ± 1.10 in the Good or Moderate group, and in the Non response group was -1.54 ± 1.05 (P = 0.049). [Conclusions] JAK inhibitors may be more effective against TNF inhibitor Non responder.

P3-070

Experience of using Tofacitinib for RA patients in orthopedic clinic

Toshiharu Okuda
Okuda Orthopedic Clinic

Conflict of interest: None

[Purpose] In our hospital, which is an orthopedic clinic, we reported on the continuation status and therapeutic effects of rheumatoid arthritis (RA) patients using Tofacitinib (TOF). [Subjects and methods] we have used TOF, and the subjects were 23 cases (2 males, 21 females) passed for more than 1 year. The average age was 67.1 years, and there were 7 bionaive cases (4 using MTX and 3 not using MTX). There were 17 cases

changed from biopharmaceuticals (TNFα inhibitor 13, tocilizumab 2 and abatacept 2), and 5 of them were used on request to change to oral preparations. The effectiveness of these cases was investigated, including continuation status and changes in disease activity. [Results] There were 12 consecutive cases at 1 year after the start of treatment. Bionaive cases continued in 4 out of 6 cases, continued in 4 cases in 13 cases where TOF change from TNFα inhibitor was continued, and 11 cases returned to previous treatments without effect. Four cases of TOF change from tocilizumab abatacept continued in all cases. In 12 cases that continued for 1 year, the DAS28-CRP mean value improved to 4.31 before administration and 2.17 in 1 year after administration. [Discussion] The use of TOF is useful for RA patients who are difficult to control using MTX.

P3-071

A case of rheumatoid arthritis (RA) with organizing pneumonia (OP) successfully treated with tofacitinib (TOF)

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Conflict of interest: None

[Objective] OP associated with RA is difficult to treat due to insufficient steroid dose reduction. Here we report a case of refractory / relapsed OP patients with RA in which OP has improved and the dose of steroid could have been reduced by using TOF. [Methods] The case was an 84 year old female. Onset of RA in X-28 year (Y). She had a history of using three biologics and, while using certolizumab, an abnormal shadow appeared in the lungs after herpes zoster, and she was hospitalized, in May XY. [Results] As a result of close examination, it was considered to be OP and was relieved by administration of 30 mg of prednisolone (PSL) for 3 weeks. After 25mg was administered for 3 weeks and reduced to 20mg, it relapsed and required 30 mg of PSL again. After 3 weeks, the dose started to decrease gradually every 2 weeks. Thereafter, RA and OP recurred simultaneously at dose of 10mg. Since side effects of PSL such as edema were severe, it was difficult to increase PSL, and TOF 5 mg monotherapy was started. When the dose of TOF was increased to 10 mg after 2 weeks, the effect was marked and the OP image disappeared. PSL has been gradually reduced to 3mg since then, but there has been no relapse. [Conclusions] TOF may have been effective for OP because it has controled multiple cytokines.

P3-072

Examination of efficacy, safety and continuation rate of JAK inhibitor for rheumatoid arthritis in our hospital

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Conflict of interest: None

[Objective] To clarify the efficacy, safety, and continuation rate of JAK inhibitors (JAKi) for rheumatoid arthritis (RA). [Methods] RA patients who had used JAKi by June 30th,2019 were targeted. We examined patient background, continuation rate, change rate of DAS-CRP and mHAQ as efficacy, and reason for discontinuation, and compared the effects of the presence and type of pretreatment drugs. [Results] Of the 95 cases, 65 were women and average age was 66. Among the discontinued cases, the reason for discontinuation within 3 months (21) was side effects (14) and ineffectiveness (7), and those after 3 months (19) was ineffectiveness (12), infectious diseases (3), malignant tumors (2). There were 77 cases (81.1%) who had used bDMARDs or b / tsDMARDs. There was no difference in the continuation rate with or without b / tsDMARDs history (Yes: 54.6% No: 72.2%, p = 0.196), in the type of b / tsDMARDs (TNFαi 57.1%, CTLA4Ig 57.7%, IL-6i 41.7%, JAKi 54.6%, p = 0.812) and in ΔDAS28-CRP after 3 months from JAKi start with or without prior treatment (Yes: -0.61, No: -0.52, p = 0.424), and in the type of b / tsDMARDs (TNFαi: 1.24, CTLA4Ig: 1.15, IL-6i: 1.18, JAKi: 0.61, p = 0.844). [Conclusions] The results suggest that the efficacy and continuation rate of JAKi may not be affected by previous treatments.

P3-073

Effects of JAK inhibitors on rheumatoid arthritis complicated with interstitial pneumonia-A study with ANSWER Cohort data-

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Conflict of interest: None

[Objective] Since JAK inhibitors (JAKi) have been given with caution in cases with interstitial pneumonia (IP), there are few reports of effects on RA with IP. Therefore, we collected cases using JAKi for RA with IP and examined the effects. [Methods] The subjects were 20 RA with IP patients who had been registered in the Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort database and were introduced with JAKi. Among them, we compared and examined parameters of 9 cases in which JAK inhibitors were continued for more than 1 year and KL-6 related to IP could be extracted. [Results] The average age of the group was 72.22 ± 7.66 years, the sex was 3 males and 6 females, the disease duration was 4.5 (0.5-31) years, and the breakdown of JAKi was tofacitinib 8 cases and baricitinib 1 case. SDAI / CDAI before introduction of JAKi was 17.75 ± 2.86 / 16.61 ± 2.84, but after introduction, it was significantly improved to 9.16 ± 1.16 / 8.61 ± 1.10. On the other hand, KL-6 before introduction was 427.57 ± 44.07 (U / ml), and KL-6 after introduction was 453.37 ± 99.10 (U / ml), and no significant difference was observed. [Conclusion] JAKi were considered to have a sufficient effect on RA with IP. There was no significant increase in KL-6 suggesting IP exacerbation.

P3-074

The efficacy of 2nd-line JAK inhibitor treatment in RA patients who had inadequate response to 1st-line JAK inhibitor treatment

Kazuki Fujioka[1], Takashi Kida[1], Hidetake Nagahara[1], Wataru Fujii[1], Shogo Toyama[2], Makoto Wada[1], Ryo Oda[2], Masataka Kohno[1], Yutaka Kawahito[1]
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Conflict of interest: Yes

[Objective] Although the effectiveness of JAK inhibitors (JAKi) against RA patients is well known, there are not a few patients who have inadequate response. However, it is unknown whether the second-line JAKi treatments are effective or not. [Methods] RA patients who had been treated with two or more JAKi in our hospital were enrolled in this study. Their background, drugs used, changes in disease activity, etc. were investigated retrospectively. [Results] There were 41 cases with the history of JAKi administration, of which 11 had the history of 2 kinds of JAKi use. Among them, 9 cases were changed from tofacitinib to baricitinib, and 2 cases were changed from tofacitinib to peficitinib. The reason for discontinuation of the first JAKi was due to insufficient efficacy in all cases. The mean SDAI at the start of the second JAKi and one month later was 28.7 ± 19.9 and 26.1 ± 19.9, respectively. There was no significant difference, but 4 cases had the 20% or more SDAI improvement at one month. Improved cases tended to show lower eosinophil counts (73±59/μL vs 225±223/μL) and larger number of bDMARDs used so far (4.8±2.1 vs

2.2±0.7). [Conclusions] In some cases, it may be effective to administer second-line JAKi treatment, but further data accumulation is desired.

P3-076

Effects of JAK inhibitors against JAK2-mediated signaling in innate immune cells

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Conflict of interest: Yes

[Background] Different cytokine signaling pathways are mediated by varying JAK complexes. JAK isoform selectivity varies depending on the type of JAK inhibitors (JAKis). We assessed the effects of several JAKis on GM-CSF-primed human innate immune cells. [Method] THP-1 cells or primary human neutrophils pretreated with tofacitinib (TOFA), Baricitinib (BARI) and upadacitinib (UPA) were stimulated with GM-CSF (20 ng/mL). JAK/STAT phosphorylation and subsequent interleukin-1β (IL-1β) were investigated using western blot and ELISA method. [Result] All JAKis blocked JAK2 phosphorylation at high concentlation (400nM) in THP-1 cells. Bari and UPA also inhibited JAK2 phosphorylation at lower concentritions (25 and 100 nM). Similarly, not TOFA but BARI and UPA suppressed STAT5 phosphorylation at higher concentrations (100 and 400 nM) in THP-1 cells. BARI and UPA significantly suppressed the IL-1β at lower concentrations (25 and 100 nM) compared to TOFA in THP-1 cells. BARI significantly suppressed IL-1β at lower concentration (25 nM) compared to TOFA in neutrophils. [Conclusion] The inhibition of JAK2-dependent cytokine signals varies depending on the type of JAKis. This suggests difference of JAK selectivity among JAKis may affect the modulation of innate immune cell activation.

P3-077

Severe uveitis in the patients with rheumatoid arthritis against biologics improving by targeted disease-modifying anti-rheumatic drugs: a case report

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Conflict of interest: None

A 39 year-old Japanese man was affected severe uveitis with rheumatoid arthritis. After glucocorticoid pulse therapy for uveitis, a combination therapy of anti-TNF drug and methotrexate was introduced for the peripheral arthritis. After two years, uveitis was recurred with high disease activity of polyarthritis. Although prednisolone 7.5mg per day was added, his disease activity was not improved. After Baricitinib, one of targeted disease-modifying anti-rheumatic drugs, was administered, the disease activity of polyarthritis with uveitis was improved immediately 4 weeks after starting it.

P3-078

The joint preserving surgery in rheumatoid hand

Ryo Oda[1], Shogo Toyama[1], Shinji Tsuchida[1], Masato Ohara[1], Hiroyoshi Fujiwara[2], Kazuki Fujioka[3,4], Masataka Kohno[3], Yutaka Kawahito[3,4], Daisaku Tokunaga[1]
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Conflict of interest: None

[Introduction] Rheumatoid hands cause various obstacles in daily life and cosmetics such as gripping and pinching. We have devised a new technique for thumb deformity and ulnar deviation due to rheumatoid arthritis. [Subjects and Methods] MP joint-preserving surgeries were performed on 10 fingers of 10 type I thumb deformities. The soft tissue was reconstructed with priority given to joint preservation for extensor tendon dislocation and ulnar deviation with swan neck deformity in 10 cases. After surgery, dynamic ROM exercises of thumb and fingers were performed. [Results] The postoperative follow-up period for thumb deformities was 20 to 68 months, with an average follow-up period of 43 months. All cases were corrected, DASH scores improved, and there was no recurrence. The postoperative follow-up period for ulnar deviation was 23 to 74 months, with an average of 48 months. There was no limitation of range of motion, and there was no recurrence of the ulnar deviation. [Discussion] Now that the control of synovitis is possible, the treatment of rheumatoid hand is entering a new era. In order to preserve the joints as much as possible and to improve the prognosis of rheumatoid hands, it is necessary to devise surgical indications and procedures.

P3-079

Characteristics and trends of surgery for rheumatoid arthritis in our department

Takayuki Shimazaki[1], Yuichi Mochida[1], Kengo Harigane[1], Naomi Kobayashi[2], Yutaka Inaba[3], Ken Kumagai[3], Akiko Nagaoka[3], Hyonmin Choe[3], Taro Tezuka[3], Shunsuke Yamada[3]
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Conflict of interest: None

[Objective] We investigated the characteristics and trends of patients with RA who underwent surgery in our department. [Methods] 408 patients with RA who underwent primary joint surgery in our department from 2013 to 2018 were investigated their characteristics and trends of medication at surgery. [Results] The number of patients under 59, from 60 to 69 and over 70 years old were 86, 126 and 196 (the rates of surgery for large joints were 33.7, 34.9, and 39.8%). MTX was administered in 74.3% of surgery for small joints, and 52.3% for large joints (average 8.1 and 7.9 mg/w). Similarly, PSL was administered in 37.7% and 41.1% (average 3.5 and 3.3 mg/w). Bio was administered in 34.2% and 45.7%. When averaged age at surgery was divided into three groups of under 59, from 60 to 69, and over 70 years old, the rates of MTX use were 69.8%, 67.5%, and 63.8% (average 9.2, 8.1 and 7.4 mg/w). The rates of PSL were 38.4%, 39.7%, 38.8% (average 3.7, 3.4 and 3.4 mg/d). The rates of Bio were 54.7%, 34.9% and 33.7%. [Conclusions] With age, the rates of large joint surgery were increased, while the rates of MTX and Biologics were decreased. Compared with small joint surgery, the rates of MTX use were a significantly lower and the rates of Bio usage were a significantly higher in large joint surgery.

P3-081

A case in which the resection gap of hand arthroplasty by the Sauvé-Kapandji method was shortened after artificial elbow replacement and osteotomy was required again

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Conflict of interest: None

[Introduction] We report a patient who underwent ipsilateral hand arthroplasty by the Sauvé-Kapandji method and artificial elbow replacement (following TEA) who needed re-osteotomy for distal ulna pain. [Case] A 73-year-old male, Rheumatoid arthritis disease duration 20 years. Right hand arthroplasty by Sauvé-Kapandji method at 55 years old, right TEA at

65 years old. At the age of 73, supination pain occurred in the right wrist joint. X-ray with shortened distal ulna and osteophyte formation. Osteophyte resection and additional osteotomy of the proximal stump of the ulna osteotomy were performed. The patient was discharged without pain 3 weeks after the operation, and passed 3 months after surgery. [Discussion] In our previous study, there was no pain in multiple cases of ipsilateral wrist arthroplasty at different times from proximal elbow shelf (Koizumi.2013.) In this case, resection of the radial head associated with TEA resulted in shortening of the resection gap of the distal ulna due to proximal movement of the radius, resulting in wrist joint pain [Conclusion] Patients with elbow joint surgery and wrist arthroplasty on the same side may not be able to maintain the forearm length and may change the situation, such as shortening the resection gap

P3-082

Clinical and radiological outcomes of Sauvé-Kapandji procedure for rheumatoid arthritis

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Conflict of interest: None

We examined the clinical and radiological outcomes of the Sauvé-Kapandji procedure for treating disorders of the distal radioulnar joint (DRUJ) in patients with rheumatoid arthritis (RA). This study included 88 wrists of 86 patients with RA underwent the S-K procedure from 2007 to 2012. The mean follow-up period was 26 months. On the basis of Larsen grade, 88 wrists were divided into Group A (grade≦ 3, n= 43) and Group B (grade≧ 4, n= 45). The clinical outcomes evaluated range of motion of the wrist, grip strength before and after surgery. Disabilities of the arm, shoulder and hand questionnaire (DASH) was used for functional evaluation. The radiological outcomes were evaluated to measure the carpal height ratio (CHR), the carpal translation index (CTI) and radioulnar ratio (RWR). The supination improved in Group A, and the pronation and supination improved in Group B. On the other hand, the volar flexion decreased in both groups. there was significantly more decrease in Group A than in Group B. The radiological outcomes indicated no significant change in both groups. The clinical and radiological outcomes are equivalent even in cases with relatively high grade, it was considered that the S-K procedure could be applied in cases of progressing bone destruction.

P3-083

Investigation for migrations of carpus after Sauvé-Kapandji procedure of the rheumatoid wrist

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Conflict of interest: None

[Objective] Sauvé-Kapandji procedure (S-K) is the arthroplasty in which the ulnar head was dissected and fixed to distal radius, working as the shelf for the carpus. In this report, we studied postoperative mid-long term migration of the carpus after S-K. [methods] We reviewed retrospectively the X-ray of the patients. We compared the ulnar shit of the carpus (UCSR) and palmar shift of the carpus (PCSR) between the X-ray taken within one month after surgery and latest X-ray of the involved wrist. [Results] We reviewed the X-ray of seventeen hand of fifteen RA patients (15 women, 1 male, 59 (33.9-75.8) years old at surgery). Median follow-up period was 8.57 (1.45-14.1) years. Median value of PCSR was 0.16 (0.074-0.28) and that of PCSR was 0.27 (0.18-0.42) on postoperative X-ray. On the latest X-ray, median UCSR was 0.22 (0.16-0.35) and PCSR was 0.23 (0.17-0.44). The difference between respective values was significant (P<.01, Wilcoxon signed rank test). Carpus migrated to ulnarly significantly, but palmar shift of carpus was significantly improved. [Conclusion] While the preventable effect of S-K on ulnar shift of carpus was limited, palmar shift was improved significantly after S-K. It is indicated that by the contact wit fixed ulnar head carpus was pushed back dorsally over time.

P3-084

Reconstruction of ruptured extensor tendons in rheumatoid hands

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Conflict of interest: None

[Objective] The purpose of this study is retrospectively evaluate the surgical outcome of RA patients who had suffered from extensor tendon rupture and undergone surgical treatment for extensor tendon ruptures in the rheumatoid wrist. [Methods] This was a retrospective study of 56 RA patients (48 women and 8 men) with extensor tendon rupture who underwent tendon repair between 2001 and 2008. RA patients were performed to move their fingers after operation under the dynamic splint. The latest evaluation was based on both subjective and objective criteria, including the range of MCP joint, PIP joint, wrist joint of flexion and extension after surgery, the extension lag at the MCP joint, PIP joint before and after surgery. [Results] Postoperative extension lag of the MCP joint in the multiple extensor tendon rupture increased significantly compared to the two tendon ruptured in the index finger, middle finger (P<0.05). In the MCP joint flexion angle and PIP joint flexion angle of the thumb, there was a significant difference between the two groups (P <0.05). [Conclusions] We considered that the MP joint extension lag can be improved sufficiently to one or two extension tendons rupture. We need that further post-treatment should be considered in the future.

P3-085

Clinical results of linked-type total elbow replacement for rheumatoid arthritis

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Conflict of interest: None

[Objective] The clinical results of semi-constrained total elbow replacement for rheumatoid elbow arthritis were investigated. [Methods] Nineteen elbows in 17 patients underwent a linked type total elbow arthroplasty in our hospital from 2004 to 2013 were enrolled in this study. The mean age at the time of surgery was 67, the mean follow-up period was 85 months. Eleven were treated with Coonrad-Morrey elbow and 8 were Discovery. Japan Orthopedic Association score (JOA score), range of motion, X-ray abnormalities, and complications were investigated before and at the final investigation. [Results] JOA score improved significantly from 40 to 81 points on average after surgery. The flexion angle improved from 116° to 132° at the time of the final examination, but the flexure contracture was almost unchanged from 31° before surgery to 27°. A radiolucent line was found in the ulna at 1 elbow from a postoperative X-ray. Two elbows suffered the periprostetic infection, 6 suffered intraoperative fracture and implant loosening at 1 elbow. [Conclusions] Total elbow arthroplasty at our hospital, postoperative results on about 7 years were generally satisfactory.

P3-086

The Revision Total Elbow Arthroplasty using an impaction bone graft for patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] The aim of this study was report of the revision total elbow arthroplasty using an impaction bone graft for patients with Rheumatoid Arthritis [Methods] A 69 year-old, he suffered from Rheumatoid Arthritis from 2003, steinblocker class2, stage4. He underwent Total Elbow Arthroplasty<TEA>with Discovery prosthesis in June 2016. Due to per-

sistent elbow pain and instability, he underwent component of ulnar revision surgery with impacted bone grafting in October 2019. Because of there were no instability after surgery among ulnar fracture, he hadn't need osteosynthesis. [Results] Postoperatively, the patients had no complications after surgery and demonstrated improvement JOA score. [Conclusions] There are many reports of complications about loosening after TEA. Because of the poor cementing technic, RA control and overuse of elbow, this patients had loosed his ulnar implant. This case presents a methods of revision TEA using impaction bone graft. We have to treat RA with csDMARDs, biologics if we get informed consent and follow up this results.

P3-087

One stage total elbow arthroplasty as the treatment strategy for the humeral supracondylar fracture in rheumatoid end-staged destructive elbow joint; a case report

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Conflict of interest: None

A female rheumatoid patient with 49 years of disease duration, 71 years old, had been suffered left humeral supracondylar fracture by fall. By the radiographic image, the fracture was classified AO-A2, and revealed the end-staged (Grade 4 according to the Larsen's classification) rheumatoid destructive articular lesion in ipsilateral elbow joint. Therefore, we selected as the treatment strategy one stage total elbow arthroplasty (TEA) for the osteosynthesis and postoperative functional improvement of the elbow joint. In the surgery, the bone cement was filled with the pressure using cement-gun, and endoprostheses were implanted, maintaining the corrective reposition of humeral fracture site in manipulation. Furthermore, to gain more ridged fixation against for the twisting force, we added osteosynthesis using locking plate system. The elbow joint was performed external fixation with splint 2 weeks after the surgery, and aggressive ROM exercise and ADL exercise were done. After 15 months from the surgery, the patient lives with improved ROM and ADL in comparison to the state before this injury without pain. And in fracture site, sufficient bone union is provided without any trouble regarding prosthesis by radiographic image.

P3-088

A case report of revision Discovery total elbow arthroplasty

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Conflict of interest: None

[Patient] 7X years old female rhematoid arthritis. [Summary] We operated a total elbow arthroplasty using Discovery total elbow system. Eight years after surgery, radiolucent line around humeral component appeared, and we diagnosed an aseptic loosening of total elbow arthroplasty. We operated revision total elbow arthroplasty. Intraoperative findings showed metallosis in the synovium around huumeral component, bearing, and condyle kit. [Conclusions] We experienced revision for aseptic loosening after Discovery elbow system, which was rarely reported.

P3-089

A case report of elbow resection arthroplasty in a patient with rheumatoid arthritis who had a massive elbow bone destruction caused by prosthesis loosening

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Conflict of interest: None

[Objective] [Objective] To report the case that had an elbow resection arthroplasty in a patient with rheumatoid arthritis (RA) due to bone massive destruction caused by prosthesis loosening. [Case] 67 years old woman. She was operated with total elbow arthroplasty (TEA) (FINE ELBOW) on her right arm at October 2006. Loosening of ulnar component was observed at one year and 5 months later post-operatedly. Revision operation was done at May 2008, one year and 7 months post-operatedly. She was operated with TEA (Coonrad-Morrey) on her left arm at May 2007. Loosening of humeral component was observed at four years and one month later post-operatedly. Her left humeral fracture also was occurred. On March 2018, her revision surgery was done with humeral component with long stem. After that, she could not flex her left elbow over 90 degrees. Then, loosening of right humeral component was observed and fracture was happened. Because of that she could not flex her left elbow over 90 degrees, she refused her right elbow revision and resection arthroplasty was done. Now she could flex her right elbow over 130 degrees with brace. [Conclusion] It is better to operate revision surgery as soon as possible if loosening of component was observed

P3-090

A Case of Infection After Total Elbow Arthroplasty Treated with Cement Spacer Placement after Removal of The prosthesis

Takuo Juji[1], Naohiro Izawa[1], Ichiro Nakamura[1,2], Katsumi Ito[3], Takumi Matsumoto[4], Jinju Nishino[4], Sakae Tanaka[4]
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Conflict of interest: None

[Introduction] Total elbow arthroplasty for elbow joint destruction in patients with rheumatoid arthritis is a useful treatment. However, postoperative infection is a serious complication. We report a case of infection after total elbow arthroplasty treated with cement spacer placement. [Case] 65 years old woman. Rheumatoid arthritis onset at age 44. Elbow arthroplasty performed at age 55. Total elbow arthroplasty performed at age 63. After surgery, infection of the elbow joint appeared. Debridement were performed. Infection improved. One year later, infection recurred. Debridement performed again. Infection improved. But 1 year and 6 months later, infection recurred. The elbow prosthesis was removed and a cement spacer was placed. The infection subsided, but the infection recurred after 2 months, so the cement spacer was replaced. There was no recurrence of infection 1 year and 7 months after surgery. [Dicussion] Joint prosthesis infection is a complication that is difficult to treat. If the infection does not subside and the prosthesis is loose, it must be removed. Cement spacers can be repositioned even if infection relapses. [Conclusions] We experienced a case in which infection after total elbow arthroplasty was treated with cement spacer placement after removal of the prosthesis.

P3-091

The effective of synovectomy against remaining arthritis to rheumatoid arthritis patients under medical treatment

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Conflict of interest: None

[Objective] We evaluated the effective of synovectomy against remaining arthritis instead of changing medication or add on medicine. [Methods] 15 surgeries were performed in 14 patients (knee7, elbow4, wrist3 and finger1), there were 14 women and 1 men, between April 2009 and April 2019. We followed DAS28 (CRP), medication and X ray in 1 year. [Results] The mean age was 59.2 (30-80) years, the mean duration of the disease was 12.8 (2-40) years, and the mean DAS28 (CRP) was 2.9 (2.1-4.9). Methotrexates were used in 11 patients, biological agencies were used in 6 patients and prednisolones were used in 6 patients. After operations were performed, the mean DAS28 (CRP) in 3, 6 and 12 month were 2.9 (1.2-4.9, p=0.057), 1.9 (1.2-3.3, p=0.012) and 1.8 (1.2-3.8,

p=0.02). 9 patients were changed their medication (5 were add-on and 4 were dose down). There were no changes in X ray but 2 total knee arthroplasties were performed over 1 year later. [Conclusions] The numbers of synovectomies reduce but we can consider to perform against remaining arthritis under medical treatment.

P3-092

Rheumatoid arthritis is a risk factor for perioperative complication after long spinal fusion

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Conflict of interest: None

[Objective] The purpose of this study was to examine whether rheumatoid arthritis (RA) affects the risk of perioperative complications such as surgical site infection (SSI) in long-spinal fusion. [Methods] Fifteen RA patients (RA group: RAG) and 50 non-RA patients (control group: CG) who underwent long-spinal fusion surgery from Nov 2010 to Des 2018 were included in this study. We examined SSI and organ-specific infections, postoperative complications other than infection. [Results] There was no difference in age (73.5 years in RAG, 72.5 years in CG), sex (female were 11 cases in RAG, 45 cases in CG) and YAM (76% in RAG, 75% in CG). The number of fixed vertebral body was significant longer in CAG (8.5) than in RAG (5.6). The mean operative time was significantly longer in CAG (487 min) than RAG (312 min), but there was no difference in bleeding (855ml in RAG, 998ml in CG). Perioperative infection rate was significantly higher in RAG (40%) than in CG (12%). SSI rate was also higher in RAG (27%) than in CG (2%). There was no difference in postoperative complication other than infection (7% in RAG, 10% in CG). [Conclusions] This result indicate that RA patients have a higher risk of SSI in long-spinal fusion than non-RA patients. Careful follow-up were necessary for RA patients.

P3-093

Nonunion odontoid fracure with anterior odontoid screw fixation in rheumatoid arthritis-2 case reports

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JCHO Tokuyama Central Hospital

Conflict of interest: None

[Case1] A 57-year-old man who has been treated rheumatoid artilitis for14 years in our hospital fell down and bumped the forehead. Because of persisting neck pain, he went for a check up to our hospital and was diagnosed with a type2 odontoid fracture in Xp and CT. Anterior odontoid screw fixation (AOSF) was performed. 1 and a half year after surgery, odontoid fracuture had nonunion. [Case2] A 73-year-old woman who has been treated rheumatoid artilitis for15 years in our hospital had neck pain after falling down from the waist. She was diagnosed with a type2 odontoid fracture by Xp and CT at our hospital. AOSF was performed and teriparatide was started after surgery. But 5 days after surgery screw was cut out from anterior cortical bone of C2, halo vest immobilization was used. 2 and a half years after surgery, odontoid fracuture had nonunion. odoncoid fracture became nonunin. [Discussion] Type2 odontoid fracture had been reported high nonunion rate for non operative treatment. AOSF is useful operative method, but nonunion cases have been reported in eldery patients with osteopenia. In our cases there was poor stability because of osteopenia with RA progression. [Clinical significance] It is possible that there is poor stability for AOSF to odontoid fracture with RA.

P3-094

The incidence of venous thromboembolism before orthopedic surgery between patients with rheumatoid arthritis and those with osteoarthritis

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Conflict of interest: None

[Objective] The aim of this study was to compare the incidence of venous thromboembolism (VTE) before orthopedic surgery between patients with rheumatoid arthritis (RA) and those with osteoarthritis (OA) and to identify the risk factors of DVT before orthopedic surgery patient with RA. [Methods] The study cohort was composed of 86 patients with RA and 106 patients with OA before lower limb orthopedic surgery between 2016-2018. Ultrasonography was performed in all patients as a preoperative examination. Logistic regression models were used to calculate the odds rate for DVT in RA patients. [Results] When the patients were matched for age, sex, and BMI, the incidence of DVT was 11% and 33% in patients with OA and RA, respectively. In the RA group with DVT, preoperative D-dimer levels and age were significantly higher than those of without DVT. NSAIDs were more frequently used daily in 71% of the patients with DVT than in 44% of the patients without DVT. Logistic regression models showed that increased age, use of steroid, not use of NSAIDs or high D-dimer level were the independent risk factor for preoperative DVT in patients with RA. [Conclusions] The incidence of DVT was more frequency in RA patients than in those with OA

P3-096

Impact of Obesity on MASEI (MAdrid Sonographic Enthesis Index) Evaluation in Spondyloarthropathy

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Conflict of interest: None

[Objective] In spondyloarthritis (SpA) such as ankylosing spondylitis (AS) and psoriatic arthritis (PsA), it has been reported that obesity contributes to disease activity and resistance to treatment. On the other hand, there are few reports showing the effect of obesity on image evaluation of adhesion inflammation in SpA. Here, we examined the effect of obesity on enthesitis using the MASEI (MAdrid Sonographic Enthesis Index) evaluation. [Methods] We retrospectively studied 98 SpA patients assessed for their MASEI score at our hospital who were divided into 44 obese patients with a BMI (Body Mass Index) ≧25 and 53 non-obese patients with a BMI < 25. [Results] There were no significant differences in VAS or HAQ between the two groups. Tendon structural abnormalities (tendon of triceps brachii and quadriceps femoris), tendon thickening (proximal patellar tendon), and osteophyte calcification (proximal and distal patellar tendons) were significantly increased in obese patients compared with non-obese patients. MASEI-inflammation did not differ significantly between the two groups, but MASEI-damage tended to be increased in obese patients. [Conclusions] These observations suggest that the obesity become an exacerbation factor of the adhesion division flame in the image evaluation in the SpA.

P3-097

Is reactive arthritis a common but overlooked disease? How do you diagnose it?

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Conflict of interest: None

[Purpose] We recently experienced three cases of ReA and discuss the diagnosis. [Case] 1) A 40y.o.F. Two weeks after tonsillitis, back pain, right anterior iliac spine pain and right lateral knee pain appeared. It also spread to the left anterior iliac spine but ceased for 2 months. 2) A 50y.o.M., Unexplained fever persisted for 2 weeks. Two weeks later, bilateral upper arm pain and right anterior chest pain appeared. Diagnosed as rheumatoid arthritis (RA) with RF positive. Using PSL 10 mg / day and MTX 10 mg /

week, and became remitted completely for 4 months 3) A 45y.o.M., 5 days after fever and skin eruption, there was tenderness in bilateral axilla and heels. They lightened after 2 months. Parvo B19IgM was positive. [Discussion] 1st., Edema of the tendon was detected by joint echography, and she was diagnosed poststreptococcal ReA. 2nd., The history was re-examined for complete remission with short term, the previous infection was confirmed, and the diagnosis was corrected to ReA. 3rd. was diagnosed as ReA after parvovirus infection based on the physical findings of enthesitis. [Conclusion] It might be true that ReA is frequent in daily clinical practice. Enthesitis is indispensable for ReA diagnosis. ReA should be reviewed in male RA and RA in remission within 6 months.

P3-098

A Case of Mono-synovitis with Family Histories of Rheumatoid Arthritis

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Conflict of interest: None

[Clinical significance] To describe that a male patient with chlamidia-associated arthritis (Chl-AA) was treated successfully using methotrexate (MTX), and that it was suggested that arthritis preceded urinary tract infection. [Case] A 30-year-old male with family histories of rheumatoid arthritis (RA) had a 10-month-history of right knee arthritis diagnosed hydrarthrosis without RA by neighborhood orthopedic sergeant and about 30 mL synovial fluid puncture was performed every 2 weeks. Since 6 months before, hand, foot and mouth disease was occurred with around 39 degrees Celsius; moreover, since 5 months before, he was diagnosed having testitis and prostatitis with around 40 degrees Celsius by a neighborhood urologist. His each disease, though, was getting well soon without biotical treatment. Since 2 months before, arthroscopy with synovium biopsy was performed and the pathology of the synvium was no malignancy but non-typical inflammatory changes. He was referred to our institute with right knee mono-arthritis. He was suggested reactive arthritis with urinary tract infection. The high cut off index of anti-C. trachomatis (CT) IgA/G antibody were detected: 9.8/11.2, respectively. Using methotrexate (MTX) made his arthritis improved. MTX was effective agent for Chl-AA.

P3-099

Study of the relationship between sternoclavicular arthritis and peripheral enthesitis by ultrasonography

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Conflict of interest: None

[Objectives] Sternoclavicular arthritis is a pathological condition sometimes observed in SpA. Since ultarasonography (US) is thought to be useful for the sternoclavicular joints, evaluation of sternoclavicular arthritis using US with an increased number of patients. [Methods] Subjects were SpA cases or suspected SpA cases (65 men,243 wemen) who underwent US in my clinic from June 2018 to August 2019. Loss of fibrillary pattern, tibia, patella tendon pole, patella quadriceps tendon, Achilles tendon, plantar fascia adhesion. Power Doppler signal (PD) was evaluated and the MASEI score was evaluated. Sternoclavicular arthritis was evaluated based on the joint US guidelines. [Results] There were 69 positive sternoclavicular arthritis cases with an average MASEI score of 15.4 and 36.8%of cases with a score of 18 or higher. On the other hand, there were 239 cases negative sternoclavicular arthritis with an average MASEI score of 10.6 and 16.3% of cases with a score of 18 or higher. [Conclusions] Cases of positive sternoclavicular arthritis with MASEI score 18 or more was 2.3 times as compared to the negative cases. Therefore, it is considered that sternoclavicular arthritis and peripheral enthesitis are closely related. Sternoclavicular arthritis is considered to be an important condition in SpA.

P3-100

Small lesions indicating bone marrow edema on sacroiliac MRI in two patients with fibromyalgia syndrome

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Conflict of interest: None

Patient 1 was 52-year-old female and admitted to the outpatient clinic with chronic pain in various parts of her body for 18 months. Laboratory testing showed CRP negative, ESR negative and HLA-A24, B7 and B61 positive. She was diagnosed as fibromyalgia syndrome using ACR 2011 criteria. Patient 2 was 35-year-old female. On admission, she complained of severe pain in her muscles and all over her body lasting for 18 years. A lot of traces of cutting were found on her extremities. Laboratory testing showed CRP 0.51 mg/dL, ESR negative and HLA-A2, B51 and B61 positive. She was diagnosed as fibromyalgia syndrome using ACR 1990 criteria. To rule out axial spondyloarthritis, MRI was performed. In both cases, small lesion with high signal intensity on STIR was detected in the right sacroiliac joint. However, their back pain was refractory to sulfasalazine. X-ray of sacroiliac joints have not shown bone destruction yet. In two patients with non-inflammatory back pain, unilateral tiny lesions suggesting bone marrow edema on sacroiliac MRI were found. Although these lesions could indicate non-specific findings in fibromyalgia syndrome, the patients should be observed carefully, because they have HLA-B61 associated with axial spondyloarthritis.

P3-101

Two cases of Stenoclavicular Joint Infection in our hospital

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Conflict of interest: None

It is difficult for a stenoclavicular joint (SCJ) pain to a diagnosis. As stenoclavicular joint infection (SCJI) is a rare occurrence, we suffer from the diagnosis and which may cause the patient the serious state by complications. Here we report two cases of SCJI in our hospital. Case1 developed into osteomyelitis. The SCJ was resected and control of the SCJI was provided. Case2 developed into a deep part abscess. We carried out drainage by retention of the pus to the deep part and treated by antibiotics, which made control of the SCJI. The compromised host such as diabetes or the steroid dosage is risk factor of SCJI. To the best of our knowledge, it takes an average of 44.4 days (3 to 180 days) by a diagnosis. X-ray and CT-scan of SCJ is almost normal, which may make a patient diagnosis difficulty and a sever state. A cure to give progressively, for example: the antimicrobial dosage, incision drainage, and SCJ resection, were reported by an image and clinical evidence. Our cases followed it, and it was with good progress. In the case of the diagnosis of the SCJ, the close inspection that is enough for mind thinks differentiation for the infection to be important.

P3-102

Clinical study of seronegative arthritis with abnormal nail capillaries

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Conflict of interest: None

[Purpose] In psoriasis, it has been reported hat abnormal findings were observed with capillaroscopy. We performed capillaroscopy in seronegative patients with peripheral arthritis and extracted eight cases with findings characteristic in psoriasis, and examined the clinical characteristics. [Methods] From November 2015 to October 2019, we examined eight

seronegative arthritis patients who showed abnormal findings with capillaroscopy (tortuous capillaries etc.). We investigated their patient backgrounds, blood tests, and imaging findings HLA-A and B, the treatment contents. [Results] The patient backgrounds; median age (IQR) 65 years (61.5-69). Clinical diagnosis was psoriatic arthritis (PsA) for 4 cases and seronegative arthritis (SNA) for 4. Image inspections revealed dactylitis in 3 cases (1 case in PsA, 2 in SNA), enthesitis in 4 (1 PsA, 3 SNA), and arthritis in all cases. HLA-A2 was positive in 5 (2 PsA, 3 SNA) and A11 was positive in 4 (3 PsA, 1 SNA). Treatment contents; Ixekizumab for 2 (1 PsA, 1 SNA +dactylitis), Secukinumab for 4 (3 PsA, 1 SNA +dactylitis), Methotrexate for 6, Apremilast for 1. [Conclusion] All cases with psoriatic findings on Capillaroscopy were HLA-A2 or A11 positive. It suggests that Capillaroscopy and HLA-A may be useful for the diagnosis of PsA.

P3-103

Histological changes in rat hip joint mono-iodoacetate induced osteoarthritis models due to differences in reagent concentration

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Conflict of interest: None

[Purpose] Mono-iodoacetate (MIA) inhibits glycolysis and damages chondrocytes, thereby causing deformed joint-like (OA) changes. In this study, we varied the concentration of MIA and evaluated local X-ray and histological evaluation of the hip joint and changes in the pain threshold. [Method] Model using 6-week-old male SD rats and MIA group (n=30), MIA 0.25mg, 0.5mg, 1.0mg, 2.0mg, 4.0mg + 25μl of saline in the right hip joint, each (n=6). In addition, as a sham group (n = 6), a model in which only 25 μl of raw food was administered was prepared. Toluidine blue staining and safranin O staining were performed, and walk analysis was performed at the same time using Cat walk® . [Result] In K-L classification, Grade increased in a concentration-dependent manner and progressed over time. In the OARSI score, the score increased in a concentration-dependent manner and progressed over time. Cat walk showed temporary pain avoidance behavior after the model was created, but it improved over time and increased to the same level as in the low concentration group at 4 weeks after the model was created. [Discussion] In the rat MIA-administered hip joint OA model, progression of joint destruction was observed over time and in a concentration-dependent manner on both X-ray and histology.

P3-104

The effect of Tramadol administration on arthritic changes in rat hip osteoarthritis model

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Conflict of interest: None

[Objective] There is no doubt that opioids are effective for the treatment of pain in osteoarthritis. In this study, we investigated the effect of opioid administration on the progression of joint deformation using a rat hip joint OA model. [Methods] Using 6-week-old male SD rats, Sham group (n = 6) administered physiological saline alone in the right hip joint, OA group (n = 6) administered MIA (0.5 mg), Tramadol 2 weeks after MIA administration The Tramadol group (n = 6) was administered intraperitoneally (20 mg / kg), and X-ray evaluation was performed at 2, 4, and 6 weeks after MIA administration for joint deformation evaluation. Local histological evaluation was performed 6 weeks after administration. [Results] **B**oth the OA group and the Tramadol group showed signs of progressive cartilage loss and degeneration, and the histological evaluation showed arthritic changes in both the OA group and the Tramadol group. The Tramadol group tended to have a stronger degree of tissue degeneration than the OA group. [Conclusions] In this study, administration of MIA 0.5 mg into the hip joint showed a relatively mild progression of OA, which was histologically more severe in the Tramadol group than in the OA group.

P3-105

Association between synovitis and pain in hip osteoarthritis

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Conflict of interest: None

[Objective] The aim of this study was to investigate the association between synovitis and pain in hip osteoarthritis. [Methods] Between February and November 2019, primary THA was performed in 90 symptomatic hip osteoarthritis cases. Of these, 7 hips were in male patients and 83 hips were in female patients, with a mean age of 69.5 years (43-89 years). We retrospectively investigated the presence of synovitis based on operative records, and preoperative clinical evaluation of hip pain was performed using JOA pain scoring system, JHEC pain score, and pain visual analog scale. We divided the patients into groups with and without synovitis. A significant difference was considered to be present when a p value less than 0.05 was obtained on a t-test. [Results] The group with synovitis included 23 hips, and the group without synovitis included 68 hips. The mean total JOA pain score, JHEC pain score, and pain VAS score in the group with synovitis were 14.2 points, 7.81 points, and 78.8, respectively. The mean total JOA pain score, JHEC pain score, and pain VAS score in the group without synovitis were 13.5 points, 7.65 points, and 80.8, respectively. There were no significant differences between the two groups. [Conclusions] Synovitis in the hip joint is not significantly associated with pain.

P3-106

Evaluation of sit-to-stand movement using a force plate system for patients with hip and/or knee osteoarthritis

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Conflict of interest: None

[Objective] Sit-to-stand movement from a chair is a mechanically demanding component of activities of daily living. We used a novel method using a force plate placed beneath the feet to quantify sit-to-stand movement. [Methods] The study enrolled 100 patients with hip and/or knee osteoarthritis (male/female ratio, 20/80; mean age, 66.8±9.8 years) who had independent walking ability prior to total joint arthroplasty. The subjects were instructed to stand up as quickly as possible on a force plate, and the sit-to-stand (STS) score was calculated as the combination of the speed (S) and balance (B) indices. We compared the STS score with the timed up and go (TUG) test, a well-known clinical test used to evaluate an individual's mobility. [Results] STS score and S was significantly correlated with TUG time (STS score; r=-0.308, S; r=-0.509). [Conclusions] STS score represents individual's mobility and can provide useful information to clinical evaluation of STS performance in patients with hip and/or knee osteoarthritis.

P3-107

Comprehensive analysis of serum peptides in patients with relapsing polychondritis

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Conflict of interest: None

[Objective] To identify candidate biomarkers for relapsing polychondritis (RP), we comprehensively analyzed serum peptides from the patients with RP. [Methods] Serum samples were obtained from 16 patients

with RP, 21 patients with rheumatoid arthritis, and 21 healthy control subjects. Peptides, extracted using weak cation exchange chromatography, were comprehensively detected by MALDI-TOF mass spectrometry. Peptide ion intensity was subjected to orthogonal partial least square-discriminant analysis to generate discriminant models for the diagnosis of RP. [Results] 160 peptide ion peaks were detected. 12 peptides showed more than 1.2-fold or less than 1/1.2-fold ion intensity between the RP and non-RP (RA+HC) groups ($p<0.05$). A discriminant model generated using ion intensity of 38 peptides clearly distinguished the RP group from non-RP group (R2X: 0.907, R2Y: 0.887, Q2: 0.0377). [Conclusions] Analysis of serum peptide profiles was useful for detection of RP biomarker candidates. Further selection from the 12 and 38 peptides may serve useful RP biomarkers for the clinical diagnosis.

P3-108

Joint destruction in hemophilic arthropathy

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Conflict of interest: Yes

[Objective] When blood vessels are damaged, bleeding is observed. Hemostasis occurs to prevent and stop bleeding. Activation of a series of blood coagulation factors occurs. Hemophilia is a inherited genetic disorder that impairs the ability to make blood clots. Although coagulation factor replacement therapy allows hemophilia patients to have stable daily life, adult patients even under the replacement therapy have joint destruction which is called hemophilic arthropathy. It is clear that bleeding induces the joint destruction, however, the details of the mechanisms of hemophilic arthropathy are unknown. Thus, we aim to clarify the pathogenesis of hemophilic arthropathy. [Methods] Factor VIII-deficient mice, which are hemophilia A model mice, were used. The joint cavity was punctured with a needle to induce bleeding, thereby obtaining a hemophilia arthritis model mouse. After puncture, joint and cytokines were determined. [Results] Bone destruction was observed in the mice five days after puncture. At one and two weeks after puncture, inflammatory cytokines were detected in the injured joint. Myeloid cell accumulation was also observed. [Conclusions] An increase in inflammatory cytokines, including RANKL and IL-6, and joint destruction was observed in the hemophilia mouse model.

P3-109

A case of erosive hand osteoarthritis successfully treated with Tocilizumab

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Conflict of interest: None

[Case] A 60-year-old Japanese woman noticed DIP arthralgia and joint deformity since X-6. PIP arthralgia appeared in X-2. The swelling also appeared afterward; she visited our hospital. The swelling and tenderness were also observed in the PIP and DIP joints. CRP and ESR were not elevated. RF 5.4 anti-CCP Ab were within a normal range. X-p revealed a gull-wing appearance and a saw-tooth erosion. The patient was diagnosed with erosive hand osteoarthritis (EHOA). Treatment with NSAID and denosumab for coexisted osteoporosis was initiated from August X-1. However joint destruction and arthralgia continued. Therefore, treatment with tocilizumab was initiated. After that, arthralgia gradually improved and the progress of joint destruction halted. [Discussion] EHOA is more likely to develop in middle-aged or older women, with rapidly progressive joint destruction and severe joint pain. Although there have been some reports that TNF inhibitors have been effective, there is no established treatment. Therefore, symptomatic treatments such as NSAIDs are mainly used. In our case, treatment with tocilizumab was effective for arthralgia and joint destruction resulting from EHOA. [Conclusion] Tocilizumab may be effective for the treatment of EHOA.

P3-110

A hemosiderotic synovitis patient with repeated knee joint hematoma was effectively treated with arthroscopic surgery

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Conflict of interest: None

[Background] Hemosiderotic synovitis is a proliferative disease synovial membrane secondary to chronic intra-articular hematoma, resulting in joint destruction. [Case] A 51-year-old woman with no particular past medical history had suffered from the swelling of the right knee joint for the past two years. She was diagnosed to have knee joint hematoma from a large amount of rust-colored knee puncture fluid. We conducted MRI and she was suspected to have pigmented villonodular synovitis. We performed arthroscopic synovectomy for the purposes of diagnosis and treatment. The outgrowth of the brown villous synovial membranes was observed and we resected the synovial membranes as much as possible. In addition, the cartilage defect was observed at the articular surface of patella and the hemorrhagic spot was seen at the same site. The patient was diagnosed to have hemosiderotic synovitis based on the pathological findings. No swelling of the knee joint was seen and no outgrowth of the synovial membranes was observed by MRI six months after the surgery. [Conclusion] When the repeated knee joint hematoma was observed in patients with no particular medical history, we need to consider that there is a possibility of hemosiderotic synovitis caused by hemorrhage from knee osteoarthritis.

P3-111

A case of Rapidly Destructive Coxarthropathy due to dialysis amyloidosis

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Conflict of interest: None

[Case] 61 years old male. He has been on dialysis for 7 years because of diabetic nephropathy. He has had left hip pain for one year, and became difficult walking for half a year. X-rays showed joint space narrowing and osteonecrosis changes, but bone destruction progressed rapidly in about one month. MRI showed extensive osteonecrosis and bone marrow edema from the left acetabulum to metaphysis. The blood was high at CRP 5-6 mg/dl, but the joint fluid culture was negative. RDC due to dialysis amyloidosis was diagnosed from the clinical course and total hip arthroplasty was performed. In synovium, HE staining revealed monocyte, multinucleated giant cell infiltration and angiogenesis, and DFS staining was partially positive. Two weeks after surgery, CRP decreased to 1.93 mg/dl and he can walk with a stick. [Discussion] In dialysis amyloidosis, B2-MG forms amyloid fibrils, causing chronic arthritis and bone cysts in the carpal bone and hip joint, etc. About 20% of patients with dialysis amyloidosis, as in this case, have reported bone cyst formation in the hip joint. Dialysis patients with diabetic nephropathy are compromised hosts, so it's important to distinguish RDC from purulent arthritis and tuberculous arthritis, and treatment methods must be carefully examined.

P3-112

Prevalence of dysphagia and the associated risk factors in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] The aim of this study was to determine the prevalence of dysphagia and the associated risk factors among elderly patients with rheumatoid arthritis. [Methods] We conducted a cross-sectional study including 61 RA patients and 25 OA patients over 65 years of age. During the period from July to October 2019, a water swallowing test (WST) and a repetitive saliva swallowing test (RSST) were performed. Oral conditions, hoarseness, temporomandibular joint symptoms, cervical range of

motion limitation, and grip strength were also evaluated. In addition, interviews were conducted to investigate swallowing ability and aspiration history. [Results] The subjects were 61 RA (average age 73.8 years) and 25 OA (75.8 years). As a result of WST and RSST, dysphagia was observed in 13 patients of RA group (21.3%) and 3 of OA group (12%). The RA patients with dysphagia were significantly older and had a longer morbidity than the non-disabled patients, however, there was no difference in disease activity or treatment. Age, Steinbrocker stage, cervical range of motion limitation, and opening disorder of jaw were identified as factors related to dysphagia. [Conclusions] RA patients had a higher rate of dysphagia than OA patients, suggesting an association with temporomandibular and cervical disorder.

P3-113

Treatment with customized insole for rheumatoid foot improve QOL and enhance physical activity

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Conflict of interest: None

[Introduction] Advances in drug therapy in rheumatoid arthritis enable us to solve the problems of ADL and QOL disturbance due to arthritis itself. However, problems such as deformities and general muscle loss have not been solved. In particular, rheumatoid foot disturb ADL and QOL. In this study, we examined the effects of insole treatment from the viewpoint of physical activity and QOL. [Patients and methods] Twelve patients who underwent insole treatment were subject and followed for 6 months. Body composition, physical activity, general and foot QOL, foot pain was assessed and compared. [Result] The average age was 71.7 years and the duration was 20.6 years. Eight had sarcopenia, and the skeletal muscle mass index was 5.7. Foot pain and QOL, and HAQ improved. The amount of physical activity related to walking increased, but the activity intensity did not change. There was no difference in body composition at 6 months. [Discussion] This study showed a high prevalence of sarcopenia and decreased QOL. Insole treatment was ineffective in body composition and activity intensity, but there were effects on the feet such as pain improvement and walking volume increase. We should first apply insole treatment to the rheumatoid foot, and then another approach is necessary.

P3-114

A multifaceted analysis of quality of life and physical activity factors in community-dwelling rheumatoid arthritis patients

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Conflict of interest: None

[Introduction] Obtaining a higher quality of life (QOL) is a primary goal of treatment for rheumatoid arthritis (RA). This study examined QOL of community-dwelling RA patients by evaluating their function based on standard tests. [Method] 71 female RA patients (65.9 ± 14.0) in 3 facilities were included (Aug.2017-Aug.2019). Subjects were divided into High and Low QOL groups based on EQ-5D. Outcomes were disease activity (SDAI), pain intensity (VAS), dysfunction (PDAS, HAQ), physical activity (Locomo25), psychological emotion (PCS, HADS) and pain perception (TSK, PSEQ). Statistical analyses were performed (Mann-Whitney U test, multiple regression analysis). [Result] Low QOL group showed high scores of SDAI, VAS, HAQ, PDAS, Locomo25, TSK and low scores of PSEQ. Further analysis showed a significant relationship between QOL and subject's physical activity, kinesophobia, pain and locomotive degree, duration of illness. [Discussion] Some patients struggle with physical and mental issues that negatively impact their QOL. It is thought to be that overall physical function and pain perception are modulated by residual pain from RA, and this leads to a reduction in total physical activity. It is necessary to focus on the correction of pain perception and promotion of active physical activity.

P3-115

Relationship of the vertebral compression fracture and the Sarcopenia index (the serum creatinine / cystatin C ratio) in the japanese woman rheumatoid arthritis patients

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Conflict of interest: None

[Objective] The purpose of this study was to clarify relationship of the vertebral compression fracture (VF) and Sarcopenia index (SI) in the Japanese woman rheumatoid arthritis patients. [Methods] A cross-sectional study was performed in the Japanese woman RA patients who were untreated osteoporosis. The VF used a semiquantitative rating system (the SQ method) and did more than grade1 if there was a bone fracture. Assessment were performed age, disease period, drug (MTX, PSL, Biologics), anti CCP antibody, creatinine, cyctatin C, CRP, ESR, MMP-3, eGFR, Bone mineral density (unilateral hips), DAS-CRP, DAS-ESR, HAQ-DI. SI calculated it in serum creatinine/cystatin C. [Results] A total of 88 patients whose average age was 71.9 years. Average SI was 0.659. There were 42 patients (47.7%) in the less than SI average. The VF occurred to 19 patients (41.3%) in less than SI average. On the other hand, occurred to 6 patients (14.3%) in more than SI average. Less than SI average significant high VF ratio more than SI average ($p=0.005$, odds ratio 4.2). eGFR and HAQ-DI was inferior to a group above the average in the results of a group below the average. [Conclusions] Less than SI average significant high incidence of the VF ratio more than SI average group. SI may be available as a screening tool of the VF.

P3-117

Intervention by Physical Therapist Utilizing Physical Exercise for Rheumatoid Arthritis Patient as Team Medical Care Reduce Joint Ache and Improve ADL/QOL: Case Report

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Conflict of interest: None

[Purpose] We report a case of markedly reduced joint ache and prominently improved ADL/QOL by intervention (IV) utilizing rehabilitation (rehab) by physical therapist (PT) in addition to medication. [Case presentation] Female of 60s with RA for 20 years visited our hospital due to worsen RA activity. Evaluation indicator of RA (EIRA) was DAS28CRP: 3.88, CRP: 7, HAQ: 2, MDHAQ: 1.2. Restriction of range of motion in thoracic spine due to poor distensibility of latismus dorsi, and patellofemoral joint pain due to inflammation and poor distensibility of rectus femoris were observed. We performed therapeutic IV twice a week for 73 days by manual correction (improvement exercise for trunk tenderness and muscle-strengthening exercise for knee joint) and coaching for voluntary training with medication. As a results, EIRA was improved; DAS28CRP: 2.7, CRP: 0.37, HAQ: 0.25, MDHAQ: 0.2. Restriction of range of motion in thoracic spine, poor distensibility of latismus dorsi, patellofemoral joint pain, and poor distensibility of rectus femoris were dramatically improved. [Discussion] This study suggests that IV utilizing profession of PT with medication is very profitable to reduce joint ache and improve ADL/QOL.

P3-118

Examination of the relationship between Locomo 25 and patient background / status at NinJa2018

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Conflict of interest: None

[Purpose] Using the NinJa 2018 data, we examined the relationship between Locomo 25, which is an index of physical condition and life status regarding locomotive syndrome, and patient background and condition. [Method] Of the cases registered in NinJa2018, 2022 people (1610 women, 412 men) with data on Locomo 25 were extracted, the Locomo 25 score and the NinJa items and were evaluated using correlation analysis. [Results] The average score for the entire Locomo 25 was 22.5 ± 22.4 (23.7 ± 22.8 for women, 17.8 ± 20.4 for men). Correlation analysis with the following NinJa items was performed: age (correlation coefficient: 0.324), age of onset (-0.013), duration of disease (0.368), number of painful joints (0.226), number of swollen joints (0.147), PtPainVAS (0.432), PtGVAS (0.474), DrVAS (0.370), mHAQ (0.881), CRP (0.176), ESR (0.247), Stage (0.313), Class (0.576), DAS28 (0.392), DAS28CRP (0.388), SDAI (0.384), CDAI (0.373), HAQ-DI (0.910), MDHAQ (0.926), EQ5D (-0.758), HADS-A (0.424), HADS-D (0.457), PSL amount (0.191), MTX amount (-0.191) and creatinine levels (0.082) were significantly correlated except onset age ($p < 0.001$). [Conclusion] Locomo 25 is suggested to be useful as an evaluation index in rheumatoid arthritis.

P3-119

Approach of early rehabilitation intervention for early rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] Through early RA cases of our hospital which early rehabilitation was effective in addition to medication, we will consider appropriate rehabilitation prescriptions according to patient profile with reference to previous reports. [Methods] We look back on the process of 4 cases who started rehabilitation within 2 months from the first visit among RA patients within 6 months of onset who visited our department from June 2018 to July 2019 and searched previous reports. [Results] Prescribing of orthotics, instruction of movement and disease education with joint protection in mind were effective and improved ADL / QOL in our cases. [Conclusions] Rehabilitation and self-care as the three pillars of RA treatment, alongside drug therapy and surgical therapy, could be expected to obtain higher effects by functioning complementarily with other pillars. [Clinical significance] It was suggested that improvement in quality of rehabilitation leads not only to disease activity and physical function, but also to psychological improvement, and it was confirmed that appropriate prescriptions can be applied to a wide range of cases.

P3-120

A case of SLE performed abortion because of disease exacerbation triggered by pregnancy

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Conflict of interest: None

[Case] 32-year-old woman. Nine years ago, she was diagnosed with SLE based on facial erythema, arthralgia, lymphopenia, ANA positive, but treatment wasn't performed. Four years ago, she had fever, LAC positive, urinary protein, and occult blood, and diagnosed with lupus nephritis type 3+4 by kidney biopsy. PSL 45mg was started, and tapered to 6mg. She had no obvious activity other than slightly low complement, and became pregnant. She was introduced at 10th week of pregnancy, but she had hypertension and hypocomplementenia. We thought SLE flared up, and she received PSL 15mg, tacrolimus, aspirin, and heparin. However, hypocomplementemia wasn't improved, and fever, hypertension, pancytopenia, and cognitive dysfunction appeared. We judged that continuation of pregnancy was difficult, and abortion operation was performed on the 14th week. After abortion, PSL was increased to 1mg/kg and IVCY for 4 times, hydroxychloroquine, MMF, and belimumab were introduced. Pancytopenia and hypocomplementemia was improved. [Clinical significance] Even if SLE activity is low at first glance, disease activity may worsen triggered by pregnancy, and continuation of pregnancy may be difficult. We should need to be careful to SLE activity and preconception care before and during pregnancy.

P3-121

A case of elderly-onset systemic lupus erythematosus presenting as interstitial pneumonia followed by thrombotic microangiopathy

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Conflict of interest: None

A 78-year-old man, without any history of autoimmune disease, developed fever and dyspnea and was diagnosed with interstitial pneumonia (IP). Although he was treated with methylprednisolone pulse therapy, no clinical improvement was shown. Furthermore, acute hemolytic anemia and thrombocytopenia occurred and schistocytosis in peripheral blood was observed during treatment. We diagnosed with thrombotic microangiopathy (TMA) and immediately started plasma exchange (PE) in addition to steroid therapy. However, his response to those treatment was still poor. He also fulfilled the Systemic Lupus International Collaborating Clinics classification criteria including positive anti-nuclear antibody and decreased level of complement. On the basis of induction therapy of systemic lupus erythematosus (SLE), we next treated with intravenous cyclophosphamide, resulting in good clinical outcome of every condition. Renal biopsy performed after 7 times of PE revealed class III (A/C) of lupus nephritis, strongly supporting diagnosis with TMA secondary to SLE. This is an atypical case of SLE presenting as IP and TMA in an elderly male patient. Renal biopsy was helpful for diagnosis and decision of treatment strategy for refractory condition.

P3-122

A case of iliopsoasitis due to systemic lupus erythematosus

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Conflict of interest: None

The patient was a 25-year-old woman who was diagnosed with systemic lupus erythematosus due to polyarthritis, lymphocytopenia, and positive of antinuclear antibody and anti-dsDNA antibody 6 years ago. She was treated with steroid pulse therapy and followed by high dose of prednisolone (PSL). After received with 5mg of PSL daily with low complement and positive of anti-DNA antibody for several years, she presented high fever. Treatment of antibiotics and 15 mg of PSL was ineffective. The swelling of the left iliopsoas was revealed in computed tomography (CT). She admitted in our hospital for the suspect of iliopsoas abscesses. On hospital day 7, she got the NSAIDs-induced aseptic meningitis and received 45mg of PSL daily (1mg/kg/day) immediately, then high fever, aseptic meningitis and iliopsoasitis were improved. The CT guided needle biopsy of iliopsoas was performed on hospital day 15, and it showed the myositis with the infiltration of CD8 positive lymphocyte, and no evidence of infection or malignancies. She discharged on the hospital day 31. [Discussion] We encountered a patient with iliopsoasitis due to SLE which high dose glucocorticoid therapy was effective. The iliopsoasitis due to

SLE was rare. We report a case of iliopsoasitis due to SLE and review the literature.

P3-123

Cerebral hemorrhage due to moyamoya syndrome in patient with systemic lupus eritematosus during pregnancy

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Conflict of interest: None

Case: A 29-years old woman, who indicated pancytopenia, proteinuria and dysfunction, was diagnosed with systemic lupus erythematosus (SLE) in the 12 weeks of pregnancy. Positivity for anti-ds-DNA antibody and antinuclear antibody was shown together with hypocomplementemia, whereas an Antiphosholipid antibody were not detected. She wes treated with intravenous infusion of methylprednisolone (0.5g daily for 3 days) and orally following prednisolone at 45 mg daily concomitantly with tacrolimus and hydroxychloroquine re, resulting in improving proteinuria and other laboratory disorders. On 26th day after initiating treatment, consciousness disturbance suddenly occurred because of intracranial hemorrhage. Brain magnetic resonance angiography revealed poor perfusion of the internal carotid, anterior cerebral and middle cerebral arteries bilaterally, as well as increased vascularity of collateral blood flow, suggesting that intracranial hemorrhage was ascribable to moyamoya syndrome (MMS). She achieved neurological recovery after surgically removing hematoma, and also could maintain clinical remission in SLE. **Conclusion:** To our knowledge, 13 cases of MMS has been described in SLE so far. Our report suggests that MMS may become the cause of cerebrovascular disorder in SLE.

P3-124

A process of 22 year follow-up of Lupus nephritis treated by blood purification therapy as initial therapy

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Conflict of interest: None

A 35-year-old woman visited our clinic complaining of fever and joint pain 22 years ago. Laboratory test revealed positive anti-nuclear antibody (ab), anti-DNA ab, pancytopenia and hypocomplementemia, leading to the diagnosis of SLE. Steroid pulse (SP) with subsequent oral glucocorticoids (GCs) was initiated and then the activity of SLE was under control for 8 years. At age 22, she developed lupus nephritis (LN). She was treated by SP with subsequent oral GCs and immunoabsorption plasmapheresis and double filtration plasmapheresis. Intermittent High-dose GCs was made for persistence of proteinuria, by which it disappeared. During GCs tapering, it appeared again and anti-DNA ab remained at around 40 IU/ml. At age 25, renal biopsy at a general hospital revealed class III (C) + V. The activity of SLE decreased after switched to GCs with belimumab. There are few reports of long-term observation of LN after blood purification therapy as the initial treatment. In this case, while remission of LN was not obtained with blood purification as the initial therapy, high-dose steroid with belimumab was effective. From this course, the effect of blood purification therapy alone as an induction therapy for LN is unclear, and it's considered essential to use an immunosuppressant in combination.

P3-125

Three patient with pericardial effusion in systemic lupus erytematotus

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Conflict of interest: None

[Objective] We examined pericardial effusion in systemic lupus erythematous (SLE). [Methods] Patients in this study were recruited from 2016 and 2019. Three patients underwent pericardial effusion drainage. [Results] The first case is a 42-year-old Japanese woman. Her pericardial effusion was Turbid yellow. The level of CRP was 15.5 mg/dL. Increasing the prednisolone dose achieve a remission. The second case is 42-year-old Japanese woman. Her pericardial effusion was clear. The level of CRP was 0.0 mg/dL. We increased the diuretic dose. However pericardial effusion was relapsed. The third case is 60-year-old Japanese woman. Her pericardial effusion was clear. The level of CRP was 0.3 mg/dL. Increasing the diuretic dose was not effective. [Conclusions] Pericardial effusion in SLE may not be necessarily to be inflammatory.

P3-126

Experience with Belimumab in the Management of Systemic Lupus Erythematosus (SLE)

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Conflict of interest: None

[Objective] We evaluated the clinical features and course of patients received belimumab. [Methods] We analyzed 8 SLE patients received intravenous belimumab in our department between April and December 2018. SLENA SLEDAI, BILAG, PGA, Lupus Impact Tracker, anti-dsDNA antibody titer and complement levels were evaluated at baseline, Month 3 and 6. [Results] Among 8 patients, 1 discontinued belimumab because of side effect (fatigue) 2 weeks later, and 1 moved. Median change from baseline to Month 6 in C3/C4 levels were 55.3/8.7 mg/dL→56.5/9.7 mg/dL. 2 patients had a high titer of anti-ds DNA at baseline and the titer decreased in both cases. Median change from baseline to Month 6 in the SLEDAI score was 7.5→9. There was one flare defined by BILAG at Month 6. Median change from baseline to Month 6 in Lupus Impact Tracker was 57.5→46.3. 2 patients achieved an SRI4 response at Month 6. Between responders and non-responders, no difference was found in the proportion or number of CD19^{+} cells at baseline. In responders, the SLEDAI score at baseline was tend to high and the disease duration tended to be short. [Conclusions] In some cases, the serological makers such as C3/C4 levels and anti-ds DNA improved after the start of belimumab.

P3-127

Usage survey of Hydroxychloroquine (HCQ) for Systemic lupus erythematosus (SLE) and related disease in our hospital part2

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Conflict of interest: None

We treated 44 patients, who are 12 SLE, 1 mixed connected tissue diease (MCTD), 1 systemic sclesosis (SSc) and 1 anti phospholipid syndrome (APS) with HCQ since January 2016. All of them are female expect of 1 patient. Their mean age is 53 years-old and mean disease duration is 17 years. On SLE patients, they complicated with 12 APS, 11 Sjogren syndrome (SS) and 2 rhuematoid arthritis (RA). 34 patients are going on adminisutration and two of them are readministration. There are 10 pateins, who are cessation of HCQ becase of skin rash and diarrhea. On 21 patients, we have been able to decrease their steroid dose. And 22 patients who receive immunosuppressants for maintenance therapy also decrease their given dose. On SLE patients, theri anit-double strand DNA antibody's titer are decreased with HCQ treatment and among them they got their improving blood sugar level. As previously reported, we conclude that HCQ is one of the improtant medecarions for SLE and related diseases and have the effect for lifestyle related diseases.

P3-128

Treatment of intractable SLE with combination of Rituximab and Belimumab

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Conflict of interest: None

[Case] 30 year old, female. About a month before hospitalization, she was aware of pain in upper extremities and a fever at night. Igratimod was prescribed for suspected rheumatoid arthritis, but it did not improve, and the general malaise and pain in the extremities became exacerbated and it became difficult to move the body, so she was taken to our hospital by emergency. Systemic lupus erythematosus was diagnosed. Treated with steroid pulses, 60 mg of prednisolone, mofetyl mycophenolate, and tacrolimus, but they were poorly improved in low complementemia and renal dysfunction. Plasma exchange was performed because hemophagocytic syndrome also occurred, but since, rituximab and berlimumab were used together. Rituximab and berlimumab showed improvement in hypocomplementemia and renal dysfunction, and autoantibodies decreased. The belimumab continues even now, and prednisolone is decreasing. [Clinical importance] Belimumab is a biologic used for systemic lupus erythematosus, a fully human monoclonal antibody targeting soluble B lymphocyte stimulator (Blys). Although it is effective for SLE, there is insufficient evidence of efficacy and safety for combination with other drugs. We report that the combination of rituximab and berlimumab may be one of the treatment options.

P3-129

Severe neutropenia in patients with systemic lupus erythematosus

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Conflict of interest: None

The patient was a 49-year-old female, who had presented with leukopenia and diagnosed with systemic lupus erythematosus (SLE) at age 21 and lupus nephritis at age 39. She was started on prednisone (PSL), tacrolimus and cyclophosphamide pulse as remission induction therapy, followed by PSL (ranging 5-40 mg/day) for maintenance. The leukocyte count gradually decreased and agranulocytosis was developed in the 2 months before admission. The bone marrow aspiration revealed hypocellular marrow without malignant cells. Her antineutrophil antibodies were negative. Therefore, we considered the agranulocytosis was induced by an autoimmune etiology associated with SLE. As the effects of granulocyte colony-stimulating factor on increasing neutrophils were limited, she was admitted and treated with 3 days of pulse steroids (1 g methylprednisolone) followed by PSL 60 mg/day and mycophenolate mofetil 2 g/day. The neutrophil count improved after the immunosuppressive therapy and has been maintained at around 4,000 /μL. In this case, there was no suspected drug affecting neutropenia and the immunosuppressive therapy was effective for improving neutropenia. We report a rare case with severe neutropenia associated with SLE.

P3-130

A case of thrombotic microangiopathy associated with SLE and lupus nephritis

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Conflict of interest: None

A 18-year-old woman was seen in the hospital because of edema, malar erythema and body weight gain. She was diagnosed as SLE and nephrosis syndrome and admitted to the hospital. She receive mPSL 1000mg pulse therapy from day 1 to 3 and PSL 1mg/kg therapy a day from day 4. In day 4, decreasing renal function and thrombocytopenia were occurred. Therefore, she was transferred to our hospital to receive more therapy and renal biopsy. Tacrolims (Tac) 2mg was started in day 4 for treatment of SLE. However, she was diagnosed as thrombotic microangiopathy (TMA) with pentalogy of Moschcowitz in day 5. In view of TMA secondary to SLE or drugs, Tac was discontinued. Plasma exchange therapy was performed in day 5 to 8, and IVCY 500mg/body therapy was done in day 7, which repeated 6 times every 2 weeks during admission. After initial therapy, PSL was tapered and HCQ 200mg was added in day 39. renal biopsy was performed in day 48, before 4th course of IVCY, she was diagnosed as lupus nephritis (ISN/RPS III (A/C)+V). MMF 1000mg was added in day 83, and she discharged and went home in day 90 with PSL 0.5mg/kg a day. We report factors and characters of secondary TMA associated with SLE in this case and those of past reports.

P3-132

A cace of lupus nephritis that treated with rituximab

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Conflict of interest: None

[Case] In 20XX-11, a 60s-year-female was diagosed as lupus nephritis (LN) classIIIA. She was treated with predonisolone (PSL) 8mg/day and tacrolimus (TAC), but protenuria was recurred. In 20XX-6, second renal biopsy revealed class V and renal ischemia due to TAC, therefore her medicne was chaged to azathioprine (AZP). Her urinarysis was normal but anti-ds-DNA antibody raised, therefore mizoribine (MZR) was added. In 20XX-2, she didn't enter remission despite of the treatment, therefore her medicine changed to micophenolate mofetil (MMF). We couldn't increase PSL because of necrosiss of femoral head. AZP and MMF were discountinued because of anemy. She was treated with PSL3mg/day and MZR. Urine analysis showed hematuria and total urinary protein excretion 3.5g/day and anti-ds-DNA antibody raised to 380IU/ml. In November 20XX-1, third renal biopsy showed classIV-G (A/C). Rituximab (RTX) was administered at a dose of 630mg/body twice and we switched to MMF1500mg/day from MZR. In August 20XX, urinary protein and anti-ds-DNA antibody declined to 0.3g/day and to 62.7IU/ml. [Discussion] In some recent reports, RTX induced remission of LN in patients who were poor controlled by standard therapy. In our case, LN was improved by using RTX without increasing PSL. We consider that RTX may be a therapy for treatment of LN.

P3-133

A case of systemic lupus erythematosus (SLE) with right pleural effusion and nephrotic syndrome during the clinical course of mycosis fungoides, which was needed to differentiate IgG4-related disease

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Conflict of interest: None

A 75-year-old male with mycosis fungoides (MF) admitted in another hospital because of right pleural effusion in winter 2019. There was no evidence suggestive of malignancy and pleural tuberculosis. Histological examination of the right pleura showed IgG4-positive plasma cell infiltrations, and suggested IgG4-related pleurisy with increased serum IgG4. In summer he presented to our hospital with a loss of appetite and exertional dyspnea. On evaluation, he fulfilled 5 out of the 11 diagnostic criteria for SLE. In addition, he presented with limb edema, hypoproteinemia and proteinuria. His renal illness was thought to be nephrotic syndrome (NS). Soon after admission, kidney biopsies were performed. It demonstrated a membranous nephropathy with mesangial proliferation without infiltration of IgG4-positive plasma cell, and presence of IgG, IgA, C3 and C1q deposits on immunofluorescence, highly suggestive of lupus nephritis (LN) class II and V. Renal disease and pleural effusion improved in response to initiation of prednisone therapy. Nephrotic range proteinuria regressed, but never completely resolved. We presented a case of LN with NS, high

serum IgG4 level and pleural effusion during the course of MF, which is very uncommon and has never been presented in the literature to date.

P3-135

A case of systemic lupus erythematosus whose anti-DNA antibody titer was negatively converted by the introduction of belimumab but relapsed with TMA

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Conflict of interest: None

[Case presentation] A 36-year-old woman who was diagnosed as SLE at 12-year old, and experienced an episode of lupus nephritis, NPSLE. She was stable with mPSL10-20 mg/day from X-10 years. She developed autoimmune thrombocytopenia in November X-3, recovered by steroid pulse therapy and followed by 1mg/Kg/day of PSL and IVCY. But her laboratory tests showed thrombocytopenia again on March X-1, anemia and the fragmented red blood cell, ADATS13 activity <10, negative ADAMTS13 inhibitor also appeared, we diagnosed that thrombotic microangiopathy (TMA) with SLE activity. Clinical course of TMA improved by increase of oral PSL and IVCY, but anti-DNA antibody titers changed into positive soon. TMA relapsed in December X-1, she was treated with rituximab (RTX), and experienced a marked improvement. Belimumab was initiated from December X, after the positive transformation of anti-DNA antibody titers. The anti-DNA antibody titers became negative, but TMA relapsed in June X+1. Re-administration of RTX was required to resolve. [Clinical importance] We encountered a case of SLE whose anti-DNA antibody titer was negatively converted by the introduction of belimumab but relapsed with TMA. We review the precautions when administering belimumab and report it with a review of the literature.

P3-136

Successful immunosuppressive treatment with cognitive dysfunction in neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

A 54-year-old woman with a history of SLE based on discoid lupus erythematosus, headache, leukopenia, antinuclear antibody and antiSmith's antibody positive since 2004 had been prescribed prednisolone (PSL), her disease activity was stable with PSL 7.5mg per day. She was taking an antiplatelet agent for old cerebral infarction and followed by neurosurgery postoperation of chronic subdural hematoma. Her disease activity was flare up from 2018, increased PSL 30mg, still be refractory. She was hospitalized urgently because of abnormal behavior during routine visits. She underwent brain MRI, which showed no new change, but her Revised version of Hasegawa's Dementia Scale (HDS-R) was 12. Other neurological examinations were normal. We prescribed pulse steroid therapy adding to meropenem.4 days later, her behavior became completely normal and HDS-R ameliorated from 12 to 30. Considering clinical course and culture findings, her cognitive dysfunction was accompanied by NPSLE and we added pulse cyclophosphamide therapy. Other infection findings were all negative and in light of the clinical course, we diagnosed NPSLE. Her clinical course has been good. <Conclusion>Successful immunosuppressive treatment with cognitive dysfunction in NPSLE without image changes is interesting. We add review of the literatures.

P3-137

A case of refractory neuromyelitis optica spectrum disorder in systemic lupus erythematosus (SLE)

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Conflict of interest: None

A 47-year-old female with a history of SLE and AIHA for 16 years was treated with prednisolone. Three years ago, she had lower extremities weakness and numbness, gait and urinary disturbance. Cervical and thoracic cord MRI revealed hyperintence signal lesions on T2-weighted images and brain MRI revealed no optic nerve involvement. She was negative for anti-aquaporin 4 (AQP-4) antibody (enzyme-linked immunosorbent assay: ELISA). The diagnosis of longitudinally extended transverse myelitis in SLE was made. After receiving steroid pulse therapy and multiple immunosuppressive drugs, her symptoms improved. However, she experienced seven times recurrences of myelitis for about two years and a half. In October 2019, she was hospitalized for recurrence of myelitis. Her serum was found to be negative for anti-AQP4 antibody (ELISA) and anti-myelin oligodendrocyte glycoprotein antibody (ELISA), but positive for anti-AQP4 antibody (cell-based assay). She was diagnosed with neuromyelitis optica spectrum disorder (NMOSD) in SLE. She was treated with steroid pulse therapy and plasma exchange, and her neurological symptoms gradually ameliorated. NMOSD is an inflammatory demyelinating disorder, whose association with SLE remains rare. We herein describe a case with reference to the literature.

P3-138

A case of neutropenia in a patient with systemic lupus erythematosus during pregnancy

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Conflict of interest: None

We report on a 37-year-old woman, who was referred to our department because of decreased WBC count, positive ANA, positive anti-Smith antibody, and positive anti-SSA antibody. Since she had no clinical symptom, the patient was followed up without the definitive diagnosis. In February X+1, when she became pregnant, the WBC count decreased and arthritis appeared. We diagnosed her as SLE and started PSL at the dose of 10mg/day at the 12weeks gestation. Subsequently the PSL dose was increased to 15mg/day (0.3mg/kg/day) at the 18 weeks gestation. However, the WBC count decreased to 1360/μl and neutrophil count 300/μl at the 24 weeks gestation. HCQ was added, but stopped due to skin rash. At the 35 weeks gestation, the WBC count decreased to 1260/μl and the neutrophil count 280/μl. Although there was no sign of infection, we gave her antibiotics and G-CSF. After receiving a total of 3 doses of G-CSF, she vaginally delivered of a 2588g healthy girl at 38 weeks 2days gestation. No infectious morbidity or adverse side-effects occurred in the mother or the infant. This is a rare case in which G-CSF may helpful for a patient with SLE combined pregnancy.

P3-139

A case of lupus aortitis successfully treated with mycophenolate mofetil

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Conflict of interest: None

[Case] a 33-year-old woman [Chief complaint] Fever and left chest pain [Present illness] She developed Raynaud's phenomenon 11 years ago, dyspnea on exertion and arthralgia sequentially, 1 year ago. She was diagnosed with MCTD based on anti-RNP antibody positivity, pleural effusion, Raynaud's symptoms, and polyarthritis, and started treatment with PSL at another hospital. Afterwards, she was referred to our hospital to raise her baby, but she was admitted to our hospital due to fever and left chest pain. On admission, she was diagnosed with SLE based on polyarthritis, hypocomplementemia, ANA positive, anti-ds-DNA antibody positive and lymphopenia. The cause of chest pain was considered to be lupus aortitis because of the thickening of the wall of the aorta on CT. PSL was increased on the 16th day, and AZP and HCQ were introduced. Serological improvement was observed, but chest pain did not improve. The CT re-examination on the 39th day showed that aortic wall thickening remained. So, when AZP was changed to MMF, the chest pain was markedly im-

proved. Thereafter, PSL was gradually reduced, TAC was introduced, and she was discharged on the 64th day. [Clinical significance] We experienced a case of lupus aortitis that was effective in MMF, so report with literature review.

P3-140

A case of systemic lupus erythematosus (SLE) accompanied with pure red cell aplasia (PRCA)

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Conflict of interest: None

[Case] A 31-year-old woman, who was diagnosed with idiopathic thrombocytopenic purpura at age 23 and was in remission without medication after prednisolone treatment. At the age of 25, she had arthritis, nephrotic syndrome, hypocomplementemia, and positive anti-dsDNA antibody. She was diagnosed with lupus nephritis by renal biopsy. She had been in remission with prednisolone + cyclosporine, but anemia appeared about 2 months ago. She became aware of palpitation and shortness of breath without responding to iron administration. She had hypocomplementia but did not have eruptions, arthritis, nephrotic syndrome, and no finding hemolytic anemia. Parvovirus B19 IgM was negative, and no thymoma was detected on chest CT. We diagnosed with PRCA secondary to SLE by bone marrow examination. [Discussion] Anemia due to SLE is often caused by chronic inflammation due to SLE itself. Other include autoimmune hemolytic anemia, iron deficiency anemia, and drugs. The cause of PRCA may be idiopathic or secondary following viral infection, drugs, thymoma, lymphoproliferative disease, autoimmune disease, and etc. Although PRCA is considered to have an autoimmune mechanisms because immunosuppressive therapy is successful, PRCA secondary to SLE is rarely, and we report this case with a literature review.

P3-141

A case of mixed connective tissue disease (MCTD) with protein leakage into the abdominal cavity

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Conflict of interest: None

[Case] A 39-year-old woman who was diagnosed with MCTD from Raynaud's phenomenon, positive of anti-U1-RNP antibody, polyarthritis, muscle weakness in X-17. She was maintained by 10mg of PSL without the serious organ damage. However, her serum complement titer was decreased in April X, alopecia in July, and she developed a fever, palpebral edema in October. She was admitted to our hospital in November. Her blood examination showed hypoproteinemia, but proteinuria was negative. CT showed no significant abnormality expect for pleural effusion and ascites. We suspected protein-losing gastroenteropathy and performed protein leakage scintigraphy. The result was protein leakage into the abdominal cavity instead of the intestine. Abdominal angiography showed narrowing, and disruption of the arteriole from the sigmoid colon to the rectum. For pleurisy and inferior mesenteric arterial vasculitis, she was treated with a combination of high-dose corticosteroid and cyclophosphamide. She experienced remarkable improvement of hypoproteinemia, pleural effusion, ascites and palpebral edema. [Clinical significance] MCTD has a variety of gastrointestinal conditions. In our case, the inferior mesenteric arterial vasculitis, which is a medium-sized blood vessel, is rare case.

P3-142

A case of severe acute pancreatitis with systemic lupus erythematosus

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Conflict of interest: None

She was 49 years-old, female and referred to our department for further examination of polyarticular pain in May, X. She had upper abdominal pain and increased hepatobiliary and pancreatic enzymes. She underwent contrast-enhanced CT and upper gastrointestinal endoscopy at gastroenterology, but the cause was unknown. She was admitted for further examination in June, X. She was suspected of systemic lupus erythematosus (SLE) based on seropositivity of anti-nuclear antibody and anti-dsDNA antibody, hypocomplementemia, and proteinuria. Within 24 hours after admission, her upper abdominal pain was getting worse, and serum pancreatic enzymes were elevated. She was diagnosed with severe acute pancreatitis due to laboratory data and contrast-enhanced CT. At the onset, she denied that she was a heavy drinker, and she had no gallstone. Therefore, it was suspected that SLE or/and steroids caused acute pancreatitis. However, the standard treatment for pancreatitis improved her acute pancreatitis, and she was found to be a heavy drinker after that. Finally, she was diagnosed with acute alcoholic pancreatitis.

P3-143

A case of intestinal perforation with MPO-ANCA positive SLE

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Conflict of interest: None

[Case] A 44-year-old woman developed a fever and numbness in both hands in October X. A nerve conduction velocity test showed right median neuropathy. She was diagnosed with systemic lupus erythematosus (SLE) based on leukopenia, positive anti-neuclear antibody, anti-DNA antibody and anti-cardiolipin antibody. Her numbness appeared in both lower legs, and she admitted in our hospital in December X. Cerebrospinal fluid showed elevation of protein and interleukin-6 levels, we diagnosed that Neuropsychiatric SLE. In addition, we confirmed positive conversion of MPO-ANCA. She was treated with combination of high-dose corticosteroid and cyclophosphamide. She experienced improvement of numbness, but perforation of small intestine and acute peritonitis were occurred, and emergency operation was performed. Pathological examination of the resected small intestine revealed SLE vasculitis. [Clinical significance] Intestinal perforation associated with SLE vasculitis is rale case. We report our experience along with some literature review.

P3-144

A SLE patient with an ulceration of the nasal septum leading to perforation

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Conflict of interest: None

A 43-year-old woman was referred for a nasal septal pain. She had been diagnosed with a systemic lupus erythematosus (SLE) 22 years before and initially treated with steroid pulse therapies. Prednisolone was tapered down to 6.5mg/day on tacrolimus, however, the dose was increased to 8.0mg/day due to the headache and arthritis. One month before, she also noticed a nasal septal pain, that otolaryngologist detected a nasal septal ulcer by a nasopharyngeal fiber-scope. Steroid nasal spray did not alleviate her symptoms. Physical examination revealed malar rash and alopecia. An oral ulcer was not detected. Laboratory results were unremarkable including PR-3-ANCA, MPO-ANCA, and a screening test for syphilis by TPHA and STS. The platelet count was decreased. A nasopharyngeal fiber-scope examination showed a nasal septal perforation with an ulcer. She was diagnosed with nasal septal ulceration due to SLE. Oral prednisone was increased at a dose of 20mg/day and hydroxychloroquine was added, that relieve her symptoms. Mucosal lesions in SLE are one of the symptoms and the oral, nasal, and pharyngeal mucosas are most frequently affected. Ulceration of the nasal septum leading to perforation is one of the critical symptoms, therefore, early detection and treatment are required.

P3-145

A case report: hydroxychloroquine has the possibility to improve obesity with long term use of steroids in lupus nephritis

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Conflict of interest: None

A 40-year-old woman was diagnosed as SLE with butterfly erythema, arthritis, and presence of anti-DNA antibody and anti-Sm antibody. She had been treated with a low dose of prednisolone (PSL) for a few years at the clinic. In 2010, she admitted to our hospital because of nephrotic syndrome (NS). Renal biopsy revealed class V lupus nephritis. Intravenous corticosteroid therapy before combination oral use of PSL and mizoribine achieved type 2 incomplete remission. Disease control was unstable because she skipped the medical examination. In 2012, proteinuria increased but DFPP and intravenous cyclophosphamide therapy could control the symptom. Long term use of oral PSL to control disease activity-induced obesity (her body mass index was 31). In May 2015 the second relapse of NS occurred. A series of intravenous corticosteroid therapy could only achieve incomplete remission. We started to used hydroxychloroquine (HCQ) to control disease activity and decrease oral PSL dose. 1 year after the introduction of HCQ, oral PSL treatment was finished under good control and she lost weight. HCQ has received insurance approval for SLE in 2015. Using HCQ is a good solution for poor control lupus nephritis with obesity like this case.

P3-146

A case of hemophagocytic syndrome (HPS) associated with systemic scleroderma (SSc) successfully treated with steroid pulse therapy

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Conflict of interest: Yes

A patient developed finger swelling, joint swelling and muscle pain on her legs eleven years before admission. She was positive for anti-U1-RNP antibody and diagnosed with MCTD. Seven years before admission, anti-U-1RNP antibody and the symptoms became negative. Three years before admission, she developed finger swelling, reynaud's phenomenon, joint pain, fatigue, photosensitivity and difficulty in swallowing, demonstrating anti Scl70 antibody strongly. One year before admission, we started to treat her with prednisolone (PSL) 30mg/day for her developing finger swelling and decreased PSL dose to 10mg/day. One month before admission, we dosed up PSL to 30mg/day because of the exacerbation of her fingers swelling and ulcers. On admission, she complained sore throat, cough, fever and skin rash, demonstrating high level of serum Liver enzymes and ferritin. We also found many activated macrophages and hemophagocytosis in her bone marrow. Therefore, we diagnosed her with HPS and treated her with steroid pulse therapy successfully. We reported a case of hemophagocytic syndrome (HPS) associated with systemic scleroderma (SSc) during management with PSL. It is interesting to consider whether her HPS was associated with some viral infection or due to her autoimmune abnormality.

P3-147

A Case of Overlap Syndrome of Rheumatoid Arthritis and Systemic Sclerosis Presenting Polyarthritis and Interstitial Lung Disease Effectively Treated with Tocilizumab

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Conflict of interest: None

[Introduction] Although both rheumatoid arthritis (RA) and systemic sclerosis (SSc) present arthritis and interstitial lung disease (ILD), an appropriate treatment hasn't been established. Recently, the effectiveness of tocilizumab (TCZ) for ILD and arthritis of SSc has been reported. We report a case of overlap syndrome of RA and SSc presenting polyarthritis and ILD that were effectively treated with TCZ. [Case] 45-year-old woman presented with worsening of a digital ulcer, arthritis and dyspnea. When she was 35 she was diagnosed with RA based on presence of polyarthritis, ILD and positive results for RF/ACPA. She had been treated with glucocorticoid and csDMARDs for RA. At age 41, a diagnosis of SSc was also made based on skin induration and testing positive for anti-centromere antibody, and she had been treated with abatacept and bosentan. A right heart catheterization revealed borderline PAH. We changed treatment to TCZ and sildenafil, which resulted in marked improvements of digital ulcer, arthritis and dyspnea. One year later, ILD was stable based on CT and respiratory function test. [Conclusion] Reports about efficacy of TCZ for ILD and arthritis of SSc have been increasing. Our case suggests the effectiveness of TCZ for arthritis and ILD of RA/SSc overlap syndrome.

P3-148

A case of mixed connective tissue disease and Sjogren's syndrome complicated with quasi-moyamoya disease

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Conflict of interest: None

A-21-year-old woman was suffered from Raynaud's phenomenon since several years ago. She was admitted to our hospital due to intermittent fever, cervical lymphadenopathy, joint pain, and extremity weakness and dysarthria since several month ago. Her physical examinations revealed swollen fingers and peripheral arthritis but no neurological abnormalities. Serum muscle enzymes levels were elevated, antinuclear antibody, anti-U1 RNP antibody and anti-Ro/SSA antibody were also positive. Lip biopsy showed focal lymphocytic sialadenitis with a focus score $\geqq 1$. Moreover, MRI revealed scattered cerebral infarction in left parietal temporal lobe and bilateral internal carotid artery stenosis, and angiography showed moyamoya vessels. Based on these findings, she was diagnosed as mixed connective tissue disease (MCTD) and Sjogren's syndrome (SS) complicated with quasi-moyamoya disease. Revascularization was performed prior to immunosuppressive therapy. Although she suffered from mixed aphasia after surgery, she gradually improved by rehabilitation. She had still prolonged fever, lymphadenitis, and peripheral arthritis, hydroxychloroquine and 20mg daily prednisolone were administered. Then, her symptoms improved. We report a rare case of MCTD and SS complicated with quasi-moyamoya disease.

P3-149

A case of systemic sclerosis complicated with focal segmental glomerulosclerosis and demyelinating myelitis

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Conflict of interest: None

[Case] A 61-year-old woman with anti-U1-RNP antibody positivity was diagnosed with systemic sclerosis based on rapidly progressive diffuse skin sclerosis one year before the present admission. After the diagnosis, she was treated with glucocorticoid. Two weeks before admission, foaming urine appeared. Since lower leg edema, body weight gain, severe proteinuria, and acute kidney injury were noticed one day before admission, she was admitted to our hospital. She had 18.2 g/day of urine protein, hypoalbuminemia, and severe hyper-LDL-cholesterolemia, suggesting nephrotic syndrome, and renal biopsy revealed focal segmental glomerulosclerosis (FSGS). Five days after admission, weakness and dysesthesia of lower extremities developed, and diffusion weighted MRI revealed multiple hyperintensity lesions in the thoracic spinal cord. Cerebrospinal fluid with an increase of myelin basic protein lead to the diagnosis of demyelinating myelitis. Although 2 courses of methylprednisolone pulse therapy improved neither FSGS nor demyelinating myelitis, intravenous cyclophosphamide therapy ameliorated both. We should be aware that these rare complications may develop in systemic sclerosis.

P3-151

A case of Sweet's disease association with immunological findings of Systemic lupus erythematosus during follow-up as Mixed Connective Tissue Disease

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Conflict of interest: None

A 20-year-old female started Raynaud's phenomenon, swelling of fingers appeared 4 years ago. Blood tests revealed positive of anti-RNP antibody and any specific antibody else negative at this time. She has diagnosed as mixed connective tissue disease and observed follow-up for 3 years. However, 8 month before admitting to our hospital, the positive anti-dsDNA antibody, low complement and low white blood cell count in the blood test were demonstrated without any clinical findings did not observed. She was referred to emergency visit with three days history of skin erythema and painful pustules in her the right neck, face with a fever over 40 degree. The findings of histopathological examination of the skin lesions were consistent with sweet disease, numerous neutrophil infiltrations revealed in the entire dermis. The skin lesion and systemic symptom improved over 10 days after systemic corticosteroid therapy.

P3-152

An autopsy case of advanced collagenous pulmonary hypertension and renal failure

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Conflict of interest: None

[Case] A 72-year-old woman was diagnosed with SLE, scleroderma, and Sjögren syndrome 25 years ago, and developed pulmonary hypertension 7 years ago. The average pulmonary artery pressure was 45 mmHg and pulmonary vascular resistance was 6.5 WU. Because her renal function and respiratory status deteriorated, she had been hospitalized in hospital A for more than 1 year, but systemic erythema worsened on the 10 days before transfer to our hospital. Later, renal disorder, proteinuria, and systemic edema appeared. Lupus nephritis was suspected, and she was transferred to our hospital. [Course] On the day of admission, 6 drugs including were administered for pulmonary hypertension. We treated with PSL 60 mg daily for 2 weeks, but renal failure, and erythema did not improve. On the 14 days after admission, she died and was necropsied. [Results] The autopsy showed pulmonary blood vessels showed plexiform lesions, dilatation lesions, thinning of arterial wall, and enlargement of arterial lumen. They are equivalent to Heath-Edwards classification Grade IV. She had no obvious findings of lupus nephritis. [Discussion] In the future, as in this case, there is a possibility that pathological and pathological findings accompanying the deterioration of the circulatory condition will increase.

P3-153

Two cases of osteonecrosis of the lunate bone in systemic sclerosis (SSc)

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Conflict of interest: None

[Case1] A 59-year-old woman had puffy fingers since October 2014. She also had Raynaud's phenomenon, anti-centromere antibody positivity and accumulation of collagen fibers in skin biopsy. She was diagnosed as limited cutaneous SSc. After 4 years of diagnosis, ultrasonography and X-ray of the wrist were performed because of her left wrist pain, but there were no findings. MRI on hands was obtained, and it showed osteonecrosis of her left lunate bone. [Case2] A 74-year-old woman had puffy fingers since July 2018. She also had interstitial pneumonia, anti-RNA polymerase III antibody positivity and accumulation of collagen fibers in skin biopsy. She was diagnosed as diffuse cutaneous SSc. MRI on hands was performed because of her bilateral wrists pain, and showed osteonecrosis of her bilateral lunate bones. There were no findings in X-ray of her bilateral wrists. [Discussion] The etiology of osteonecrosis of the lunate bone with SSc remains to be elucidated, but vasculopathy may cause osteonecrosis of the lunate bone, because SSc patients had microvascular abnormalities. If patients with SSc had a joint pain of the wrist, we need to suspect osteonecrosis of the lunate bone and magnetic resonance imaging on hands have to be performed for diagnosis.

P3-154

A case of systemic sclerosis with pericarditis

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Conflict of interest: None

[Chief complaint] Dyspnea, face and lower leg edema. [Clinical history] The case was a 75-year-old woman. Stiffness and edema of both limbs appeared from May 2013, positive for antinuclear antibody (320 times), positive for anti-Scl-70 antibody, and introduced to our department in August of the same year. Systemic sclerosis and accompanying interstitial pneumonia were diagnosed. In January 2014, prednisolone (0.5mg/kg) and azathioprine were started. In March 2019, exacerbation of interstitial pneumonia was observed, and combination with tacrolimus was started. The patient's condition was stable after that, but since mid-June, he had difficulty breathing, and edema of the face and both legs, so he was admitted to the department for the same month. [Course] Echocardiography showed moderate amount of pericardial effusion. Pericardial puncture was performed, and diagnosed pericarditis associated with systemic sclerosis, and was given steroid (1.0mg/kg) and cyclophosphamide. As a result, no increase in pericardial fluid was observed, and dyspnea and edema gradually improved. [Discussion] We experienced a case of systemic sclerosis with pericarditis. There have been reports that systemic administration of steroids has been effective, but it is often refractory. This is reported with literature review.

P3-155

ILD is a shared organ involvement in patients positive for myositis specific autoantibodies including anti- SRP and -Mi2 Abs

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Conflict of interest: None

[Objective] To determine whether interstitial lung disease (ILD) is frequently found in patients with ant- SRP and anti-Mi2 Abs as well as those with anti-ARS Ab. [Methods] Subjects were 126 patients positive for anti-ARS, -SRP, -Mi2 or Ku antibodies. Myositis-specific/related Abs were measured by Euroline Myositis profile 3. When the intensity of each Ab was (2+) or more, the antibody was judged as positive. ILD was detected HRCT scans. [Results] The subjects were 126 patients (M/F; 39/87, mean age; 58.2 years). Anti- ARS, SPR, Mi-2 and Ku Abs were positive in 68, 17, 11 and 32 patients, respectively. ILD was found in 52/68 (78%) of ant-ARS Ab+ patients. Interestingly, ILD was also found in 8/17 (47%) of anti-SRP Ab+, in 5/11 (46%) of anti-Mi2 Ab+ and 9/32 (28%) of anti-Ku Ab+ patients. In myositis patients, ILD was found in 95% of anti-ARS Ab+ patients, in 56% of anti-SRP Ab+, in 80% of anti-Mi2 Ab and 67% of anti-Ku Ab+ ones. Similarly, in patients without myositis, ILD was detected in 47, 37, 17 and 13% of anti-ARS, SRP, Mi-2, and anti-Ku Ab+ patients, respectively. [Conclusions] ILD is a shared organ involvement in patients positive for myositis specific autoantibodies including anti-SRP and -Mi2 Abs.

P3-156

An autopsy case of anti-melanoma differentiation-associated gene-5 antibody positive dermatomyositis with prominent hyperferritinemia

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Conflict of interest: None

[Case] A 81-year-old woman was referred because of Gottron's signs and peripleural ground-glass opacity (GGO) accompanied by traction bronchiectasis on computed tomography (CT) of the chest. Because she had few physical findings suggesting myositis and the skin biopsy findings were typical of dermatomyositis, we diagnosed clinically amyopathic dermatomyositis (CADM). Anti-MDA5 antibody in serum obtained at 5 days before admission was found to be positive. Methylprednisolone pulse therapy followed by oral prednisolone and subsequent treatment with oral tacrolimus and intravenous cyclophosphamide did not improved the patient's status. CT on Day 8 of admission showed a patchy multilobar distribution of GGO. She got a fever with chills on Day 18 and we started antibiotics. Laboratory investigations revealed increased aspartate aminotransferase, alanine transaminase and lactate dehydrogenase levels and serum ferritin was 48323 ng/mL on Day 21. She died on Day 27. An autopsy was performed, invasive fungal pulmonary infections and an ischemic liver injury were revealed. [Conclusions] We should take other causes of the elevation of ferritin like sepsis or ischemic liver injury into consideration despite serum ferritin level correlates with the activity of CADM.

P3-157

A case of inclusion body myositis (IBM) in which MRI findings facilitated definitive diagnosis by muscle biopsy

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Conflict of interest: None

[Case presentation] A 54-year-old female had been aware of muscle weakness since year X-17. Serum levels of myogenic enzymes were elevated in year X-14. Muscle biopsy was refused for economic reasons; myogenic change was recognized in electromyogram and was diagnosed as polymyositis in year X-6. She received PSL and immunosuppressants; however, her CPK levels did not improve. In year X, she was referred to our institution because of increased difficulty walking and raising her arms. MRI revealed fat infiltration in the bilateral femoris muscles; muscle biopsy then showed inclusion bodies in muscle fibers, which led to a definitive diagnosis of inclusion body myositis (IBM). Her PSL was discontinued, and she started rehabilitation. [Discussion] Muscle biopsy is problematic in some cases, and other modalities are employed. We then reexamined the CT findings of the 5 IBM cases diagnosed by muscle biopsy, and found bilateral fat infiltration in the subscapular, quadriceps femoris, gastrocnemius medialis, and flexor digitorum profundus muscles. Thus, muscle biopsy should be performed to definitively diagnose IBM and thereby avoid useless immunosuppressive therapy in patients with refractory inflammatory myopathy who show bilateral fat infiltration in specific muscles by CT or MRI.

P3-159

A case of myositis of the cardiac muscle and extraocular muscle

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Conflict of interest: None

A 74 years old woman was admitted to our hospital because of right eye movement disorders, right blepharoptosis, and diplopia. Two weeks before admission, eye movement disorders, blepharoptosis, diplopia developed. Ten days before admission, she had a medical examination in previous hospital. MRI suggested myositis of right medial and inferior rectus muscles. She was diagnosed as extra-ocular myositis and transferred to our hospital. On admission, there were no extremity-muscle weakness and skin rush. The blood tests on admission showed CK 3872 U/L, troponinI 9295 pg/mL, anti-mitochondrial antibody positive. ECG revealed diffuse ST depletion. Coronary CT angiography was normal. Myocarditis was suspected but there was no cardiac symptom. On the fourth hospital day, left blepharoptosis developed. On the 31st day, ocular symptoms were worsened. On the 35th day, the blood level of CK and troponinI increased to 5640 and 4117, respectively. Biopsy on the right medial rectus muscle revealed autoimmune myositis. High dose prednisolone was started. The blood level of CK and troponin I decreased and ocular symptoms improved. Because myositis localized to extra-ocular and heart muscles is rare, we report this case with the literature review.

P3-160

Two cases of dermatomyositis with pneumomediastinum

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Conflict of interest: None

Case1: A 50s-year-old woman diagnosed dermatomyositis had been treated by oral steroid therapy for eight years. She developed cervical swelling and diagnosed cervical subcutaneous emphysema and pneumomediastinum. In spite of steroid pulse and cyclosporine therapy, they showed no improvement. Two months later, they disappeared spontaneously. Case2: A 50s-year-old man who had been treated for diabetes. One year ago, he suffered from lower limb weakness. The elevation of serum creatine kinase (CK) level was observed and the serum anti-ARS antibody was positive. Based on these findings, he was diagnosed as dermatomyositis. After a course of treatment by steroid pulse and tacrolimus, he developed cervical swelling, and diagnosed subcutaneous emphysema and pneumomediastinum. After two weeks of conservative treatment, cervical swelling and pneumomediastinum disappeared spontaneously. Discussion: Pneumomediastinum with collagen disease is reported more often in patients with dermatomyositis. Possible mechanisms include alveolar rupture due to increased airway pressure, microinfarct of pulmonary vasculitis, and tissue weakness due to steroids. Since both cases developed in a relatively short period of time and improved spontaneously, there can be causes other than the above.

P3-161

Efficacy of warfarin and diltiazem for calcinosis cutis with dermatomyositis

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Conflict of interest: None

A 43-year-old female was diagnosed with dermatomyositis (DM) with interstitial pneumonia (IP) in August X-3. She was treatment with predonisolone, cyclosporine, and intravenous cyclophosphamide, and IP was improved. In October of the same year, CT was performed for the purpose of excluding malignant diseases showed suspected calcinosis cutis around the left inguinal region and the buttocks. In December of the same year, severe pain was observed in both elbows, and the inflammatory response was high. Therefore, she was diagnosed with cellulitis and was administered with antibiotics. Although inflammatory response and pain were improved, CT was performed, because induration remained. As a result, calcinosis cutis were suspected not only in the groin and buttocks, but also in both elbows and knees. A biopsy of the skin was performed from the left elbow, calcification was observed. Calcinosis cutis had been worsening, and she was treated with warfarin and diltiazem. CT in October X-2 and March X-1 showed a trend toward improvement in calcinosis cutis without relapse. Calcinosis cutis complicated with DM is a rare condition in adults compared to children. Although the treatment has not been established, we report a good therapeutic effect with warfarin and diltiazem.

P3-162

Case of polymyositis with anti-Ku antibodies to be resistant to steroid therapy

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Conflict of interest: None

We report the case of a 78-year-old woman who seemed arm and thigh weakness 2 months before admission to our department. Laboratory findings were high titer of serum CK/MG and positive for antinuclear antibody (ANA; 1:1260) with a speckled pattern. Anti-aminoacyltRNAsynthetase (ARS) antibody and anti-topoisomerase I (anti-topo I) antibody, anti-RNA polymerase III, anti-centromere antibody were negative, but Anti-Ku antibody was positive. Electromyogram showed myogenic change. Muscle biopsy was not consistent with polymyositis. Therefore, the patient was diagnosed with polymyositis with anti-Ku antibody. Treatment with an oral prednisolone was started. Subsequently, serum CK decreased 3000 to 900 IU/L and stayed. Azathioprine was added, but serum CK kept same level. Instead of azathioprine, cyclosporine was started. Thereafter serum CK decreased to normal range. Anti-Ku antibody was fined in polymyositis patient complicated systemic sclerosis. Generally, patients having Anti-Ku antibody improve by prednisolone therapy. In spite of measurement of Anti-Ku antibody is expensive, it is important to accumulate similar patients to make it clear.

P3-163

A case report: Anti-MDA5 Ab-positive dermatomyositis patient with a minor chest CT finding at onset resulted in rapid progression to death

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Conflict of interest: None

[Case] A 58-year-old woman. She presented with a month of malaise and arthralgia. Dermatomyositis (DM) was suspected from heliotrope rash, Gottron's s papules, elevated CK, myalgia, and dysphagia. She was admitted to our hospital. Chest CT showed small nodules in subpleural region. With a recent dental treatment, antibiotic was used for septic pulmonary embolization suspicion. She was diagnosed with DM from skin and muscle symptoms. Pulse mPSL was done from DAY6, and Tacrolimus was added from DAY9 as anti-MDA5 Ab+ was found. IVCY was also given on DAY25 when ferritin and interstitial pneumonia (IP) worsened. 2nd IVCY was given on DAY44 after UTI treatment. Steroid psychosis interrupted the treatment and hypoxemia progressed. 3rd IVCY was given on DAY64, but she died of respiratory failure. [Discussion] Anti-MDA5 Ab-positive DM is known as amyopathic and is highly related to acute IP with poor prognosis. Thus immediate combined immunosuppressive therapy is recommended. Elevated ferritin, AaDO2 gap, right middle lobe GGO have been reported to be poor prognostic factors. In this case, we could have used IVCY from initiation for elevated ferritin and AaDO2 gap. Further consideration is needed that complications, infection and steroid psychosis, had such a big impact on treatment course.

P3-164

Anti-PL-7 antibody positive dermatomyositis with myositis and interstitial pneumonia after onset of fasciitis alone

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Conflict of interest: None

In patients with dermatomyositis (DM), fasciitis is found from onset of DM and is a frequent. We report a case of DM that occurred for fasciitis. The case is a 56 year-old-woman. Muscle ache of both arms developed from February, 2019. She noticed femoral ache at walk. She visited our hospital in April. Fasciitis was detected in MRI, and she was referred to our department. AntiPL-7 antibody was positive. Pain of her arms did not disappear in internal use of NSAIDs. Interstitial pneumonia (IP) was detected in CT. Eruption of DM developed from same time. Because CPK rose, and muscle ache persisted, she started prednisolone (PSL) 30 mg. but CPK was as high as 1280 U / l, and myositis findings were observed on femoral MRI. Therefore, we increased her PSL to 45 mg and was admitted to our department. She continued PSL 45 mg, and CPK decreased. However, she used 3 mg of tacrolimus (TAC) because IP worsened. We increased TAC to 6 mg and reduced PSL to 25 mg and became discharge. She continued TAC 6mg and reduces PSL to 15 mg in outpatient, but CPK was within the normal range, and IP was not getting worse. We experienced DM that occurred for fasciitis. Muscle ache has been attributed to fasciitis in many cases with DM in previous studies. Our case was compatible with it.

P3-165

A Case of Hansen Disease with Vasculitic Neuropathy and Serum PR3-ANCA

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Conflict of interest: None

[Case] A woman in her 30s, born and raised in Myanmar, had suffered from sensory disturbance in the right hand for 7 years. A year ago, fever and nodular erythema (EN) developed. She had been treated with prednisolone (PSL) as idiopathic EN. Once resolved, but her rash and fever recurred as her dosage of PSL was tapered. Her skin biopsy revealed vascular destruction with granulomas. Based on these findings and positive PR3-ANCA, she was tentatively diagnosed with ANCA-associated vasculitis, and high dose PSL and IVCY were administered. She became afebrile, and her rash improved, but her peripheral neuropathy persited. As her dosage of PSL was tapered, painful skin nodules, fever, and lymphadenitis recurred. Her biopsy revealed foamy macrophages, positive mycobacterial staining, and positive PCR for *M. leprae*, and thus her diagnosis of Hansen's disease was confirmed. [Clinical significance] Hansen's disease is a long-term infection by *M. leprae*, which can lead to damage of the nerves, respiratory tract, skin, and eyes. Although no new Japanese patient with Hansen's disease has been diagnosed since 1980, it is still common in South and Southeast Asia. It should also be noted that rare cases with Hansen's disease and vasculitic neuropathy or serum ANCA have been reported.

P3-166

Cytomegalovirus reactivation and high initial serum creatinine can predict subsequent severe infections in patients with ANCA-associated vasculitis

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Conflict of interest: None

Objectives The aim of this study was to examine prognostic factorsfor early severe infections, especially in cytomegalovirus reactivation (CMV-r), in patients with antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV). **Methods** We recruited 128 consecutive hospitalized patients newly diagnosed with AAV at KCH between 2006 to 2019 retrospectively. Thirty-four patients with CMV-r during remission induction therapy compared with 94 patients without CMV-r. The univariate and multivariable analysis for severe infections within 180 days were performed, and prognostic value of CMV-r for subsequent severe infections were also analyzed. **Results** Revised-FFS ≧2, renal involvement, initial serum creatinine ≧1.5 mg/dl at diagnosis, hemodialysis, and CMV-r were associated with severe infections in the univariate analysis. Among these variables, CMV-r (OR 4.09; p= 0.012) and high initial serum creatinine at diagnosis (OR 4.01; p= 0.025) were independent risk factors for severe infections within 180 days. Although the positive predictive value (PPV) of CMV-r to predict subsequent severe infections were 36%, when

including high initial serum creatinine, PPV were 71%. **Conclusion** CMV reactivation andhigher initial serum creatinine can predict subsequent severe infections.

P3-167

A Case of Microscopic Polyangiitis that Developed Central Diabetes Insipidus

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Conflict of interest: None

[Case] An 87-year female. The subject noticed dry mouth in February 2019, followed by general malaise noticed in early June. In July, interstitial pneumonia, MPO-ANCA positive, fever, and weight loss lead to a diagnosis of microscopic polyangiitis. Urinary osmotic pressure was low, and there was notable decrease in serum ADH (0.8 pg/mL). Contrast MRI could not confirm an area of high signal intensity in the posterior pituitary, and central diabetes insipidus was discovered. With the start of immunosuppressive therapy, the amount of urine decreased, and DDAVP treatment was not necessary. It was assumed to be central diabetes insipidus that developed as a complication of microscopic polyangiitis due to pituitary vasculitis. [Discussions] Central diabetes insipidus is a rare complication of ANCA-associated vasculitis. The cause for central diabetes insipidus is assumed to be pituitary vasculitis or granulomatous lesion in the same site. Most reports of central diabetes insipidus as a complication of ANCA-associated vasculitis are about PR3-ANCA positive granulomatosis with polyangiitis, where MPO-ANCA positive microscopic polyangiitis is rarely reported. Through the present case, we examine characteristics of central diabetes insipidus as a complication of ANCA-associated vasculitis.

P3-168

Two cases of ANCA-associated vasculitis with large vessel involvements

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Conflict of interest: None

[Introduction] ANCA-associated vasculitis (AAV) is an inflammatory disease involving small- and medium-sized vessels. Large vessel involvements (LVI) in AAV were rarely reported. [Case 1] 74 year-old male with idiopathic interstitial pneumonia had been observed. Because of jaw claudication and weight loss, he was suspected for having giant cell arteritis and introduced to our hospital. Sonographic examination revealed a thickened wall of his right superficial temporal artery. The biopsy showed necrotizing vasculitides of medium-sized arteries around the temporal artery. Further examinations detected mononeuropathy multiplex and positive for MPO-ANCA, so we diagnosed as LVI with AAV. [Case 2] 90 year-old female had suffered from a refractory otitis media. She had a persistent fever and stomachache for two months. A CT scan revealed soft tissue mass surrounding abdominal aorta. A biopsy of the mass detected the infiltration of inflammatory cells around the walls of venule. MPO-ANCA was positive, so we diagnosed as periaortitis with AAV. [Conclusion] AAV sometimes develops LVI like our cases. If physicians found interstitial pneumonia, otitis media and so on, which are not generally seen in large vessel vasculitis, they should consider the coexisting LVI with AAV.

P3-169

Clinical characteristics in patients with MPO-ANCA: A single center study

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Conflict of interest: None

[Objective] We investigated patients who were positive for MPO-ANCA and examined the difference in therapies and prognosis between patients who met the diagnostic criteria for microscopic polyangiitis (MPA) and those who did not. [Methods] Among the patients who were positive for MPO-ANCA in our hospital from August 2014 to August 2019, we classified the patients who met the diagnostic criteria for MPA of Ministry of Health, Labor and Welfare as MPA group and those who did not as MPO-ANCA group. [Results] Thirty-three patients were classified as MPA group, and eight patients as MPO-ANCA group. Between the MPA and MPO-ANCA groups, no significant differences were observed in age, averages of MPO-ANCA and CRP levels, and dose of prednisolone for induction therapy. The score of BVAS was 14.5 in MPA group, and 6.4 in MPO-ANCA group (P=0.003). Five patients died in MPA group, and one in MPO-ANCA group: he developed alveolar hemorrhage six month later and met the diagnostic criteria for MPA. [Conclusions] Even if the patients who didn't met the diagnostic criteria for MPA at diagnosis, they would require glucocorticoid therapy. Careful follow-up is required, because they could meet the criteria and die in their disease course.

P3-170

Two case of severe microscopic polyangiitis (MPA) successfully treated with plasma exchange (PE) and rituximab (RTX)

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Conflict of interest: None

[Case1] A 68-year-old male visited with left hemiplegia and motor aphasia, diagnosed as multiple cerebral infarction. Decreased renal function, infiltrative shadow of both lower lung fields, and MPO-ANCA elevation (>=300IU/ml) were observed. He was diagnosed with MPA and then treated with steroid pulse, RTX (375mg/m^2/week x4), and hemodialysis for RPGN. After 2 doses of RTX, progression of anemia and exacerbation of lung field shadow was observed and diagnosed as alveolar hemorrhage (exacerbation of MPA disease activity), second steroid pulse, PE for 2 days were done. Successful treatment, normalization of renal function was possible. [Case2] A 69-year-old female visited with fever and general malaise. Severe pneumonia was observed, but treatment of antibiotics was not effective and severe anemia (Hb 4g/dl), RPGN, MPO-ANCA elevation (133IU/ml) was seen. Anemia was diagnodes as alveolar hemorrhage caused by MPA. We started Steroid half pulse, PE for 3 days, RTX (375mg/m^2/week x4). Administration of ventilator was required, but withdrawal from the ventilator was possible after treatment. [Discussion] Both cases were severe MPA and successfully treated with steroid pulse, RTX, and PE. We report literature considerations on usefulness of RTX and PE for severe MPA.

P3-171

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.

P3-172

A case of microscopic polyangiitis with posterior reversible encephalopathy syndrome, alveolar hemorrhage, and rapid progressive glomerulonephritis

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Conflict of interest: None

A seventy-eight female was transported to our hospital due to disturbing and dyspnea. Her blood pressure was 154/94mmHg. Physical examination revealed nose bleeding, pitting edema and purpura on legs. Chest plane CT revealed bilateral consolidation. Diuretic agent did not ameliorate her symptoms and anemia worsened, which implied alveolar hemorrhage. Her serum creatinine level increased to 2.6mg/dl and granular cast appeared, indicating rapid progressive glomerulonephritis. Skin biopsy revealed leukocytoclastic vasculitis. Brain MRI revealed high intensity area of bilateral posterior white matter lesions in the FLAIR and ADC map, indicating posterior reversible encephalopathy syndrome (PRES). Under the diagnosis of microscopic polyangiitis, methylprednisolone pulse therapy was initiated followed by administration of prednisolone 40mg. Intravenous cyclophosphamide therapy and plasma exchange was performed. Nifedipine was administrated for PRES. After induction of the immunosuppressive and antihypertensive therapy, her clinical symptoms and laboratory data resolved. PRES refers to a disorder of reversible subcortical vasogenic brain edema in patients with acute neurological symptoms. If acute neurological symptom occurs in patients with MPA, PRES should be considered.

P3-173

A case of refractory scleritis and proptosis as the initial clinical manifestation of ANCA associated vasculitis

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Conflict of interest: None

A 75-year-old man felt appetite loss and weight loss. He also had ocular hyperemia and pain of left eye. Two months later, he visited ophthalmologist. He showed conjunctival congestion and corneal ulcer of left eye. He was started with eye drops of antibiotics and steroid. Because the ocular symptoms were recurrent four months later, he was visited to our hospital. He was diagnosed scleritis. Nevertheless, he did not show fever, rivedo, symptom of sinusitis and otitis media and renal dysfunction, the laboratory data indicated elevated levels of CRP (0.37mg/dl), MPO-ANCA (28.9U/ml). The HRCT revealed consolidations and pleuritis in the right upper lobe. The orbital MRI did not reveal granulomas and mass. He was diagnosed with unclassified type ANCA associated vasculitis (AAV). He was administrated both 40mg/day PSL and AZA for initial treatment. After this treatment, his symptoms were remarkably improved. When the initial symptoms were only ocular symptoms of AAV, it was considered that it needed time to diagnose. As a result, there was possibility of ophthalmic poor prognosis. Even if there were no typical signs of AAV such as nasal symptoms, lower respiratory tract symptoms, and renal impairment, in the case of refractory scleritis, we should consider to assessing ANCA.

P3-174

A case of ANCA-related vasculitis with elevated hepatobiliary enzymes

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Conflict of interest: None

[Case] A 80-year-old woman visited our hospital with fever and bilateral thigh pain. Laboratory data showed increased serum CRP and hepatobiliary enzymes. We followed up with levofloxacin because there were no findings in physical examinations and cervical/abdominal CT. After one week, her symptoms had been persisted and she was hospitalized. Laboratory data showed a high titer of MPO-ANCA. Urinalysis, whole body enhanced CT and head enhanced MRI showed no significant findings, but femoral MRI showed diffuse high intensity areas in both thigh muscles with FLAIR. We performed a muscle biopsy of the right lateral thigh muscle, but there were no findings of vasculitis. After admission, serum ALP increased gradually. Abdominal ultrasonography and MRCP showed no specific findings, so we performed liver biopsy. Pathological findings showed interface hepatitis. The possibility of giant cell arteritis (GCA) was considered due to high serum ALP and fever. Therefore, we performed PET-CT but did not find any significant findings. Based on various laboratory findings, we diagnosed ANCA-related vasculitis. After we started the prednisolone, her symptoms and laboratory data improved immediately. We report a rare case of ANCA-related vasculitis with elevated hepatobiliary enzymes.

P3-175

A case of polymyositis (PM) with MPO-ANCA positive granulomatosis with polyangiitis (GPA)

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Conflict of interest: None

A 69-year old woman with PM was admittede to our hospital because of persistent dry cough. At 12 years ago she was diagnosed with interstitial pneumoniae. The patient had been diagnosed with PM 4 years earlier based on the presence of Raynaud phenomenon, myalgia, with muscle weakness, increased serum CK, and positive anti-Jo-1 antibody. She was treated with PSL 50 mg daily, and she responded. The PSL dose was tapered slowly to 4 mg/day. She had suffered from antibiotics-resistant dry cough, middle low grade fever and chronic middle otitis. Chest CT showed bronchial wall thickening. Bronchoscopy showed bronchial edema and stenosis. MPO-ANCA was positive with titer of 38 EU. Beside on these findings, a diagnosis of GPA was made. Administration of PSL 50 mg/day and intermittent pulse intravenous cyclophosphamide therapy (IVCY) improved her general status and MPO-ANCA. Cyclophosphamide treatment was switched to azathioprine 25 mg/day and the PSL dose was tapered to 4mg/day. She was suffering from middle otitis. She presented with dry cough and Chest CT showed bilateral multiple lung nodules and ground-glass opacity. Serum MPO-ANCA flared. 30mg of PSL was effective. We report a case of PM complicated with GPA. This is very rare case that ANCA-associated vasculitis with PM.

P3-176

A case of granulomatosis with polyangiitis by intranasal lesions improved after treatment

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Conflict of interest: None

[Case] 45-year-old woman. Six years ago, she presented with nasal obstruction and nasal bleeding. The biopsy performed from the left lower turbinate was diagnosed with tuberculosis granulation. The treatment started with anti-tuberculosis drugs, but didn't succeed. Five years ago, she presented saddle nose and PR3-ANCA increase, and diagnosed with granulomatosis with polyangiitis (GPA) by reexamination of pathological tissue and re-biopsy. She was treated with prednisolone, and her symptoms improved. However, she stopped medication by herself judgement. Two months ago, she caused tonic convulsion. Brain MRI showed the non-uniform mass extending headward from the ethmoid sciatic plate. She was diagnosed with symptomatic epilepsy due to intracranial extension of intranasal lesions, and introduced to our hospital. We couldn't biopsy be-

cause the mass was where might cause cerebrospinal fluid leakage. She was started to treat with prednisolone 50mg per day and intravenous cyclophosphamide for three times, and azathioprine by remission maintenance therapy. She followed a good course, and the lesion reduced from 27 to 23mm on MRI. After tapering prednisolone, the lesion is not growing on MRI. [Clinical significance] Intracranial lesion is rare for GPA, but it is important to consider.

P3-177

A case of ANCA-associated vasculitis complicated with invasive pulmonary aspergillosis

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Conflict of interest: None

A 78-year old woman presented with AKI. Laboratory data showed an elevated Cre (4.57mg/dl) with hematuria and proteinuria, an elevated CRP (7.34mg/dl), and a positive MPO-ANCA (84.4U/ml). Possible diagnosis of ANCA-associated RPGN (Grade II) prompted to the administration of PSL 40mg/day. However, her renal function deteriorated and led to the initiation of hemodialysis on 21 day. Her clinical course was good with the tapering of PSL (20mg/day), but she had fever on 56 day. Chest CT revealed a thick wall pulmonary cavity in the right lung. Testing for T-SPOT was negative. Conversely, βD-Glucan (300 pg/ml) and aspergillus antigen (5.0) were extremely elevated. A bronchoscopy revealed that aspergillus antigen was positive and A. terreus was cultured from bronchoalveolar lavage fluid. Thus, she was diagnosed as invasive pulmonary aspergillosis (IPA), and successfully treated with VRCZ. βD-Glucan and aspergillus antigen decreased to 118pg/ml and 0.7, respectively. On 133 day, she was discharged after PSL was tapered to 5mg/day with negative MPO-ANCA. I reported a rare case of ANCA-associated vasculitis complicated with IPA. When a pulmonary cavity was found in patients using steroid with reduced immunity, prompt diagnosis and treatment may be necessary considering IPA.

P3-178

A Case of ANCA-Associated Vasculitis in Central Nervous System Developed by Recurrent Cerebral Infarction with Headache as An Initial Manifestation

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Conflict of interest: None

[Case] 51-year-old female [Present illness] She had headache for 2 months and was diagnosed with cerebral infarction, but her symptom and MRI findings were recurrent even after anti-platelet therapy. She also observed numbness in her bilateral lower legs and hematuria, admitted to our hospital. [Clinical course] CRP was elevated to 5.22 mg/dL. MPO-ANCA was positive with 69.3 U/ml. Slight hematuria without creatinine elevation was observed. Nerve conduction velocity revealed multiple mononeuropathy. Enhanced MRI revealed new multiple infarctions with leakage of enhancer indicating vasculitis. We diagnosed her with ANCA-associated vasculitis (AAV). High dose corticosteroid (CS) combined with intravenous cyclophosphamide (IVCY, 500mg/m^2/2weeks) following steroid pulse therapy was started. On day 42nd, followed-up MRI observed new small infarcted lesions, but we tapered CS with continuing IVCY because CRP and MPO-ANCA certainly decreased without newly occurred symptom. On day 55th, no new MRI lesion was found though CS was tapered. [Clinical significance] CNS vasculitis typically manifest recurrent infarction with hemorrhage after reperfusion. In cases of persistent headache with cerebral infarction refractory to anti-platelet therapy, AAV should be one of the differential diagnoses.

P3-179

A case of hypertrophic pachymeningitis with a decrease in visual acuity developing with granulomatosis with polyangiitis

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Conflict of interest: None

[case] A 74-year-old Japanese woman was diagnosed with granulomatosis with polyangiitis (GPA) six years ago, due to fever, myalgia, peripheral neuropathy, sinusitis and MPO-ANCA (+). She had been treated with oral corticosteroid and intravenous cyclophosphamide. She developed a decrease in the right visual acuity 6 months ago. She was diagnosed with retrobulbar optic neuritis and treated with steroid pulse at an ophthalmologist. After steroid pulse therapy, her right visual acuity improved. Afterward, she had been aware of headaches and right facial neuralgia since 3 months ago. She developed a decrease in the right visual acuity again and visited the ophthalmologist. She was diagnosed with retrobulbar optic neuritis and MRI revealed hypertrophic pachymeningitis. Her right visual acuity quickly improved and facial neuralgia and headache gradually improved administrations of rituximab following steroid pulse therapy. Five weeks later, hypertrophic pachymeningitis improved by MRI. [clinical significance] Hypertrophic pachymeningitis occasionally accompanies GPA. Headache is the most common symptom of hypertrophic pachymeningitis, but nonspecific. We should remember hypertrophic pachymeningitis, when ANCA associated vasculitis patients present headache and neurological symptoms.

P3-180

Myalgia as a presenting symptom in ANCA-associated vasculitis

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Conflict of interest: None

A 72-year-old man had muscle pain of the lower legs a month ago, and he was admittd to a hospital two weeks ago. The serum creatine kinase level was normal, the electromyogram and the nerve conduction velocity were not remarkable. MPO-ANCA was high, and CT of the chest showed bilateral ground glass opacity, which was compatible with interstitial pneumonia. ANCA associated vasculitis (AAV) was suspected, he was introduced to our hospital. Physical examination showed muscle tenderness of the lower legs bilaterally, but no muscle weakness. Renal function was normal, and urinary testing did not suggest the presence of glomerulonephritis. MRI of the lower legs showed T2W1 high signal intensity lesions. Muscle biopsy revealed small-vesssel vasculitis. A clinical diagnosis of AAV was made, and Prednisolone (30mg/day) was initiated. Myalgia rapidly improved, and ANCA levels gradualy decreased. ANCA associated vasculitis (AAV) is preferentially involving the kidneys, lungs, skin, and nerves, but muscles can infrequently become a target organ. Muscle biopsy was useful for suspected case of muscle vasculitis due to AAV, when biopsy of the other organs is impractical. We investigate some case reports about muscle vasculitis due to AAV and report clinical charactristics of them.

P3-181

Clinical features and treatment results of the patients with eosinophilic granulomatosis with polyangiitis in Ehime university hospital

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Conflict of interest: None

[Objective] Eosinophilic granulomatosis with polyangiitis (EGPA) is a disease with various damages by eosinophilia and ischemic injury associated with vasculitis. We aim to analyze the clinical features of EGPA patients in our university hospital. [Methods] We analyzed 18 patients with EGPA followed more than one year after treatment between April 2006 and April 2018. [Result] Eighteen patients (11 females, 7 males) were between 17- and 76-year-old (mean 57). Mean values are as follows: eosinophil count 8810/ul, total IgE 1340 IU/ml, and CRP 5.13 mg/dl. Neurological symptoms occurred in 17 patients, cutaneous lesions in 7, pulmonary involvement in 13, cardiac lesions in 5, and nasal sinus lesions in 13. Of those, 7 showed a positive MPO-ANCA. Patients with negative ANCA had pulmonary and nasal sinus lesions significantly, compared with positive ANCA. All patients were treated with corticosteroid therapy. Cyclophosphamide, intravenous immunoglobulin, and mepolizumab were administered to 7, 10, and 2 patients, respectively. [Discussion] ANCA-positive patients tend to relapse, compared with ANCA-negative patients in our hospital. We report clinical features and treatment results in our hospital with a review of the literature.

P3-182

The efficacy and safety of rituximab on granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] To evaluate the efficacy and safety of rituximab (RTX) therapy in patients with granulomatosis with polyangiitis (GPA) in our hospital. [Methods] Eighteen patients with GPA were treated with RTX. RTX was administered weekly for consecutive 4 weeks. Thirteen patients with GPA had been given cyclophosphamide (CY) before RTX therapy and seven in those patients relapsed after discontinuation of CY. Six patients were refractory to CY therapy and switched to RTX therapy. The average follow-up periods was 18 months (6-43). The efficacy of RTX therapy was determined as follows; 1) reduction of BVAS up to 30%. 2) reduction of steroids doses was possible. [Results] Twelve patients treated with RTX achieved clinical remission during observation period. Four patients did not reach the clinical remission while dose reduction of steroids was possible in there patients by RTX therapy. Two of twelve patients relapsed after the remission by RTX therapy and repeated RTX therapy exhibited therapeutic effects again. One patient died for severe infection after RTX therapy. Two of eighteen patients developed severe allergic reaction and RTX was stopped. [Conclusions] Efficacy and safety of RTX therapy was confirmed for relapsing GPA.

P3-183

An effective case of rituximab for refractory sinus lesions in eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

A 52-year-old man was diagnosed with allergic rhinitis in childhood. In September 2019, he presented to emergency department with fever and chest compression. We suspected coronary disease because ECG showed ST depression, but it was ruled out after hospitalization. Transbronchial lung biopsy for infiltrative and ground glass shadows in lungs was associated with eosinophil infiltration. He was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) by asthma, eosinophilia, polyangiitis, MPO-ANCA positive and pathological findings. Glucocorticoid therapy (prednisolone 55mg/day) was effective, but eye pain appeared when the dose was betamethasone (BMZ) 1.5mg/day. We increased BMZ 3.0mg/day for relapse as sinus lesions were enlarged, but not improved. Remission induction therapy by intravenous methylprednisolone pulse therapy, intermittent pulse intravenous cyclophosphamide therapy and mepolizumab was done. However, he complained of eye pain again during maintenance therapy with azathioprine. Finally we used rituximab for refractory sinus lesion, his symptoms and CT findings were improved. We report on the efficacy of rituximab in patients with sinus lesions of EGPA, which was not improved with glucocorticoids, cyclophosphamide, and mepolizumab, including a literature review.

P3-184

A case of eosinophilic granulomatosis with polyangiitis complicated by dissecting aneurysms of bilateral internal carotid arteries at the onset and the relapse

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Conflict of interest: None

A 50-years-old man presented with hemiparalysis, fever, numbness of the feet in X-4 years. MR angiography (MRA) showed dissecting aneurysms of right internal carotid artery (ICA). Intravascular stenting and coil embolization of the right ICA was performed. He was also diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) based on his symptoms and chronic allergic sinusitis, eosinophilia, elevation of MPO-ANCA, IgE, and CRP. High-dose prednisolone (PSL) and 2x intravenous cyclophosphamide (IVCY) followed by tapering PSL resulted in remission of his symptoms. In year X, he had fever, dyspnea, numbness of the feet, and bilateral mandibular pain. Laboratory studies showed hematoproteinuria, eosinophilia, elevation of MPO-ANCA and CRP. Chest CT showed interstitial pneumonia and renal biopsy revealed necrotizing glomerulonephritis. MRA showed dissecting aneurysms of left ICA. He was diagnosed with the relapse of EGPA complicated with aneurysms of left ICA. mPSL pulse therapy, high-dose PSL and 6x IVCY resulted in remission. Intravascular stenting and coil embolization were performed for left ICA. Vasculitis and aneurysm of ICA is not a prominent feature of EGPA, but our case suggests EGPA should be considered as the differential diagnosis of ICA dissection or aneurysms.

P3-185

A case of eosinophilic granulomatosis with polyangiitis complicated with severe alopecia areata and ulcerative colitis successfully treated with tofacitinib

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Conflict of interest: None

A 28-year-old woman was treated with mesalazine (5-ASA) for ulcerative colitis. She later developed allergic rhinitis, interstitial pneumonia, gastrointestinal ulcer. Her blood test showed eosinophilia and PR3-ANCA positive. She was diagnosed with eosinophilic granulomatosis with polyangiitis. She was treated with prednisolone (PSL), Cyclosporin-A (CyA) and 5-ASA. When PSL was taperd, her UC symptoms was exacerbated. CyA was changed to tacrolimus (TAC), and 5-ASA dosage was increased. But she developed erythroderma and severe alopecia areata. TAC and 5-ASA was stopped. CyA was restarted. After erythroderma was improved, infliximab (IFX) was started. Her UC symptoms was relieved but her EGPA symptoms was exacerbated. IFX was stopped, and Mepolizumab (MEP) was started. But her UC symptoms was exacerbated. MEP was stopped and Tofacitinib was sterted. Her UC, EGPA symptoms and severe alopecia areata was improved.

P3-186

A case of eosinophilic granulomatosis with polyangiitis, associated with rapidly progressive multiple mononeuropathy, diagnosed at the same time with rheumatoid arthritis

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Conflict of interest: None

(Case) 50's female (Chief complant) Fever, dysesthesia and purpura of legs (Clinical course) She had the history of asthma. She was admitted to our hospital, complaining of hand stiffness and dysesthesia of her left leg. The blood test showed the increase of CRP, positive anti-CCP antibody, and eosinophilia. The next day, the purpura and the gait disturbance appeared. Eosinophilic granulomatosis with polyangiitis (EGPA) was suspected from the history of asthma, fever, purpura, dysestesia, and eosinophilia. Nerve conduction study showed multiple mononeuropathy of axon type in motor and sensory nerve. The biopsy specimen of her skin showed the infiltration (mainly eosinophils) and the nuclear dust around small blood vessels in dermis. Nerve biopsy showed the eosinophil infiltration around small vessels. After treatment of prednisolone (PSL) 50 mg/day, eosinophils and CRP levels returned to normal. The purpura and fever quickly resolved, although dysesthesia deteriorated. Under the usage of mepolizumab (300 mg/4 weeks), PSL was tapered to 20 mg/day. (Clinical significance) A complication of EGPA and RA is rare. It was interest that both diseases were simultaneously diagnosed.

P3-188

A case of hemophagocytic syndrome caused by coxsackievirus and herpes simplex virus during treatment for eosinophilic granulomatosis with polyangiitis (EGPA)

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Conflict of interest: None

[Case] 50s male [Chief complaint] Fever, liver damage [Present illness] The patient was treated with PSL (max 80 mg/day) and MTX for EGPA in April 20XX. Bullous eruptions were observed on the lips, oral cavity, and palms. AST 3618 IU/L, ALT 7211 IU/L were noted. We adjusted the drug, but this was not improved. The patient had fever, the right lung infiltrated shadow was found, so we diagnosed pneumonia. Antibiotics were administered but this was not improved, and the skin eruption was worsening. Fever persisted, and cytopenia, liver damage, high ferritin, high LDH, low haptoglobin, and atypical lymphocytes were suspected to hemophagocytic syndrome (HPS). A bone marrow puncture was performed, and we diagnosed HPS. After diagnosis, a steroid pulse was administered, the findings improved. The rash was diagnosed by dermatology as hand-foot-mouth disease and cold sores. Serologically, coxsackie virus and herpes simplex virus infection were confirmed, and these were considered to be the cause of HPS. [Discussion] The activity of EGPA was controlled, and liver damage appeared. Drug change and administration of antibiotics did not improve. The patient was diagnosed with HPS due to viral infection. We reported a rare case of HPS in adults with coxsackievirus and herpes simplex infection.

P3-189

A case of adult-onset IgA vasculitis with gastrointestinal ulcer and renal disorder

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Conflict of interest: None

[Case] A 56-year-old man was complained of abdominal distension and was admitted to the hospital because of small intestinal ileus. Abdominal symptoms improved after insertion of the ileus tube, but the inflammatory response re-elevated and purpura appeared on both lower legs. He was diagnosed with IgA vasculitis from the result of skin biopsy and treated with high dose prednisolone (PSL) daily. The inflammatory response and intestinal lesions improved. A capsule endoscopy showed multiple ulcer lesions in the duodenum and ileum, but no active bleeding. However, level of serum creatinine remained increasing, and bloody stool and anemia were exacerbated. He was transferred to our hospital for intensive therapy. We started 1000mg of daily i.v. methylprednisolone pulse therapy for 3days, followed by 60mg (1mg/kg/day) of PSL, and combination therapy that single filtration plasma therapy and i.v. cyclophosphamide. Bloody stool and renal dysfunction were improved after our treatment. [Conclusion] IgA vasculitis rarely occurs in adults and has a poor prognosis compared to children. We encountered a case of severe gastrointestinal tract lesions and renal dysfunction that had a good course with intensive treatment.

P3-191

A case of refractory IgA vasculitis with fatal hemorrhagic small intestinal ulcer

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Conflict of interest: None

A 63-year-old man with diabetic renal failure was admitted to our hospital due to high fever lasting 10 days. Laboratory studies were as follows; WBC 35,300/μL, CRP 20.9 mg/dL, BUN 81.2mg/dL, Cr 8.3 mg/dL. Because pyelonephritis was suspected, we started antibiotics and hemodialysis (HD). Additionally, he started to complain of arthralgia, purpura and bloody stool. Abdominal CT showed thickening of wall of intestine. Antinuclear antibodies, MPO-ANCA and PR3-ANCA were negative. Histological examination of skin showed leukocyte vasculitis with IgA deposition on the vessel wall. We diagnosed IgA vasculitis. We started methylprednisolone pulse therapy (500mg/day for 3 days) followed by oral prednisolone (1mg/kg). However, his symptoms were not responded. Upper gastrointestinal endoscopy showed severe reflux esophagitis and ulcer of the duodenum. Plasma exchange were performed, but he got hemorrhagic shock. Active bleeding from jejunum was observed at contrast-enhanced CT, TAE and intravenous cyclophosphamide therapy were performed. But active bleeding from the intestine was difficult to control, and he died on the 31st hospital day. Gastrointestinal symptom in IgA vasculitis are occurred frequently, but hemorrhagic shock is rare. We consider this a valuable presentation.

P3-192

Effective treatment with Tofacitinib in a patient with rheumatoid vasculitis

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Conflict of interest: None

A 75 years old male was suffered limb joint swell in January 2017. He visited our hospital in February 2017, and he was diagnosed as RA. Treatment with PSL 5mg/day and MTX 8mg/week was started, but subluxation of fingers was appeared. Treatment with GLM 50mg was started, but liver disorder was appeared. Treatment with GLM was changed to TCZ, but skin rash was appeared, so treatment with TCZ was changed to GLM 100mg in February 2018. Livedo Reticularis was appeared on the lower leg in April 2018, so he was admitted to our hospital in March 2018. Laboratoly data was CRP 6.2mg/dL, CH50 40.7U/mL, C1q ≦1.5μg/mL, DAS28 was 5.96, and SDAI was 35.27. Biopsy on lower leg revealed vasculitis, so he was diagnosed as rheumatoid vasculitis. After the treatment with PSL and IVCY, general malaise and purpura were improved, and serum CRP turned to negative. 6th IVCY therapy was finished in November 2018, treatment with TOF was started. RV was not relapsed. JAK inhibitor's efficacy to middle and large vessel vasculitis such as GCA and PAN has reported, but efficacy to RV has not reported. JAK inhibitor suppress pathogenic immune responses in vasculitis, so treatment with JAK inhibitor may be a useful option for RV.

P3-193

A case of vasculitis syndrome affecting the various-sized vessels and multiple organs

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Conflict of interest: None

[Case] A 71-year-old woman was admitted to our hospital because of malaise and appetite loss. The numbers of WBC and serum CRP levels were elevated (WBC 11600/μL, CRP 14.55 mg/dL). In addition, her urinalysis revealed proteinuria (3+) and pyuria (WBC4+). Therefore, she underwent antibiotic treatment after diagnosed as a urinary tract infection. However, she did not have improvement of symptoms and then was found to be positive for MPO-ANCA and HLA-B51. A contrast-enhanced CT scan revealed showed mucosal thickening of thickening of pericardium, wall thickening of the aortic root, severe stenosis of the celiac artery, andpancreaticoduodenal artery pseudoaneurysm. In addition, FDG-PET/CT showed FDG accumulation in the ascending aorta and epicardium. In several days after admission, since X-ray photograph revealed the development of pericardial effusion and bilateral pleural effusions, she was treated with PSL 50 mg/day in combination with IVCY and gradually made a symptomatic improvement and a decrease in MPO-ANCA with no complications. [Clinical significance] The case with vasculitis syndrome affecting the various-sized vessels and multiple organs was few. FDG-PET/CT was an usuful image examination to expose the complication such as large vessel vasculitis and pericarditis.

P3-194

Hepatitis-B virus associated cryoglobulinemic vasculitis with various complications treated by corticosteroids, mycophenolate mofetil and cryofiltration

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Conflict of interest: None

We report a 59-year-old man with repeated purpura and urticaria which resolved spontaneously every few days. Only a few cryoglobulin (CG) could be recognized, and type I membranoproliferative glomerulonephritis was diagnosed by renal biopsy in the previous year. We diagnosed type II cryoglobulinemia related to Hepatitis-B virus (HBV) with cutaneous leukocytoclastic vasculitis, glomerulonephritis, and hypocomplementemic urticarial vasculitis (HUV). Entercavir induced to the negative conversion of serum HBV-DNA, moreover CG could not be detected by treatment with glucocorticoid (GC) and mycophenolate mofetil (MMF) for a long time. However, HUV were not improved and renal function deteriorated. In addition, because of anemia caused by MMF, it was forced to control with GC single agent. Consequently, CG increased again. Thereafter, cryofiltration combined with GC and MMF slightly improved general malaise and HUV. However, B-cell lymphoma newly developed and rapidly progressed. In consequence, he died. HBV-associated cryoglobulinemic vasculitis (CV) is rare and its treatment is unclear. There are CV with persistent symptoms, even if CG is not detected. This case showed the refractory pathophysiology of complications related to CV and progression of lymphoma due to uncontrolled CV.

P3-195

A case of hyper coagulability and hyper fibrinolysis after starting of steroid therapy in sarcoidosis with multiple organ invasion

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Conflict of interest: None

[Case report] A 47-years-old woman was aware of a nodule on the forehead in 2015. Laboratory data showed elevated levels of ferritin, CRP, ACE, and sIL2-R. FDG PET-CT showed the pulmonary reticular opacities, hepatosplenomegaly, systemic lymphadenopathy and uptake on the liver, spleen, and systemic lymph nodes. Skin and liver biopsy was done and diagnosed with sarcoidosis. Though she had been followed up without treatment, she presented remittent fever, weight loss since April 2018. FDG PET-CT showed the progression of hepatosplenomegaly, and new uptake on the bones such as thoracic spine. We started treatment with prednisolone (40mg/day) in January 2019. Though the symptoms and elevated levels of ferritin and CRP resolved, laboratory data showed hyper coagulability and hyper fibrinolysis (D-dimer 64.4μg/ml, TAT 2.9 ng/ml). Despite of close examination, there was no thrombus. Though DIC diagnostic criteria was met, her general conditions remained good and D-dimer improved spontaneously. [Discussion] This case suggest that the granulomas was collapse due to the therapy and fibrin contained in the granulomas might have deposited in the blood vessels. In case of sarcoidosis with multiple organs lesion, there may be a risk of hyper fibrinolysis when starting steroid therapy.

P3-196

Gulain-Barre syndrome in a patient with polymyalgia rheumatica

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Conflict of interest: None

A 78-year-old male patient with polymyalgia rheumatica was treated with low-dose prednisolone 5mg daily and methotrexate 10mg weekly for one year and maintained remission. He suffered from diarrhea soon after taking influenza virus vaccine. He was referred to our hospital because of continuous abdominal pain and watery diarrhea and was diagnosed with acute enteritis. His symptoms naturally improved. However, four days later, he felt rapidly progressed muscle fatigue in head and all extremities and difficulty in walking. The physical exam showed significant muscle weakness (MMT: 3/5) and absent deep tendon reflexes. Cerebrospinal fluid study showed albumin-cytologic dissociation. Altogether, he was diagnosed with Guillain-Barre syndrome. He was treated with intravenous immunoglobulin and symptoms improved. We report this as a rare case with a literature review.

P3-199

A case of TAFRO syndrome with anti-centromere antibody

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Conflict of interest: None

[Case] A 56-year-old woman presented with systemic edema, abdominal pain and malaise. Laboratory results included thrombocytopenia, elevation of C-reactive protein. Anti-nuclear antibody and anti-centromere antibody were positive. The computed tomography (CT) scan revealed cervical and para-aortic lymphadenopathy and pleural effusion and ascites. Lymph node biopsy showed atrophic germinal centers with enlarged nuclei of high endothelial cells. Bone marrow biopsy showed mild fibrosis. Then, we diagnosed TAFRO syndrome. Methylprednisolone 80mg/day was started but plural effusion and ascites were getting worse. She also needed hemodialysis because of oliguric renal failure. After tocilizumab (400mg/body/week) was started, platelet elevated and pleural effusion and ascites decreased gradually. 2 months later, her pleural effusion and ascites disappeared. After systemic edema disappeared, her skin was not thick. [Discussion] In this case, we regarded as TAFRO syndrome from her clinical course and her lymph histopathology. TAFRO syndrome with anti-centromere antibody is not to be common.

P3-200

A case of TAFRO syndrome with marked neutropenia after the first administration of tocilizumab (TCZ)

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Conflict of interest: None

(Case) A 33-year-old Japanese man complaint with fever and epigastralgia developed ascites, pleural effusion, pericardial effusion after hospitalized previous hospital. He was transferred to our hospital for further examination and treatment. He had anasarca, renal dysfunction (BUN: 54.4mg/dl, Cre: 2.02mg/dl), thrombocytopenia (PLT: 32000 /μl) and organomegary. We diagnosed he had TAFRO syndrome. We treated with Methylprednisolone: 1 mg / kg / day and TCZ: 8 mg / kg. Marked neutropenia occurred on the 7th day after TCZ administration. Lenograstim was administered from the 10th to 13th day after the TCZ administration. After the neutrophil count was recovered, TCZ dose was reduced and administered weekly. He was discharged on the 30th day of hospitalization. His condition worsened immediately after discharge and he was admitted again. After the TCZ dose was increased to 8 mg / kg, neutropenia did not occur and treatment was continued. (Discussion) We experienced a case of TAFRO syndrome that showed marked neutropenia after the first administration of TCZ. IL-6 is involved the process in neutrophil production in the bone marrow and recruitment into the peripheral blood. Tocilizumab administration in a state of high IL-6 may cause marked neutropenia due to sudden IL-6 suppression.

P3-202

A case of idiopathic hypereosinophilic syndrome associated with extensive venous thrombosis

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Conflict of interest: None

[Case] 46-year-old man [chief complaint] left periocular swelling [current medical history] He was diagnosed as left orbital cellulitis at a medical practitioner. Antibiotics did not have effects and he was hospitalized. He had fever, hypereosinophilia, thrombocytopenia, glomerular hematuria and lung consolidations. After 1 mg/kg/day of prednisolone was initiated, fever, hypereosinophilia and glomerular hematuria improved but thrombocytopenia and lung consolidations got worse, so he was transferred to our hospital. Deep venous thrombosis was observed in both lower limbs by echosonograph and contrast-enhanced CT showed pulmonary thromboembolism and pulmonary infarction, so we diagnosed him as hypereosinophilic syndrome. Anticoagulant therapy was started, and thrombocytopenia and lung consolidations improved immediately. [Consideration] It has been reported that thrombosis is observed in hypereosinophilic syndrome. This is a valuable case and we report the treatment process with literature review.

P3-203

A case of TAFRO syndrome complicated with hemophagocytic syndrome and thrombotic microangiopathy

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Conflict of interest: None

A 64-year-old female patient was hospitalized because of high fever, high inflammatory response, thrombocytopenia in April 201x. On admission, she was diagnosed with DIC from FDP 49.8μg/mL and thrombocytopenia. The underlying disease was unknown and antibacterial drugs were used. On the 3rd day, she was diagnosed as hemophagocytic syndrome (HPS) based on bone marrow examination. We started steroid therapy and cyclosporine. However, the therapeutic effect was poor, and renal dysfunction and edema were observed. On the 5th day, the respiratory condition worsened and CT showed pleural effusion and infiltrative shadows. She became ventilated as a complication of ARDS on the 7th day. TAFRO syndrome was diagnosed based on thrombocytopenia, pleural effusion, fever, organomegaly and renal dysfunction. Tocilizumab (TCZ) was administered on the same day. Although it temporarily improved, re-elevation of LDH and hyperbilirubinemia were obsereved. She was diagnosed with thrombotic microangiopathy (TMA), and plasma exchange was started. She gradually improved, and withdrew from ventilator on the 20th day. She continued TCZ and improved, she was discharged on the 95th day. TAFRO syndrome is a novel concept, and is reported the effectiveness of TCZ. We report a case of TAFRO syndrome complicated with HPS and TMA.

P3-204

Cardiac sarcoidosis presenting with acute left heart failure due to severe mitral regurgitation

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Conflict of interest: None

(Introduction) Previous studies reported that cardiac sarcoidosis (CS) may involve any part of the heart. (Case) A 65-years-old woman with dyspnea on exertion for a month, presented fever and orthopnea. She was tachypneic and caught her breath between sentences. Physical examination revealed pansystolic murmur at the apex and wheeze. Chest radiograph showed pulmonary edema and cardiac dilatation. Transthoracic echocardiogram showed septal hypertrophy, left ventricular tract (LVOT) obstruction and severe mitral regurgitation (MR). We diagnosed acute left heart failure (LHF) due to MR, so urgent surgical treatment was conducted. The hypertrophy of ventricular septum contributed MR and LVOT obstruction without mitral valve abnormality. Then she has undergone mitral annuloplasty and the myectomy introduced by Andrew Morrow. Endomyocardial biopsy revealed noncaseating granuloma. (Conclusion) Clinical features of CS depend on the location, extent, and activity of the disease, however hypertrophy of myocardial wall is less common in CS than basal septum thinning. We report a case of ventricular septal hypertrophy associated with CS

P3-205

Preiser disease developed during RS3PE syndrome treatment

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Conflict of interest: None

A 72-year-old woman had joint pain in both wrists and edema of the limbs appeared, and she visited a praimary care doctor in June. In August, the doctor suspected rheumatoid arthritis and introduced to ouh hospital with PSL 8mg/day started. RF and anti-CCP antibody were negative, and she had polyarthralgia and indentation edema of the extremities. I diagnosed RS3PE syndrome and started treatment at PSL 15mg/day. Although edema was improved, joint pain remained. I increased the dose of PSL 30mg/day and added MTX 8mg/week. The Symptoms improved, and after that, I gradually decreased PSL, but there was no sign op relapse. In September next year, swelling of the right wrist appeared without incentive, and when performing wrist joint MRI for the purpose of finding the cause, necrosis of the scaphoid bone was observed. I thought she developed Preiser disease. Preiser disease is a rare disease, so I report this case.

P3-206

A case of rheumatoid arthritis with significant improvement in scleritis due to increased amounting of Golimumab

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Conflict of interest: None

[Objective] We report a case of RA of 25 years' duration. In 1994, the patient was diagnosed with RA and prescribed prednisolone and oral disease modifying anti-rheumatic drugs such as salazosulfapyridine. [Case] In 2004, as the symptoms aggravated, the drugs were switched to MTX, and then, tacrolimus was added. In 2013, as her knee arthritis aggravated, subcutaneous injection of GLM 50 mg once every four weeks was started. GLM was highly effective, and remission was achieved early. Lens reconstruction was performed for bilateral cataracts in 2016 and 2017, respec-

tively. In 2019, the patient consulted an ophthalmologist due to bilateral eye pain. The patient presented with bilateral redness of the conjunctiva and was thus diagnosed with scleritis. Ophthalmologic treatments such were started, but the eye symptoms did not improve. In June 2019, although her RA was in low-disease activity, with the hope of improving the eye symptoms. The eye symptoms markedly improved after increasing the dose of GLM. [Clinical significance] Scleritis is commonly associated with persistent pain, and it often takes a long time to resolve. The present case suggests that the use or increased dose of GLM can improve not only joint symptoms but also eye symptoms.

P3-207

A Case of cutaneous polyarteritis nodos and multiple gastrointestinal ulceration associated with myelodysplastic syndromes

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Conflict of interest: None

Patient is an 82-year-old man with anorexia and weight loss appearing two years prior. Serum CRP elevation and FDG accumulation in the spine were observed. One year prior, purpura of bilateral lower limbs appeared. Vasculitis was not revealed by skin biopsy, but myelodysplastic syndromes (MDS) was diagnosed by bone marrow biopsy. He had no chromosomal abnormalities, including trisomy 8, and was in the low-risk group of IPSS-R classification. Serum CRP elevation persisted, prompting hospitalization. Skin biopsy from the purpura was performed again, revealing small- and medium-vessel vasculitis. We diagnosed with cutaneous polyarteritis nodosa. In addition, multiple punched-out ulcers were found in the stomach, terminal ileum, and colon, but the cause was not identified. His condition improved upon PSL initiation at 30 mg/day, however he subsequently developed intestinal perforation. It has been reported that MDS is accompanied by inflammatory and autoimmune disease (IAD), including vasculitis and Behçet's-like syndrome, but that some cases do not satisfy the diagnostic criteria and cannot be classified into specific diseases. In this case, multiple gastrointestinal ulceration may be IAD-associated. Thus, such unknown inflammation in patients with MDS may be a complication of IAD.

P3-208

A case of rheumatoid arthritis complicated with AIH-PBC overlap with clinical remission and improvement of liver dysfunction with sarilumab

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Conflict of interest: None

A 50 female has been suffered from polyarthralgia and chronic liver damage three years before introduction of SAR. The patient was diagnosed with RA with Sjogren syndrome. Liver biopsy was performed. The patient was diagnosed with PBC-AIH overlap and started treatment with PSL 15 mg and ursodeoxycholic acid (UDCA). AST 38U / L, ALT 34 U / L, ALP 1128 U / L, γGTP 298U / L, IgG 1985mg / dl, IgM 345mg / dl, ANA160 times, SSA +, AMA +, anti-SMA+. SAR was administered because of HDA. tender 7, swollen 18, CRP 7.8mg / dl, ESR 56mm / h, MMP-3 1555 ng / ml, ALP555 U / L, γGTP103 U / L, (T-Vs) 77 (%).3 months later: 0 tender, 3 swollen, CRP 0 mg / dl, ESR 4 mm / h, MMP-3 190 ng / ml, ALP 283 U / L, γGTP 57 U / L, T-Vs 8.6 (%) Clinical remission was obtained by administering SAR to highly disease active RA with PBC-AIH overlap. The combined PBC-AIH overlap syndrome also resulted in normalization of ALP and γGTP. For treatment of AIH, PSL and AZA are used, and for treatment of PBC, UDCA and fibrate are used. Recently, there are reports of the effectiveness of immunosuppressive drugs such as MMF. There are reports that immunological abnormalities in PBC are elevated cytokines such as IL-6, and inflammation is involved in the pathology of PBC, including other literature.

P3-209

Two cases of iliopsoas bursitis mimicking iliopsoas muscle abscess

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Conflict of interest: None

[casse 1] A 42-year-old man with SLE in clinical remission presented with a one-month history of left hip pain. MRI revealed a multilocular cystic mass of approximately 5 cm diameter extending anteromedially from the hip on fat-suppressed T2WI, indicating iliopsoas bursitis. CT-guided needle aspiration of the iliopsoas bursa demonstrated macrophage-enriched yellowish fluid with no deposition of crystals and no growth of fluid culture. The patient was clinically diagnosed with non-infective iliopsoas bursitis mimicking iliopsoas abscess. [casse 2] A 93-year-old woman with ANCA-associated vasculitis in clinical remission presented with one week lasting fever. MRI revealed a multilocular cystic mass of approximately 4 cm diameter extending anteromedially from the hip on fat-suppressed T2WI, indicating iliopsoas bursitis. US-guided needle aspiration of the iliopsoas bursa demonstrated yellowish fluid with no deposition of crystals and no growth of fluid culture. The patient was clinically diagnosed with non-infective iliopsoas bursitis mimicking iliopsoas abscess. [Conclusions] The present cases should remind readers to consider extensive iliopsoas bursitis as a cause of iliopsoas muscle mass with hip pain.

P3-210

The two cases diagnosed as EBV-positive mucocutaneous ulcer (EBVMCU) during the treatment of methotrexate

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Conflict of interest: None

EBVMCU is a recently proposed lymphoproliferative disorder associated with iatrogenic immunosuppression or age-related immunosenescence in the revised 2016 WHO classification. EBVMCU cases clinically present isolated, well-circumscribed mucosal or cutaneous ulcers located in the oral cavity, skin and intestine without systemic symptoms. Histologically, it is characterized by the proliferation of EBV-positive polymorphous atypical lymphocytes. Most cases have a benign course and respond well to conservative management, such as reduction of immunosuppressants. Therefore, we should keep in mind of this rare disorder during immunosuppressive therapies. The first case is a 79-year-old man who was diagnosed as rheumatoid arthritis 12 years before and had been treated with weekly 10mg of MTX and monthly golimumab. He had a painful gingival ulcer on his left upper jaw. The second case was 56-year-old woman who was diagnosed as dermatomyositis 7 years before, and took weekly 12mg of MTX and daily 9mg of PSL. She suffered from persistent ulcer in her right oral cavity. Biopsies from these lesions histologically revealed the proliferation of EBV-positive atypical lymphocytes, and they were diagnosed as EBVMCU. Both conditions had improved spontaneously after discontinuation of MTX.

P3-211

An observational study on the risk of and prognosis following the development of avascular necrosis of the hip among patients with collagen vascular diseases treated with high-dose glucocorticoids

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Conflict of interest: None

[Objective] To clarify the risk of and prognosis after the development of avascular necrosis (AVN) of the hip among patients with various collagen vascular diseases (CVDs) who received treatment with high-dose glucocorticoids (HDGC). [Methods] HDGC was defined as such if steroids ≧ 30 mg prednisolone equivalent per day were given for ≧2 weeks, and

medical records of the CVD patients admitted in 2002-2011 who had received HDGC were reviewed in details. [Results] Thirty-two out of the HDGC-treated 281 patients in total were diagnosed with AVN the median (range) of 3.9 (0.7-13.6) years after HDGC introduction. The AVN-afflicted patients comprised of 5 males and 27 females included 16 patients with SLE, 4 microscopic polyangiitis (MPA), 4 Still's disease, 3 inflammatory muscle disease, 2 small-sized vasculitis, 2 Sjogren syndrome, and 1 Behcet's disease; 13 among them received ≧2 HDGCs and 14 received pulsed steroid. The ten-year estimated risk of AVN ranged from 8.1% in Behcet's to 37.8% in MPA. Unilateral damage occurred in 14 while 18 had both sides damaged, and 24 patients underwent hip replacement surgery in the end. [Conclusions] AVN occurred after HDGC in various CVDs similarly as in SLE, and was shown to be a debilitating complication of steroid treatment in the long term.

P3-212

Long-term course of steroidal femoral head necrosis, from our cohort

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Conflict of interest: None

Many patients have experienced an avascular femoral head necrosis (ANF) after high-dose steroid therapy. We experienced a case in which a strong symptom was appeared and so orthopedic procedure was considered, but then her symptom disappeared with no additional treatment several years after and the bone necrosis was improved on MRI. We will examine how many cases of natural remission are seen from our cohort created in 2012. [Objective] To clarify the long-term course of ANF associated with high doses of steroids. [Methods] This study was conducted for a case in which hip MRI was taken twice or more from a cohort of steroid mass therapy experienced in our hospital created in 2012. Diagnosis of ANF and judgment of improvement depended on radiology report. [Results] From April 2009 to December 2011, 111 cases were treated with high-dose steroids in our hospital. The primary disease included 57 cases of SLE and 23 cases of PM / DM. 74 cases received the first MRI examination. Of these, ANF was observed in 53 limbs of 32 cases. Of the cases that were ANF-positive in the first examination, 19 cases were subjected to the second MRI examination. In the second examination, 11 out of 34 limbs where ANF was present improved. [Conclusions] A significant percentage of ANF cases recovered

P3-215

A case of RA pataient infected with cytomegalovirus during treating of amyloidosis and lymphoproliferative disorder

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Conflict of interest: None

A 75-year-old woman was introduced to our hospital with abdominal pain, diarrhea and vomiting. She had been treated RA since 40y. o, and had taken MTX since 50y.o. She was detected multiple lung nodules, and admitted to previous hospital. She was diagnosed amyloidosis with biopsy of duodenum and ileocecal region. She was also suggested Oii-LPD with elevated serum levels of sIL2R. She stopped taking MTX and food, and took intravenous steroid and nutrition. Though lung nodules and inflammatory reaction improved, diarrhea and undernutrition persisted. Anti IL6 recepter antibody was administered to her. Her nutrition did not get well. Ground glass opacityof lung appearedandserum levels of βD-glucanelevated, we treated as pneumocystis pneumonia, but she died of respiratory failure. Autopsy was performed and we found that lung nodule was mostly necrosis, amyloid deposition in vessel walls of multiple organs, and also intranuclear inclusion in the erosion of stomach, small intestine and colon. We thought cytomegalovirus infection was likely to be the main cause of her death. Long-standing RA patients, even though their disease activity is already low, are high risk of amyloidosis and Oii-LPD. Early detection and treatment is important, and we also care of opportuneistic infections in such situation.

P3-216

A case of systemic juvenile idiopathic arthritis accompanied by secondary syphilis who suspected as recurrence of sJIA

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Conflict of interest: None

(Case) A 22 years old woman diagnosed as systemic juvenile idiopathic arthritis (sJIA). She has been administered with prednisolone (PSL) at 10 years old. Tocilizumab (TCZ) was added to PSL at 12 years old. After that, She had a recurrence of sJIA at 19 and 21 years old. Therefore, TCZ was stopped, cyclosporin was introduced at 21 years old, remission was obtained. However she had a intermittent fever, sustainability erythematous papule, high CRP level at 22 years old. She was initially treated with escalating dose of PSL, but this treatment did not improve her symptoms. After detailed examination, she was diagnosed as secondary syphilis and genital chlamydial infection. We administered with amoxicillin and doxycycline. Her symptoms were resolved by their antibiotic agents. (conclusions) Recently syphilis is rapidly increasing in Japan. It may mimic sJIA clinically, and delayed diagnosis can lead to serious results. We should be aware of sexually transmitted infections for the differential diagnosis of the recurrence of sJIA.

P3-217

A study of RA cases with nontuberculous mycobacterial pulmonary disease (NTM-PD) and with NTM-PD like lung disease (NTM-LLD)

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Conflict of interest: None

[Purpose] In RA with NTM-PD, there are many cases in which the use of biologics (bio) is discouraged and also in the case with NTM-LLD. We examined the clinical course of RA and pulmonary disease in these cases. [Methods] NTM-PD was diagnosed with 2 positive sputum cultures. We analyzed the clinical course of 11 RA patients with NTM-PD and 8 NTM-LLD. [Results] (1) NTM-PD. Average age: 74 years old. Average observation period: 7.9 years. Bacterial species: M. Avium 8, M. Intracellular 2, M. Abscessus 1. RA treatment before NTM-PD diagnosis: Bio5, TOF1, MTX6, TAC3, MZB1. Antibacterial agent was used for 7 cases. RA treatment after NTM-PD diagnosis: ABT2, MTX1, TAC1. Subsequent clinical course of NTM-PD: No deterioration except a M. Abscessus case. (2) NTM-LLD. Average age: 62 years. Average observation period: 7.0 years. NTM was detected once in sputum culture in 2 cases and anti-MAC antibody was positive in 2 cases. Biologic agents were used in 6 cases, image deterioration in 2 of them. [Conclusion] (1) Biologics can be used for MAC disease in combination with antibacterial treatment, but can not for M. Abscessus. (2) In case of NTM-LLD, it is necessary to carefully follow the course during biotherapy.

P3-218

A case of disseminated nocardiosis diagnosed by supraspinatus abscess that developed during the course of systemic lupus erythematosus

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Conflict of interest: None

[Case] 52 year old man. He was diagnosed with SLE at X-8 years, and started to treat with prednisolone, cyclophosphamide, rituximab, and mycophenolate mofetil. However, he repeated flares of SLE, and received dialysis from Jan. X. In September, he complained the pain of the right

shoulder, and visited our hospital. At that time, he took prednisolone 14mg, tacrolimus 1.5mg, mycophenolate mofetil 1000mg and belimumab. His right shoulder showed swelling, redness, and warmth. We punctured the abscess diagnosed by echography and MRI. Gram staining showed Gram-positive actinomycetes, and kinyoun staining showed weak acidity, so we suspected nocardia. As another finding, CT revealed a thickened cavity in the apex of the right lung. We started imipenem/cilastatin, and added incision and drainage. Lung lesions disappeared in CT on the 18th day and nocardia was detected from the culture, so we diagnosed with disseminated nocardiosis. After 4 weeks, we changed to minocycline and continued. [Consideration] Disseminated nocardiosis is the very rare, but should be considered in immunosuppressed patients. Since nocardia is resistant to conventional antibacterial drugs, it is important to estimate the causative bacteria by Gram staining, and to administer appropriate antibiotic therapy.

P3-219

The efficacy and safety of vaccination in RA patients with who are treated with corticosteroid or DMARDs: systematic review

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Conflict of interest: None

[Objective] To develop 2020 Japanese guideline for the management of RA, we conducted a systematic review for the efficacy and safety of vaccination in RA patients treated with corticosteroid or DMARDs. [Methods] Cochrane Central Register of Controlled Trials, PubMed, and Ichushi were electrically searched. [Results] We included 26 studies (RCT: 6 studies, cohort study: 20). In terms of immunogenicity for seasonal influenza vaccination, RA patients who were treated with MTX, TNFα inhibitors, tocilizumab, or tofacitinib generally have non-significant differences in seroresponse and seroprotection proportion compared with patients without. Serorepsonse and seroprotection proportion for some types of influenza, however, was decreased. Vaccination decreased the proportion of influenza, its complications, and death. As for pneumococcal vaccine, RA patients treated with MTX, TNFα inhibitors, tocilizumab, abatacept, or tofacitinib have non-significant differences in seroresponse and seroprotection proportion compared with patients without. Vaccination did not, however, decrease the proportion of infection. The safety of vaccine was not comprehensively examined. [Conclusion] Immunogenicity for vaccination was maintained in RA patients although quality of evidence was low or very low.

P3-220

Two cases of pneumonia in patients with rheumatoid arthritis during treatments of IL-6 inhibitor (Sarilumab, Tocilizumab)

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Conflict of interest: None

We experienced two cases of rheumatoid arthritis which caused pneumonia during a 14-day interval administration of IL-6 inhibitor subcutaneous injection (case 1: salilumab, case 2: tocilizumab). Though the clinical findings at the onset of pneumonia were limited to slight general fatigue and mild wet cough (no rales) in both cases, chest computed tomography revealed bronchial pneumonia in more than three lobes of lungs. The effects of IL-6 inhibitors masked other clinical findings suggesting infectious diseases, such as fever, elevation of C-reactive protein, and elevation of white blood cell count and neutrophil fraction. Both cases showed a flare-up of disease activity after cessation of IL-6 inhibitors (case 1: increased number of painful swollen joints and increased MMP-3 level, case 2: increased number of painful swollen joints). Case 1 resumed salilumab 5 weeks after the last dose of salilumab, and Case 2 resumed tocilizumab 4 weeks after the last dose of tocilizumab. As is well known, IL-6 inhibitors mask the signs of infectious diseases, such as clinical symptoms and increased inflammatory response, special care must be taken during routine treatment of RA. These cases warned the importance of examination of internal medicine.

P3-221

A case of dermatomyositis with VZV myelitis during treatment

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Conflict of interest: None

[Case] A 60-year-old male. He became aware of dullness of the lower legs and visited our hospital because of decreased muscle strength of the lower leg. He was diagnosed with dermatomyositis and started treatment with corticosteroids. CPK gradually decreased and skin and muscle symptoms improved. However then he complained of difficulty swallowing and became difficult to ingest. Head MRI was performed because of dysphagia, dysarthria and abnormal facial perception. A high intensity area was detected outside the right medulla, and a new cerebral infarction with lateral medullary syndrome was suspected. Then blisters appeared from the right cheek to the auricle, he was diagnosed with shingles in the V2 region of the trigeminal nerve. Valacyclovir was administered for 10 days. When cervical spinal cord MRI was additionally performed, a long lesion up to the C2 level was found on the right dorsal side of the medulla, suggesting myelitis due to VZV. He was transferred to the K University Hospital. Swallowing function training was performed, but no improvement was observed. [Discussion] Herpes zoster during corticosteroid treatment is often experienced, but few cases have myelitis. Early detection and antiviral treatment were important. We report the subsequent progress with literature reviews.

P3-222

One patient whom meningoencephalitis and a brain abscess by Listeria monocytogenes developed in during hospitalizing of the relapsing polychondritis

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Conflict of interest: None

[Case] A 79-year-old man presented with conjunctivitis, auricular cartilage swelling, an airway lesion, and RP was diagnosed by an auricular cartilage biopsy. The activity was ameliorated by 60 mg of prednisolone (PSL) and methotrexate 8 mg/week, but he suddenly developed fever, vomiting, convulsions and a persistent disturbance of consciousness (GCS E1V1M1) in PSL40mg, and was on an artificial ventilator. CSF showed increased cell number and the bacterial culture was negative, but L. monocytogenes was detected in blood cultures and had a diagnosis of Listeria monocytogenes meningoencephalitis. Furthermore, a brain abscess was detected in brain MRI at his left lateral ventricle. The state of consciousness was gradually improved by ABPC (eight weeks) and GM (two weeks) administration and he recovered to the degree that communication and a dietary intake were possible. [Discussion] The prognosis of meningoencephalitis, the brain abscess by L. monocytogenes is poor. When sudden fever, disturbance of consciousness, suggestive of meningitis were seen in patients with CTD during immunosuppressive therapy, L. monocytogenes infection should be considered.

P3-223

A case of pneumocystis pneumonia (PCP) causing alveolar hemorrhage in the course of treatment for Microscopic polyangiitis (MPA)

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Conflict of interest: None

[Case] 73-year-old woman. Interstitial pneumonia (IP), arthralgia, and acute kidney injury appeared in July, X. MPO-ANCA was positive (≧300IU/ml), and renal biopsy showed crescent formation. She was diagnosed as MPA and started steroid pulse therapy. She improved after receiving steroid therapy and intravenous cyclophosphamide therapy (IVCY). When she got hospitalized to do fourth IVCY, ground-glass opacity (GGO) appeared in both lung fields. PCP was suspected, but β-D glucan was not

so high (15 pg/ml). AZM was started in consideration of atypical pneumonia. Bronchoscopy revealed alveolar hemorrhage, and pulmonary inflammation and bacterial infection were suspected. ABPC/SBT was started, and the dose of PSL was increased to 40mg. On the 3rd hospital day, β-D glucan had risen to 33.91 pg/ml. PCP was strongly suspected, and atovaquone was started. She was diagnosed as PCP, because there was no increase in MPO-ANCA, no causative bacteria were detected in sputum culture, and Carinii-PCR was positive. When the effect of atovaquone was insufficient, she changed to sulfamethoxazole/trimethoprim and turned into herself. [Discussion and Clinical Significance] There are few reports of PCP with alveolar hemorrhage, and this case needs discrimination.

P3-224

Implants preservation after debridement for infected TKA with autoimmune disease: two case reports

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Conflict of interest: None

Two stage revision surgery is the common strategy for artificial joint infection with autoimmune disease. We experienced two cases which we could preserve implants after debridement for infected total knee arthroplasty (TKA). [Case 1] 79 year old female with Sjogren's syndrome (SS) who took right TKA 4 years ago. She was brought to the ER complaining of right knee pain. Her BP dropped on day 2 of hospitalization. We suspect implant infection after TKA and performed arthroscopic debridement on the same day. E. coli was identified from synovial fluid culture. Administration of SBT/ABPC lead to negative CRP on day 58 of hospitalization. [Case 2] 83 year old female with SS and rheumatoid arthritis who took left TKA 12 years ago. She came to outpatient office complaining of left knee pain. MRSA was identified from synovial fluid. We performed open debridement and exchanged polyethylene insert. Administration of LZD and then DAP lead to CRP 0.69mg/dL, which was the same level as pre infection. Recurrence of infection has not occurred after quitting antibiotics in both cases. [Clinical meaning] We try to preserve implants for cases without loosening of that. Debridement and administration of antibiotics from the early phase would improve preservation rate of TKA implants after infection.

P3-225

The effectiveness of hydro release for patients with rheumatoid disease

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Conflict of interest: None

[Objective] Hydro release is an interfacial or perineural injection treatment, and has been increasingly used as a novel treatment for musculoskeletal pain, including neck and shoulder pain, and low back pain. The aim of this study was to assess the efficacy of hydro release for musculoskeletal pain in patients with rheumatic diseases. [Methods] We retrospectively studied patients with rheumatic diseases who received hydro release at Tama-Nambu Chiki Hospital. A mixture of normal saline (10ml) and lidocaine 1% (1ml) was injected with ultrasound guidance. [Results] Between May and October 2019, 52 patients (41 RA, six PMR, two SLE, two RS3PE, one SAPHO syndrome, one SSc and one SjS) received 142 hydro release (49 knees, 48 shoulders, 39 low back and six others). The numerical rating scales before treatment and at the next visit were as follows: 6.22 and 3.21 in knees ($p<0.05$),6.83 and 4.90 in shoulders ($p<0.05$), 7.95 and 4.0±3.73 ($p<0.05$) in low back, and 6.5 and 3.17 in others ($p=0.09$). Two cases (1.4%) needed corticosteroid injection. [Conclusions] Hydro release is effective in patients with rheumatic diseases. This novel treatment and corticosteroid injection should be properly used in dependence on characteristics of pains.

P3-226

Analysis of blood glucose fluctuation of glucocorticoid induced diabetes using CGMS

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Conflict of interest: None

[Objective] We evaluated circadian blood glucose fluctuations examined by CGMS when using prednisolone (PSL). [Methods] Patients who took PSL from January 10, 2018 to March 31, 2019 were included. [Results] There were 19 cases, of which 7 were GID (glucocorticoid induced diabetes), and 12 were non-GID. GID cases had significantly higher pre-treatment blood glucose levels and HbA1c and PSL doses. Mean blood glucose levels and estimated HbA1c shown by CGMS were 103 ± 4 mg / dL, 5.2 ± 0.1% for non-GID cases, 137 ± 5 mg / dL, 6.4 ± 0.2% for GID cases ($p<0.01$). Hypoglycemia tends to be more common in non-GID cases. The blood glucose waveform can be classified into three types. 1: monophasic waveform after lunch. 2: a biphasic waveform showing higher blood glucose after lunch than after dinner. 3: A stepped waveform in which blood sugar does not decrease by the next meal. All monophasic waveforms were non-GID, and all GID cases were stepped waveforms. The blood glucose peak was either 1-2 hours after lunch (7 hours after internal use, n = 8) or 1 hour after dinner (11 hours after internal use, n = 10). The blood glucose level increases from the day of internal use. [Conclusions] When using PSL, there are three types of blood glucose waveforms. GID cases show a stepped waveform.

P3-227

The effect of prophylactic dose of trimethoprim on serum creatinine in Japanese patients with connective tissue diseases

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Conflict of interest: None

[Objective] We conducted this study to evaluate the effect of prophylactic dose of trimethoprim (TMP) in patients with connective tissue diseases (CTD). [Methods] We extracted all the cases with CTD, treated with low dose TMP from 2004 to 2018. Acute kidney injury due to other cause were excluded. Retrospective medical chart review was performed to collect following data for 12 weeks; baseline patient characteristics, serum creatinine (SCr), creatinine clearance (CCr), urine test, SCr elevation value after initiation of TMP. We examined the factors that have affected SCr elevation using single and multiple regression analysis with variables as follows; baseline CCr, Dose of TMP, NSAIDS, Antihypertensive agents, diuretics, diabetes mellitus. [Results] 273 cases (female; n=186, mean age; 56±18 y.o. including as follows; RA n=78, SLE n=76, Vasculitis n=39, PMR n=29, SSc n=32, PM/DM n=10, MCTD n=5, others n=56) were included. Mean of baseline creatinine level was 0.67mg/dL. Mean dose of TMP was 104±32mg/day. Multiple regression analysis showed tendency to get SCr elevated if baseline CCr is low. 5 cases (2%) had creatinine elevation more than 0.3 mg/dL. [Conclusions] Low dose TMP rarely shows remarkable elevation of creatinine. We may consider other causes if SCr is elevated more than 0.3 mg/dl.

P3-228

Consideration of the relationship between the disease state and blood IL-6 / VEGF levels after the start of tocilizumab in a patient with Sjogren's syndrome / dermatomyositis complications with TAFRO syndrome

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Conflict of interest: None

A 51-year-old woman. Currently visiting our department for Sjogren's syndrome and dermatomyositis. Hospitalized for cough, fever, general malaise. Massive pleural effusion and ascites appeared several days after admission. A marked increase in hepatobiliary enzymes and thrombocytopenia were also observed. There was a tendency to improve the disease once due to strengthening of immunosuppressive treatment. However, thereafter, pleural effusion and ascites tended to increase again. The existence of a condition similar to TAFRO syndrome was considered. While IL-6 in blood was slightly increased to 5 pg / ml, IL-6 in pleural effusion was at a significantly high concentration of 5890 pg / ml. Periodic administration of tocilizumab showed decreased pleural effusion and ascites, improved general edema tendency, and recovery of platelet count. Blood IL-6 and VEGF levels showed an increasing trend even after the start of tocilizumab administration, but decreased when the general condition stabilized for a long time. It was suggested that blood IL-6 / VEGF concentration is unlikely to be an indicator of disease state in the short term, but can be an indicator of disease state in the long term in TAFRO syndrome-like pathology.

P3-229

Clinical features of collagen disease cases that required emergency hospitalization due to unexpected steroid discontinuation

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Conflict of interest: None

[Background] We diagnosed clinical condition with adrenal insufficiency symptoms as steroid withdrawal syndrome by having been in a condition of decessation of steroid from state of persistent steroid use suddenly. In recent years, due to aging and a rise in single rate, there are many opportunities to experience cases requiring hospitalization due to unexpected steroid discontinuation. [Method] We retrospectively examined cases requiring hospitalization due to unexpected steroid discontinuation from 2007 to 2019. [Results] There were 6 patients who required hospitalization because of discontinuation of steroids. All patients had not been measured ACTH but were clinically diagnosed with steroid withdrawal syndrome. Average age was 82 ± 4.1 years, 3 males and 3 females. Collagen disease were RA in 3 patients, SLE in 1 patient, and GPA in 2 patients. Reasons for discontinuation were 6 adherence reductions, 4 poor appetites, and 1 pneumonia. Average steroid dose before discontinuation was 8.2 ± 1.9 mg. Elevated CRP was observed in all. Symptoms improved by steroid replacement. [Conclusion] Patients who presented with discontinuation of steroid were elderly. We considered that increase in single rate due to aging and nuclear families was one of reasons for decrease in drug adherence.

P3-230

Clinical Characteristis of 10 Cases of Hereditary Angioedema in our hospital

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Conflict of interest: None

[Objective] Hereditary angioedema causes repeated edema of the skin, gastrointestinal tracts, and upper respiratory tract. If laryngeal edema is severe, it may be fatal. Tranexamic acid are used as prevention, and tranexamic acid and C1 inactivator are administered for the treatment. Icatibant is approved in 2018, and the administration by the self-injection becomes possible. In order to determine in which cases it is desirable to propose icatibant, we examined the characteritics of hereditary angioedema in our hospital. [Methods] On 8 cases in our hospital in point of time in October, 2019, symptoms, fit frequency, preventive medication, administration frequency of C1 inactivator, etc. were examined retrospectively. [Results] The male to female ratio was 1: 1, and the mean age was 48 years (26 -78 years old). Type III was observed in 1 patient. The symptoms were abdominal pain in 6 cases, peripheral swelling in 6 cases, and laryngeal edema in 4 cases. C1 inactivator was used in 2 cases since October, 2018. It was used for abdominal pain, and for laryngeal edema. In case 1, the preventive medication was not used. The case 2 was under the tranexamic acid increase. [Conclusions] The introduction of the icatibant seems to be fundamentally desirable in the multiple use of the C1 inactivator.

P3-231

Rituximab for severe thrombotic thrombocytopenic purpura which plasma exchange and steroid treatment are not enough effective

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Conflict of interest: None

[Back ground] Thrombotic thrombocytopenic purpura (TTP) is one of the severe hematologic disease, in which thrombus are made in systemic microvessels. ADAMTS13 breaks von Willebrand factor specifically. In aquired TTP, ADAMTS13 inhibitor supressed ADAMTS13 activation. Some reports have showed rituximab (RTX) supressed its inhibitor production and treat with TTP. [Case] Case1: A healthy 54-year-old woman had peripheral purpura and oral bleeding. Labo data showed hemolytic anemia, thrombocytopenia, low ADAMTS13 activity and high ADAMTS13 inhibitor, so we diagnosed aquired TTP. We start plasma exchange (PE) and steroid treatment, but neurological symptoms appeared and got worse. Though We infused rituximab (RTX) for her, her TTP was uncontrollable and convulsions are appeared. Two days later, she died. Case 2: A healthy 43-year-old woman had also peripheral purpura and nausea. As is case1, she was diagnosed TTP. As her neurological symptoms got worse, PE and steroid treatment was started. after that thrombocyte count increased and her symptoms dissapeared. Two weeks later she was discharged. [Conclusions] We can use RTX from August 2019 in Japan. We experienced two cases of TTP treated by not only PE and steroid but also RTX. We consider the adaptation and effectiveness of RTX for TTP.

P3-232

Diffuse alveolar haemorrhage in a case of the rheumatoid arthritis

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Conflict of interest: None

[case] 72 years old, male [chief complaint] dyspnea [clinical history] Rheumatoid arthritis developed at 62 years old and received medical treatment in PSL2.5mg and MTX14mg. Activity aggravated it when treatment of the articular rheumatism was discontinued in the end of August, 2019, and organized pneumonia developed. We started treatment in TOF10mg from September 25. Activity of the rheumatoid arthritis decreased and discharged hospiptal. After the discharge, dyspnea appear suddenly and administration again. [clinical course] Antimicrobial treatment was performed from the first day of illness. However, lacked in the reactiveness of the antimicrobial agent, we started administration of mPSL500mg as relapse of the organized pneumonia for three days from the fifth day of illness. We intubated it on the sixth day of illness and became the respirator management. By bronchoscopy, diffuse alveolar haemorrhage was detected and we gave IVCY500mg on the ninth day and performed a plasma exchange for three days from the tenth day of illness. We extubated on the 17th day of illness and passes without a recurrence. [discussion] We experienced the pulmonary alveolar haemorrhage that occurred in a case of the rheumatoid arthritis, report it with discussion from literatures.

P3-233

A case with eosinophilic granulomatosis with polyangiitis and breast cancer during the therapy for rheumatoid arthritis

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Conflict of interest: None

A woman came to our hospital with polyarthralgia and joint swelling. She had got bronchial asthma around forty years old and sinusitis at fifty years old. She was diagnosed with rheumatoid arthritis and treated with methotrexate, added with iguratimod, tacrolimus, infliximab sequentially, and she was getting better. As arthralgia appeared again, infliximab was changed to tocilizumab and her condition of the disease improved and iguratimod was discontinued. About two years later, at the age of fifty five her lower limbs became numb and swelling of upper limbs, face edema and urticaria appeared. Marked eosinophilia and slight drop foot were observed, and nerve conduction study suggested mononeuritis multiplex. In conjunction with bronchial asthma, it was considered that she got eosinophilic granulomatosis with polyangiitis. In addition computerized tomography showed tumor in right mammary gland and she was diagnosed with breast cancer. Methotrexate, tacrolimus and infliximab were discontinued, prednisolone was added with 20mg per day and treatment with intravenous immunoglobulin was performed. Symptoms such as swelling of upper limbs disappeared, numbness improved and eosinophil count became normal. After reduction of breast cancer with chemotherapy, total mastectomy was performed.

P3-234

A female case of tattoo-associated uveitis and sarcoidosis like reaction

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Conflict of interest: None

A 31-year-old Japanese female presented for recurrent fever up, general fatigue, and right femoral lymphadenopathy, since she started part-time works one month ago. Workup included infection and inflammation were negative, and computed tomography demonstrated enlargement of right femoral and para-aortic lymph nodes. Lymph node biopsy showed reactive histiocytosis and phagocyte the pigment granule, and excluded malignant lymphoma. Her tattoos in thigh and back were performed ten years ago, and became nodular papules and were accompanied by sensations of burning skin, that coincident with systemic symptoms. Four-month later, bilateral eye pain nonresponsive to topical corticosteroids was getting worth, so uveitis and optic nerves edema aggravated. Oral prednisolone 20mg was started, however, uveitis flared up by slight dose reduction of prednisolone. Thus, tattoo excision for the radical cure of systemic sarcoidal reaction was operated, resulting in dramatic improvement. Pathological findings showed non-caseating granulomas and multinucleated giant cells within black tattoo pigment. We diagnosed tattoo-associated granulomas with uveitis (TAGU). Tattooing is a popular cosmetic practice and the technique has been adopted, though TAGU would become more frequent regardless of gender.

P3-235

A case of histiocytic sarcoma diagnosed with various collagen disease-like symptoms

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Conflict of interest: None

68 years old male [c. c] Joint pain [PMH] Peritoneal dialysis was confirmed in 2006, and hemodialysis in 2014. [SH] Smoking: 20 bottles/day (16 years old to present), Alchohol: Beer 350ml 2 bottles/day [FH] Mother: Cerebral Infarction, Father: Cerebral Hemorrhage [HPI] From around X-years, he was aware of wrist joint pain and showed a slight increase in inflammatory response. Later, pain was observed in many joints, and the inflammatory response was also worsening. Swelling and pain were observed in many joints, synovitis and adhesion inflammation were observed in joint echo, and multiple nodules in the liver/spleen were detected by CT when he was hospitalized. [Physical] Enlargement of both hands, extensor lateral erythema, left palmar nodule, forehead nodule [Blood test] Increase in white blood cells and CRP [Clinical course] Nodular erythema was biopsied, but it was not diagnosed only by infiltration of inflammatory cells-Follow-up CT showed a new nodule shadow in the lung, biopsy of subcutaneous nodule, a part of histiocytic infiltration was observed, and noncaseating granuloma was not observed. He was diagnosed with histiocytic sarcoma, and started chemotherapy. [Discussion] This is a valuable case of arthritis that was referred to our department and confirmed a blood tumor.

P3-236

Two cases of connective tissue disease related interstitial pneumonia undergoing brain death lung transplantation

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Conflict of interest: None

[Case 1] A 54-year-old female. NSIP pattern of interstitial pneumonia (IP) was pointed out twelve years ago. MPO-ANCA was positive, and a surgical lung biopsy showed that IP was associated with vasculitis. After treatment with steroids and immunosuppressants was induced, lung fibrosis progressed year by year. An antifibrotic drug and home oxygen therapy were added four years ago, and she was registered for the Japan Organ Transplant Network. Two years later, bilateral lung transplantation was performed and respiratory failure improved. [Case 2] A 58-year-old male. NSIP pattern of IP was pointed out six years ago, and steroids and immunosuppressants were started. Three years later, the presence anti-ARS antibody and skin biopsy revealed dermatomyositis-related IP. Despite of intensifying immunosuppressant, lung fibrosis progressed. Two years later, home oxygen therapy was added, and he was registered for the Japan Transplant Network. A right-lung transplant was performed about one year after registration, and respiratory failure improved. [Conclusions] Connective tissue disease often occurs in young people and cause IP. If IP shows a course of resistance to immunosuppressive therapy, lung transplantation should be considered as an option.

P3-237

A case of malignant lymphoma with pancytopenia that was diagnosed Sjögren's syndrome and Evans syndrome before treatment

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Conflict of interest: None

Introduction: Malignant lymphoma is a part of non-Hodgkin lymphoma (NHL) which consists of a diverse group of malignant neoplasms. Case: A 72-year-old female admitted to her family doctor for weakness. LDH and ALP were elevated. She admitted to the general hospital after 3 months. She had anemia, thrombocytopenia, high soluble IL-2 receptor. Hepato-spleenomegaly was detected on CT scan. Bone mawwow biopsy was undergo and the result was not specific. Anti nuclear antibody, anti SS-A /Ro antibody were positive. The amount of haptoglobin was decreased and PAIgG was positive. Anemia and thrombocytopenia was progressing. So she was diagnosed with Sjögren's syndrome and Evans syndrome. Glucocorticoids therapy was started. Because her symptoms didn't response to glucocorticoids treatment for one months, she were transferred to our hospital. She had skin rash on her face, chest, abdomen and extremities. Skin biopsy and bone marrow re-bipopsy was done. Skin biopsy showed the proliferation of lymphoma cells within the blood vessels. Bone marrow biopsy this time showed the the large size tumor cells which was CD20 (+). She was diagnosed with malignant lymphoma. Chemotherapy was planned. Conclusion: Patients with pancytopenia should be aware malignant lymphoma.

P3-238

A Case of Renal-limited Vasculitis and Autoimmune Autonomic Ganglionopathy Successfully Treated by Glucocorticoid, Intravenous Immunoglobulin, and Rituximab

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Conflict of interest: None

Case presentation: A 54-year-old man admitted to our hospital because of orthostatic hypotension last for over 10 years. He developed worsened constipation, dyshidrosis, and erectile dysfunction. On admission, laboratory findings revealed elevated CRP, creatinine, and proteinuria. MPO-ANCA was positive in the immunological test. Afterwards we knew anti-gAChR antibody, that leads to a diagnosis of autoimmune autonomic ganglionopathy (AAG), was positive at that time. Result of renal biopsy showed pauci-immune crescentic glomerulonephritis. There was no evidence of organopathies except renal dysfunction that we diagnosed him with renal-limited vasculitis (RLV). We administered predonisolone (PSL) at dose of 1mg/kg/day. Intravenous immunoglobulin (IVIG) 400mg/kg/day for five days and weekly rituximab at a dose of 375mg/m^2 for four times were added. After this treatment, proteinuria decreased. Results of 123-I-MIBG myocardial scintigraphy and the coefficients of variation of R-R intervals improved before and after the therapy. We thought that treatment for RLV was effective for AAG too. Discussion: Although a standard treatment strategy of AAG has not been established, combination therapy as a treatment for RLV was successful. This therapy may be effective option for treating AAG.

P3-240

A case of systemic lupus erythematosus with severe hepatic dysfunction induced by ibandronic acid

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Conflict of interest: None

[Background] Hepatic dysfunction due to ibandronic acid (IBN) is occasionally observed (less than 1% on the package insert), but a few cases are reported to discontinuation. We report a severe hepatic dysfunction caused by IBN. [Case] A 51-year-old female. On the first hospital day (HD), she was transferred to our department for treatment with SLE, CNS lupus, DM, and SSc. At that time, hepatic dysfunction due to fatty liver (AST 29U/L, ALT 55U/L) was observed. 30th HD, glucocorticoid-induced osteoporosis treatment was changed to IBN on 58th HD. AST and ALT levels were raised after the second administration of IBN (AST 45U/L, ALT 125U/L →AST 165U/L, ALT 297U/L). On 71st HD, AST and ALT were elevated to 250U/L and 712U/L, respectively. No viral hepatitis was observed, autoantibodies related to AIH/PBC were negative, and abdominal echo showed a fatty liver only. Medications other than IBN that may cause hepatic dysfunction were discontinued, but AST and ALT did not improve. As a result, hepatic dysfunction due to IBN was suspected, and administration of glycyrrhizin was started. On 73rd HD, AST and ALT were decreased (AST 124U/L, ALT 473U/L) and improved to the standard values (AST 14U/L, ALT 22U/L) on 164th HD. [Clinical significance] IBN rarely cause severe hepatic dysfunction.

P3-242

Mid-term results of the S-ROM® femoral prosthesis after previous intertrochanteric valgus osteotomy

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Conflict of interest: None

(Objective) We report mid-term results using S-ROM® (Depuy) in THA after previous intertrochanteric valgus osteotomy. (Subjects and Methods) We studied 16 joints in 14 subjects. The mean follow-up period after THA was 8y. The mean age at THA was 57 y. Our clinical evaluation included JOAscore, and radiological findings. (Results) Mean JOA score was 53 in the preoperative period and 80-point at follow up evaluation. We find stress shielding graded 3-4 degree in 7 joints (44%). In three joints (19%), the alignment of the stem changed from neutral to varus alignment. (Conclusion) S-ROM has good clinical results, existing the alignment of the stem changed in some cases.

P3-243

Stabilization of total elbow arthroplasty for unstable elbows in rheumatoid arthritis

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Conflict of interest: None

[Objective] Total elbow arthroplasty (TEA) is an effective treatment for elbow joint destruction by rheumatoid arthritis (RA). Bone defect in RA and unstable elbow is a dood indication for TEA, but postoperative elbow joint instability and implant looseness become ploblems. Therefore, we report the use of animplat that is one size larger than the conventional size in order to prevent initial fixation and loosening of the implant. [Methods] We mesured Patient-Related Elbow Evaluation (PREE), Mayo Elbow Performance Score (MEPS), and the elbow flexion angle of 4 patients who used TEA after January 2019 and used an implant that is one size larger than the conventional size. [Results] Preoperative results were PREE 67±11, MEPS 65±38, flexion angle 115±23 °. The results at 3 months after surgery were PREE 23±10, MEPS 97±3, flexion angle 135±5 °. [Conclusions] In TEA for unstable elbows due to RA, the clinical results at 3 months after the surgery were improved in all cases compared to preoperative. The possibility of improving the elbow instability by using one larger size of implant was suggested.

P3-244

A case report of Ankylosing spondylitis patient performed with pedicle subtraction osteotomy

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Conflict of interest: None

[Purpose] In EULAR 2016, spinal corrective osteotomy is recommended in severe cases. We report a severe Ankylosing spondylitis (AS) case whose kyphosis were corrected by the pedicle subtraction osteotomy (PSO) and achieved favorable patient satisfaction. [Case] A 37-year-old male. He has started to experience low back pain several times from 17 years old. His spinal column gradually bent forward, and he has felt persistent bilateral coxalgia from several years ago. He was referred to our department for the indication of surgical treatment after diagnosed as AS. The whole spine and the sacroiliac joints were ankylosed and showed bamboo spine, and bilateral hips showed joint space narrowing by plain radiography. He walked with flex position of hip and knee and could not look upward because of the kyphosis. For this patient, One-level lumber PSO was performed and corrected his kyphosis about 20 degrees. Three months later, his gait was obviously improved. [discussion] The correction of sagittal imbalance is reported to improve physical and psychological changes of AS. However spinal corrective osteotomies are highly invasive and reported relatively high rate of complications, therefore the surgery was required the high skilled surgeon and should be performed to limited cases.

P3-245

Bilateral snapping knee caused by systemic inflammatory disease

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Conflict of interest: None

[Case] A 43-year old male who had both knee pain. X month ago, he felt multiple joint pain. He consulted the other hospital, and diagnosis was the Sjögren' s syndrome suspected and erythermalgia. After a while, snapping phenomenon was appeared in both knees. The patient observed bilateral knee pain and snapping in the lateral patello-femoral joint with knee flexion. The rheumatoid factor, the antinuclear antibody, and the anti-SS-A antibody were positive in the blood test. The lateral synovial plica was suspected in the imaging examination. Arthroscopic surgery was performed for resection the plica. An arthroscopy revealed that hard scar-like tissue between the lateral patello-femoral joint in both knees. From the result of pathological examination, the granulation tissue with inflammatory cell infiltration and vascular hyperplasia was observed. After the operation, the snapping phenomenon and pain disappeared during flexion of both knee joints. In this case, inflammation of the knee joints was caused by an inflammatory disease, the scar tissue of the articular capsule was degenerated, and it was thought that the snapping knees were caused by impingement the patello-femoral joint. We experienced a very rare case which caused bilateral snapping knee by an inflammatory disease.

P3-246

A Case of Bil TKA with difficulty in diagnosis of EORA

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Conflict of interest: None

[Case] 76-year-old female [CC] Bilateral Knee Pain [Clinical course] First visit was 2018.1 worsening of both knee pain. Physical examination, inflammatory knee arthritis Confirmed the presence. RA check in blood test is negative, but CRP: 9.2 was high, considering other inflammatory diseases. Kenacolt intra-articular administration+PSL started to improve CRP to 3.5 but DM worsened, so PSL increase is impossible. Since both knee OA (KL: Grade III / III) originally existed, Lt TKA was performed on March 19, 2018, and the contralateral symptom was improved. However, 7.12 Rt TKA was performed because 6.12 right knee pain reworse. The postoperative course was good, but the improvement feeling was not as good as the left postoperatively, and the swelling of the knee joint also recurred. So MTX+ETN was introduced with the diagnosis of EORA, and the joint swelling is also improved now The postoperative course is also good. [Discussion] Many elderly patients who have gonalgia have OA findings. EORA cannot be confirmed. In this case, there was TKA hope first, and TKA was performed, but it was difficult to choice TKA or Bio therapy for EORA. if inflammatory changes are left unattended, it may cause loosening on implant. It is difficult to decide which treatment should be selected first.

P3-247

Pigmented villonodular synovitis was difficult to diagnose and distinguish from rheumatoid arthritis

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Conflict of interest: None

[Introduction] Pigmented villonodular synovitis (PVS) is rare benign neoplastic diseases. It is common in the knees and can be difficult to differentiate from rheumatoid arthritis (RA). It is recommended that we should diagnose using 2010 ACR / EULAR RA new classification criteria. However, it is often difficult to diagnose. This time, we experienced a case of PVS diagnosed by biopsy for arthroscopy. [Case] A 54-year-old male. There has been pain in the right knee joint about 11 years ago. The right knee joint had swelling tenderness and limited range of motion. Blood biochemistry of CRP was within the normal range, but rheumatoid factor and anti-CCP antibody levels were high. There was Geode at near the femur and tibia for Xp and CT scans, and MRI showed low signal in the T1 and T2-weighted images of the synovium and surrounding soft tissue. The ACR / EULAR scored 5 points and did not meet the standard. We performed knee arthroscopic synovial biopsy for diagnostic purposes. The pathological diagnosis was PVS. [Discussion] RA should be diagnosed appropriately. It is important to make a histological diagnosis for difficult cases.

P3-249

Patient Comprehension of Methotrexate Dosing Method and Instruction for Secure Use

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Conflict of interest: None

[Objective] Comprehension and management of side effect of MTX, including temporary cessation of MTX under side effect is essential for safety use. The aim of this study is to clarify the patient comprehension of MTX dose method searching for effective instruction. [Methods]. Of 189 RA patients who visited our department from June to November in 2019, Eighty-four patients had questionnaire asking correct dose method, temporary cessation under side effect and free answer about devices avoiding misdose of MTX. Nurses instructed correct dose method on the basis of the result of the questionnaire. Result was quantified and collected retrospectively. [Results] Proportion of patients who obtained full marks were as low as 23.8%. Over 90% of the patient correctly answered as for dose method. Around 60% correctly answered as for temporary cessation under side effect. The group with low points had significantly higher proportion of the patients who leave expert doctor to decide treatment plan. Better comprehension was obtained by repeated instruction. The devices to avoid misdose include medicine calendar, medicine case, marking calendar and alerting function in the smart phone. [Conclusions] Repeated instruction of MTX dose method can improve patient's comprehension, leading to safe treatment.

P3-250

Survey on telephone consultation for patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] Many patients with rheumatoid arthritis (RA) suffered from various problems including physical, psychological and social problems consult the hospital by telephone. The purpose of this study is to clarify the current condition of telephone consultation for RA patients. [Method] The subjects were RA patients who visited our hospital from January 1, 2018 to October 15, 2019. We conducted a retrospective survey concerning the telephone consultations. [Results] There were 127 telephone consultations from 63 patients. The average age was 66.7 ± 13.7 years, 7 males, 56 females, and the average disease duration was 15.9 ± 14.7 years. There were 13 cases related to symptoms of RA, 67 cases related to general physical condition, 14 cases related to treatment, 28 cases related to changing the consultation date and prescription, and 5 other cases. None of the patients who consulted about their general physical condition fell into a serious condition. [Conclusions] The EULAR recommendation suggests that RA patients should get consults with nurses to increase treatment satisfaction. This study suggests that the telephone consultation leads to early problem resolution and prevention of complications. The knowledge and assessment skills of nurses are essential for good phone support.

P3-251

Analysis of questionnaire about self-injection of certolizumab pegol for patients and nurses

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Conflict of interest: None

[Objectives] There are two self-injection devices of Certolizumab pegol (CZP), which one of them is syringe, and the other is auto-clicks. We investigate the effectiveness of CZP self-injection devices with questionnaire for patients and nurses. [Methods] We performed the questionnaire for 38 patients who used CZP injection and 18 nurses who instructed CZP self-injection. We evaluated satisfaction, injection pain (Visual analogue scale; VAS), merit and drawback for each device. [Results] In two devices, 87% of patients chose auto-clicks, and 57% of them changed from syringe into auto-clicks. 84% of these patients and 57% of the patients who used auto-clicks at first acquired satisfaction. The injection pain of auto-clicks (VAS=38.4) were lower than that of syringe (VAS=55). Auto-clicks was easier for nurse to instruct self-injection, and it took shorter time (20.6 minutes) to instruct it compared to syringe. On the other hand, many nurses felt the difference between real drug and demonstration device. [Conclusion] In CZP self-injection, auto-clicks acquired higher satisfaction for both patients and nurses, and it was easier to get the injection skill. Improvement of self-injection devices resulted in the elevation of satisfaction.

P3-252

The current state of drug administration route and treatment satisfaction in outpatients with rheumatoid arthritis in OMC-RMA (Osaka medical college-Rheumatic disease medical stuff association) study

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Conflict of interest: None

[Objective] To investigate the degree of treatment satisfaction and desired of drug administration routes for patients with rheumatoid arthritis in OMC-RMA study. [Methods] A total of 97 outpatients with RA in our 3-hospitals were included. The questionnaire will investigate current treatment satisfaction, desired for the route of drug administration, and their reasons. [Results] 25 males, 72 females, ages 20s-90s, Patients were treated with MTX (39.1%), Biologics (44.3%), and tsDMARDs (4.1%). 69% were satisfied, 5% were dissatisfied and 26% were neither, and patients treated with biologics were significantly more satisfied. ($p=0.011$) One of the most important factors when treating were drug effect 39%, side effects 25%, life rhythm 20%, drug price 16%. The desired route of drug administration was 64.8% for oral, 20.5% for in-hospital subcutaneous injection,10.2% for self-subcutaneous injection, and 4.5% for intravenous drip, of which 21.6% wanted to change the drug. Oral administration hope was 60% in patients who were dissatisfied with their treatment, and 90% in those who were satisfied. [Conclusion] Biologics make RA patients satisfied with their treatment. It is suggested that there is a potential for RA patients want to change to oral treatment.

P3-253

A survey on telephone consultations by patients with rheumatoid arthritis in Japan

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) often seek consultation via phone. As nurses answer patients' questions in the front-line, better understanding of patient concerns would identify educational needs of nurses. This study aims to clarify and categorize telephone call details of RA patients. [Methods] Call data was collected from 2017 medical records in 2 hospitals and 2 clinics and categorized. [Results] 188 patients called, totaling 328 calls with 341 questions. 58 were symptoms unrelated to RA [32 requiring physician consultation [PC]; 47 concerning infection and appointment changes [PC: 39, 32 respectively]; 41 deterioration of RA symptoms [PC: 22]; 39 medication concerns [PC: 25]; 22 side effects [PC: 12]; 20 self-injection [PC: 17]. Calls unrelated to RA included stomach pain, high blood pressure, anxiety, etc. Respiratory infections were the most frequent [26 calls] among infections. Regarding medication, patients asked if they should suspend. Self-injection calls were divided into 2 patterns; about injection kit or skill, and asking if they should postpone injection. [Conclusions] Nurses were consulted about various kinds of issues, most of them were referred to rheumatologists. This result will be useful to consider the necessary support for nurses in Japan.

P3-254

Survey on patient's wishes; Route of Administration and Frequency of Biologics in Rheumatoid Arthritis ~from OMC-RMA~

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Conflict of interest: None

[Objective] To clarify the patient's wishes regarding the frequency of administration, self-injection, and injection at hospitals of biologics in RA. [Methods] In 2019, a questionnaire survey was conducted on RA patients managed by OMC-RMA (Osaka Medical College Rheumatic disease Medical stuff Association). The survey items were related to the frequency and method of administration, and lifestyle of self-injection. [Results] The subjects were 97 (25 males, 72 females), average age group 60s, average disease duration was 3-5 years. Employment status was 11% employees, 4% self-employment, 12% part-time workers, 71% unemployed, and 1% leave. Patients receiving bDMARDs: Subcutaneous ETN 3, ADA 4, GLM 11, TCZ 5, SARI 2, ABT 6, Infusion IFX 3, TCZ 3, ABT 6. Favorite method of administration was infusion 16.2%, self-injection 29.7%, and hospital subcutaneous injection 54.1%. The frequency of administration was 8.2% once a week, 21.9% once every 2 weeks, and 69.9% once every 4 weeks. The importance of self-injection is ease of administration 26%, treatment costs 21.1%, fewer doses 20.3%, less pain 13%, length of visit interval 7.3%, refrigerator space 5.7%, take-out ease 4.1%. [Conclusions] Subcutaneous injection in hospitals, and the longer administration interval, was desired.

P3-255

Evaluation of Difference in Role of The Certified Nurse by Japan Rheumatism Foundation between Nurse Administrator

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Conflict of interest: None

[Objective] Status of The Certified Nurse was assessed in nationwide to investigate whether they were able to practice RA treatment with motivation for their work, and examined the difference in recognition between The Certified Nurse and Nurse Administrator. [Methods] The Certified Nurse and Nurse Administrator were subjects for survey research were

developed by 42 sub-items from EULAR recommendations on the role of nurses in the management of chronic inflammatory arthritis. [Results] The subjects of the analysis were 303 The Certified Nurse and 107 Nurse Administrator. There is a significant difference ($p < 0.0001$) in 35 items among 42 items in the way The Certified Nurse and nursing managers perceive, indicating that Nurse Administrator had little understanding of the role of The Certified Nurse. When the role of The Certified Nurse and if The Certified Nurse were assigned to where they are desired to be assigned or not, there were significant differences in 42 small items and 26 small items. [Conclusions] There is a significant difference in the role awareness, not sharing common perception between of The Certified Nurse and Nurse Administrator, indicating that rheumatic nurses are not practically fulfilling their role.

P3-256

Rheumatoid care nurse and registered sonographer who was involved in treatment as a rheumatoid arthritis patient with schizophrenia

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Conflict of interest: None

[Case] 40 years old woman [Medical history] In July 2014, the patient was diagnosed with RA, treated with a combination of MTX, IGU, and ABT. After achieving remission, ABT was stopped and the disease was stable. However, since 2016, the drug has been on the decline and arthritis has relapsed. When she visited our hospital, mental symptoms were unstable, She was referred to a rheumatic care nurse outpatient clinic. J [Clinical course] I listened to the current living environment and tried to improve internal adherence adherence, but my mental condition worsened again in October 2018. There was a wave of psychiatric symptoms, such as a whole body fracture caused by jumping. Joint echo was continuously performed in addition to joint symptoms and disease evaluation. When each disease activity parameter at each visit was compared with the echo test results, there was a large variation in Pt VAS, suggesting the effect of schizophrenia. However, by carefully observing the walking state, facial expressions, conversational tone, etc. over time, and performing joint echoes as appropriate by care nurse, it is possible to judge the disease state of RA and proceed with treatment smoothly with the doctor, which is valuable. It was an experience.

P3-257

Significance of "Talking Salon" and needs for patients with rheumatoid arthritis (RA) revealed from questionnaire

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Conflict of interest: None

Objective: Recently, the importance of peer support is increasing. We held a "Talking Salon" at our clinic for the purpose of exploring whether there is a significance and patient needs in establishing a place for communication between patients. Method: A free talk "Talking Salon" was held between patients. After completion, we conducted a questionnaire survey. Results: There were 58 participants, and the number of valid responses in the questionnaire was 51 (87.9%). The average age of the participants was 68.0 years, 42 patients with RA (72.4%), 4 patients with collagen disease (6.9%), disease duration was 6.7 years, and our clinic visit history was 4.2 years. The responses regarding the satisfaction were very satisfied 71%, satisfied 27%, slightly satisfied2%, normal 0%, slightly dissatisfied 0%, dissatisfied 0%, very dissatisfied0%. Among the free answers, 37 participants (72.5%) answered that it was good to have a free conversation and enjoyable communication between the rheumatic diseases' patients. Discussion: Because of the high level of satisfaction, it is meaningful to establish a place for communication between patients, and there is a need for patients. We think holding a "Talking Salon" that is more beneficial for patients is a future issue.

P3-259

Survey of patients with rheumatoid arthritis who experienced pregnancy, childbirth and childcare

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Conflict of interest: None

[Purpose] The purpose of this study is to conduct interviews with RA patients who experienced child-raising while treating RA, to understand the actual situation, and to use it for future patient support. [Methods] An interview survey was conducted with RA patients in their 20s to 40s, who were visiting our hospital who experienced pregnancy, childbirth and childcare. Based on the information obtained, the current problems and future countermeasures were examined. [Results] Case 1: "When I want to hold my baby, my joint symptoms are strong, and I can't hold my baby so much. Case 2: "I want to receive support for childcare after birth. " Case 3: "I would like to request detailed information for patients with rheumatoid arthritis and their families who wish to become pregnant, give birth, or raise children. " The above is a part of the interview surveys obtained so far. Based on the results, we report "nursing support for RA patients raising children" with a literature review. [Conclusions] This interview revealed the problems of RA patients who are raising children while being treated.

P3-261

Survey on switching device for adalimumab (Humira®) from subcutaneous syringe to PEN in patients with rheumatic diseases

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Conflict of interest: None

[Objective] To clarify the benefits, satisfaction, and convenience of switching from adalimumab (ADA; Humira®) syringe to PEN in rheumatic disease patients. [Methods] A survey was conducted in rheumatic disease patients using ADA who were switched from syringe to PEN, impressions after use of each, and changes due to the switch were verified. [Results] Twenty-one patients proposed a switch from ADA syringe to PEN and 14 (66.7%) switched. The group who did not wish to switch had significantly longer syringe use than those who did ($p=0.006$). In the impressions survey after switching, improvement was observed in "anxiety and fear, " "motivation and positive outlook toward treatment, " "ease of recalling method of use, " "ease of injection, " "ease of handling syringe, " "pain at injection, " and "overall satisfaction. " In self-injecting patients, switching also decreased the number of failures, the "instances of forgetting to self-inject, " and "number of times self-injection was not performed due to not wanting to, " while "motivation and positive outlook toward treatment" significantly increased ($p=0.02$). [Conclusions] Switching from ADA syringe to PEN may be useful in alleviating anxiety, fear, and pain associated with injections, as well as improving motivation towards treatment.

P3-262

Survey of life guidance provided by nurses for patients undergoing biologic therapy. -Changes in recognition and performance after training-

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Conflict of interest: None

[Objective] The actual situation of life guidance for nurses was investigated. As a result, guidance for infection other than common cold was

not sufficient. After that, we reviewed the recognition and performance of the importance of guidance. [Methods] The targets were 32 nurses related to patients who received biotherapy at our hospital. Using 17-item survey, we compared the recognition and performance status of guidance. [Results] The effective response rate is 94%. After the training, there was a significant difference in the importance of guidance and 14 out of 17 performance items. The items that are recognized to be important but have a low level of performance are “gingivitis”, “otitis media”, and “sinusitis” . The reason for this was that guidance methods and guidance contents differed depending on the time of introduction of Bio, treatment history, and frequency of visits, and it was difficult to provide guidance according to the individuality of patients. [Conclusions] Nurses share instruction methods with others in the nursing practice and lead to patient guidance with personality.

P3-263

Shared Decision Making of Rheumatoid Arthritis by patients who have withdrawn or changed their Biological treatmentStrategy for the future support system

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Conflict of interest: None

[Objective] A biological treatment of rheumatoid arthritis is in the central location as in bringing a remission at present. There are some cases which left biological treatment as for a remission, However, there are some cases that require withdrawal from treatment or drug change by inadequate side effects, relapse even if signs of improvement appear, or financial problems Choice of medication varies depending on the physical status and the symptom. However, the endless change of therapeutic drugs is a major anxiety factor for patients. Anxiety reduction is one of the important aim of patient in Shared Decision Making (SDM) This time, we conducted a Bio questionnaire and SDM scale tool SDM-Q9 for patients who changed or withdrawn from Bio. We report what the medical care that patients require in RA-Bio and what are the elements of medical staff necessary for SDM intervention.

P3-264

Practical report of educational admission for rheumatoid arthritis patients that used critical path and the problems for rheumatology nurses to tackle in the future

Emiri Nakamura
Kitasato University Hospital

Conflict of interest: None

[Objective] In our hospital, Since February 2019, using critical path, we have 3-day, 2-night educational hospitalization the for patient who have been diagnosed with rheumatoid arthritis and introduced a biologic or JAK inhibitor. Doctors, pharmacists, and rheumatic care nurses collaborated to create manuals, and operate them. In addition, we focused on observing the feet of rheumatic patients and decided to convert them into data. [Methods] Digitalization of the activity content and the practice results from November 2018 to October 2019. [Results] From February to October 2019, there were 33 hospital admissions, For the concrete support the patients hoped for, we resulted in: 5 cases of economic insecurity, 3 cases wishing for explanation about self-help devices, 2 consultation cases about desire to bear children, and 11 cases about their foot problem. [Conclusions] The need for foot care became clear. As for future issues, I think it is necessary to review the critical path and introduce foot care. As a rheumatic care nurse, we will create a manual with the cooperation of doctors and physical therapists so that we can introduce foot care that leads to self-care, insoles, and custom-made shoes. In addition, we want to lead to a highly satisfactory educational hospitalization.

P3-265

Supporting the suffering of rheumatoid arthritis patients who needed to change their treatment due to drug-induced lupus erythematosus

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Conflict of interest: None

[Objective] We experienced a case in which drug-induced lupus erythematosus caused by etanercept was suspected and treatment change was necessary. We wanted to investigate the actual situation of self-care along the trajectory of long-term illness of 16 years and clarify the support method. [Methods] Based on Orem’s self-care deficit nursing theory, semi-structured interviews will be conducted on patient, and consideration will be given to how patients should be supported from their actual self-care. [Results] DAS28 was 6.43, mHAQ was 1.50 and there were restrictions on activities in daily life, so she used a lot of time and energy to make herself personal. Pain is a symptom that makes various activities for daily life difficult and makes mental and physical anning a critical situation, and the approach tends to be judged from past experience. She may try to relieve symptoms in another way if she doesn’t feel she is recovering after taking the medicine as prescribed. [Conclusions] In order to practice medical treatment based on scientific grounds, patient-centered communication is necessary, and support for maintaining relationships with medical professionals was also an important issue.

P3-266

A Relationship between treatment and psychological QOL improvment on rheummatoid arthritis

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Conflict of interest: None

[Case] He was 68 years old man. Chief complaint was gait disturbance due to joint pain. He was diagnosed with RA at age of 40. MTX and PSL were treated during about 10 years. At our first visit, he had active synovitis on his right wrist, left MP3 joint and right shoulder, revealed with joint ultrasound. Thus, SASP was added and PSL was became reduced. Since the symptoms improved, he restarted the cleaning industry, but gradually re-exacerbation of joint pain and increased the serum levels of CRP. And he was readmitted again. [Methods] We examined Relationship between treatment and psychological QOL improvement on RA, using the MMSE, HDSR, FAB, POMS, compared in the time of discharge at the time of hospitalization. [Results] DAS28-CRP: 5.62, MMSE: 19/30, HDSR: 18/30, FAB: 8/30, Motivation13/42, TEG: ACdominant type” dependent type”, POMS: “anger”, “depression”, “confused” showed high levels of value. At his discharge DAS28-CRP 3.81, MMSE: 22/30, HDSR: 22/30, FAB: 15/18, Motivation11/42, POMS: High in” confused”, “angry” and “depression” improved to the average of general healthy person. [Discussion] Holistic pain was a combination of physical, mental, social and spiritual pains. This is an example that suggests prevention and improvement in psychological QOL as well as physical QOL

English Poster Session

EP1-001

Greater patient's pain score is a risk factor of worsening clinical disease activity index at three months after attaining remission

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Conflict of interest: None

[Objective] In treating with rheumatoid arthritis (RA), it is needless to say essential treatment goal with first priority. On the other hand, patient's pain influences on clinical indices deeply, however, pain score is not been regarded as most important despite that correlates with patient reported outcome. We have investigated clinical significance of remnant pain score although attaining clinical disease activity remission statistically. [Methods] RA patient who have attained remission with clinical disease activity index (CDAI) were picked up. These patients were divided into three groups according to pain score with visual analog scale (PS-VAS); less than 10mm (A), 10 to 29mm (B), and no less than 30mm (C). CDAI at three months later from first remission attained date, were monitored and CDAI remission rate for each group were compared with chi-square test. And furtherly, the CDAI score and CDAI remission were set as dependent variant, for clinical background factors, and clinical parameters at first CDAI remission attained were set as dependent variants, and then these parameters were evaluated statistically with multivariate regression analysis (MLR) and binary regression analysis (BRA). [Results] 393, 297, and 300 cases were collected for group A, B, and C, respectively. CDAI remission ratio at three months later was 68.2, 65.4, and 63.0% for group A, B, and C, respectively. There demonstrated no significant difference, however, PS-VAS, modified Health Assessment Questionnaire (mHAQ), and the CDAI score at first remission attained demonstrated significant correlation with the CDAI score at 3 months later with MLR, while PS-VAS, the CDAI score and the Total Sharp Score demonstrated significant correlation with the CDAI score at 3 months later with BRA. [Conclusions] PS-VAS is suggested of the factor that predicts the CDAI score at three months later from first CDAI remission.

EP1-002

Predicting clinical efficacy of JAK Inhibitors by cluster analysis in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify the characteristic group of oral Janus kinase inhibitors (JAKi) resistance (JAKi-R) in patients with rheumatoid arthritis (RA) by cluster analysis. [Method] This retrospective study comprised 40 RA patients who were treated with JAKi (Tofacitinib and Baricitinib) between July 2013 and September 2019. The disease status at the baseline, 12 weeks after JAKi treatment and the time of withdrawing JAKi was assessed using the Disease Activity Score (DAS28) or the American College of Rheumatology (ACR) response criteria. JAKi-R was defined as follows, primary non-response at 12 weeks after JAKi treatment: ACR20 non-response or an increase in DAS28-CRP (ΔDAS28-CRP>1.2 from baseline), secondary non-response: withdrawal of JAKi without clinical remission after 12 weeks. Hierarchical cluster analysis was performed with the following variables: gender, age, disease duration, Steinblocker classification (Stage, Class), complication of rheumatoid lung disease (RA-ILD) or other autoimmune disease (AID), anti-citrullinated protein antibody (ACPA) at diagnosis, and rheumatoid factor, use/dose of methotrexate (MTX) and prednisolone, serum ESR/CRP, tender/swollen joint counts, visual analog scale by patients, and treatment history of biologic DMARDs. [Result] Among 40 enrolled patients, 4 groups were classified by cluster analysis, Group A (n=10): seronegative RA + MTX user, Group B (n=7): female + RA-ILD/AID + MTX non-user + Stage III, IV + Class 3, Group C (n=12): ACPA positive + non-RA-ILD + MTX user + Class 1,2, Group D (n=11): male, MTX user + Stage I, II + Class 1,2. The rate of JAKi-R was A: 50%, B: 29%, C: 8%, D: 18%. Seronegative RA (p=0.0001) and Class 3 (p=0.001) were identified as the predictors of JAKi-R by multivariate logistic regression analysis. [Conclusion] Seronegative RA and Class 3 may be considered as the predictors of JAKi-R in patients with RA. Cluster analysis is an exploratory tool that aids in the analysis of huge multiple data.

EP1-003

Status of use of Abatacept 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 Abatacept for rheumatoid arthritis in our hospital with using the NOSRAD registry. [Patients and Methods] 104 patients (18 men and 86 women) of rheumatoid arthritis who introduced Abatacept between November 2010 and August 2019 in our hospital were included in this study. The average age at the start of t administration was 70.2 (40-89) years. The average observation period was 1.9 years. The examination items consist of 1) Changes in DAS28 from the start up to 12 months after the administration of Abatacept 2) Cumulative survival rate of Kaplan-Meier method 3) Combined rate and combined dose of MTX and PSL at the start of administration 4) DAS28 and survival rate in combined with or without MTX 5) DAS28 and survival rate of each bio-naïve and switch cases 6) Reasons for discontinuation. [Results] DAS28 gradually improved over the course of 12 months, 3.1 before administration, 2.5 after 3 months, 2.2 after 6 months, and 2.0 after 12 months. The cumulative survival rate of the Kaplan-Meier method was 65% for 1 year and 56% for 2 years. There were 41 MTX combination cases (39.4%) at the start of administration, and the average dose was 6.8 mg / week. There were 59 PSL combination cases (56.7%) at the start of administration, and the average dose was 5.9 mg. With or without MTX, DAS28 significantly decreased in the group without MTX, and survival rate was significantly higher in MTX non-combination group (54% for 1 year, 47% for 2 year in combination group, 74% for 1 year, 63% for 2 year in non-combination group). In comparison between bio-naive and switch groups, there was no significant difference in DAS28, and the survival rate was 73% for 1 year, 62% for 2 year in bio-naive group, and 52% for 1 year, 47% for 2 year in bio-switch cases. The reasons for discontinuation were 17 cases for primary and secondary ineffectiveness and 5 cases for infection. [Conclusion] These findings tended to be different from other biologics.

EP1-004

Prevalence of age-related comorbidities among Japanese Rheumatoid Arthritis patients who initiated their first DMARD treatment: A claims database analysis

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Conflict of interest: Yes

[Objective] Therapies targeted to elderly Rheumatoid Arthritis (RA) patients in Japan have gained prominence recently, due to the rapidly aging RA patients and general population. This study aimed to describe demographics and comorbidities among Japanese RA patients initiating their first disease modifying anti-rheumatic drug (DMARD) treatment. [Methods] This study included adult patients (aged ≧18 years) with RA in the Medical Data Vision (MDV) hospital claims database. Patients with RA were identified via International Classification of Diseases 10th Revision (ICD-10) codes and initiated their first DMARD between 4/2009-4/2018, with the index date (ID) defined as the date of DMARD initiation. Patients were required to have 12-months continuous enrollment pre- and post-ID,

and could not have a record of any DMARD claims during the pre-ID period. Prevalence of background comorbidities was assessed via measuring the ICD-10 code groupings, and Charlson Comorbidity Index (CCI) was used to measure overall pre-index comorbid disease burden. [Results] Of the 47,201 patients initiating their first DMARD, 64.4% of the population were ≧65 years (mean age 65.9 years, 74.2% female). The mean Charlson Comorbidity Index (CCI) score was 0.507, with age-related comorbidities such as hypertension (8.8%), osteoporosis (8.3%), osteoarthritis (7.7%), heart failure (6.3%), disorders of lipid metabolism (6.3%), type 2 diabetes (4.7%), renal impairment (4.6%), and chronic obstructive pulmonary disease (3.1%) also being prevalent. [Conclusions] In this MDV database analysis, patients initiating their first DMARD treatment had a mean age of 66 years further highlighting the aging RA population. A high prevalence of age-related comorbidities was observed, therefore with the aging RA population in Japan, these comorbidities should be carefully considered among this elderly RA population.

EP1-005

Serum hepcidin and iron metabolism are related indirectly and directly to osteoporosis in patients with rheumatoid arthritis: A cross-sectional study

Hiroe Sato[1,2,3], Chinatsu Takai[3], Masanori Sudo[2], Ayako Wakamatsu[2], Eriko Hasegawa[2], Daisuke Kobayashi[2], Naoki Kondo[4], Takeshi Nakatsue[2], Asami Abe[3], Satoshi Ito[3], Hajime Ishikawa[3], Takeshi Kuroda[1], Ichiei Narita[2]

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Conflict of interest: None

[Objectives] Hepcidin, a major regulator of iron metabolism and homeostasis, is regulated by inflammation. Recent studies have suggested that hepcidin and iron metabolism are involved in osteoporosis. This study examined serum hepcidin level of patients with rheumatoid arthritis (RA) and its relationship with osteoporosis. [Methods] In total, 262 patients with RA (mean age, 67.5 ± 11.4 years; 77.5% female) were enrolled; 52.7% used methotrexate and 33.6% used biological disease-modifying antirheumatic drugs (bDMARDs). The serum hepcidin level was measured by liquid chromatography-tandem mass spectrometry. Multiple regression analysis was performed with adjustment for age, sex, body mass index, estimated glomerular filtration rate, C-reactive protein (CRP) level, and bDMARDs use. The Jonckheere-Terpstra trend test, Spearman's Rank method and Mann-Whiteney U test were also performed. [Results] The serum iron, ferritin, and hepcidin levels were correlated with each other, and with the hemoglobin level, CRP, disease activity score-28 CRP and bDMARDs use. Regarding osteoporosis and bone markers, the serum iron level was correlated with the femoral T- and Z-scores (ß = 0.123, p=0.034 and ß = 0.128, p=0.038, respectively), while the serum hepcidin level was not. The serum hepcidin and ferritin levels were correlated with the serum 25-hydroxy vitamin D (25OHD) level (ß = 0.209, p=0.001), which was in turn correlated with the femoral Z-score (p=0.049). [Conclusions] Iron overload was not related to osteoporosis in patients with RA. Contrary to expectations, however, higher iron levels were related to higher bone mineral density (BMD). The serum hepcidin level was not associated with BMD or bone metabolic marker levels, but was correlated with the serum 25OHD level (which in turn was negatively correlated with BMD). In this cross-sectional study of patients with RA, serum hepcidin was indirectly and iron metabolism was directly related to osteoporosis.

EP1-006

Efficacy and safety of Abatacept in elderly patients with rheumatoid arthritis aged 75 years old or older: a single center study

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Conflict of interest: None

Objective: Recently Abatacept (ABT), a biologic agent suppressing T cells by blocking co-stimulation signal, is reported to be safer compared to other biologics in rheumatoid arthritis (RA). However, reports regarding ABT efficacy and safety in Japanese elderly RA patients aged 75 years old or older is still limited. This study is conducted to elucidate the efficacy and safety of ABT in elderly RA patients (75≦) in comparison with younger RA patients (75>) in real world. We also investigated which combination therapy with methotrexate: MTX or tacrolimus: TAC, were better for maintaining drug retention of ABT in RA patients. Methods: This study was designed for a retrospective, observational cohort study. RA patients treated with ABT from 2010 to 2018 in our department were included. Of 30 patients received ABT, 29 patients were enrolled (one patient excluded for drug allergy) and clinical records were retrospectively reviewed. Results: ABT is effective in elderly RA patients (11 cases) as well as younger RA patients (18 cases) in daily clinical practice (DAS28CRP after 6 months: 1.9 vs 2.21, respectively), however, some differences were observed: elderly patients significantly tended to receive TAC for combination therapy rather than MTX compared to younger patients (TAC, 63.6% vs 22.2% and MTX, 9.1% vs 55.6%, respectively, p<0.05). Overall ABT retention probability in combination with TAC (11 cases) was significantly higher than those with MTX (11 cases) (75% vs 26.5%, respectively. p=0.02). Patients receiving MTX combination were tended to be younger, and ABT was administered more late timing (3rd biologics or more) than TAC group (p=0.07). On the other hand, the rates of lung complication (concomitant interstitial lung disease) and severe infections did not differ between elderly and younger RA patients. Conclusions: ABT was effective in elderly RA patients (75≦) and combination therapy with TAC can be considered in elderly RA patients for better drug retention.

EP1-007

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

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Conflict of interest: None

[Objective] Cartilage damage in rheumatoid arthritis (RA) has been evaluated by joint space narrowing (JSN) in X-ray, despite the fact that it is not a direct evaluation of cartilage. We previously reported that direct evaluation of finger joint cartilage thickness evaluated by ultrasound (US) is useful for patients with RA. We aimed to examine the temporal changes of US cartilage evaluation in RA patients. [Methods] We enrolled patients with RA in whom the cartilage thickness of finger joints was measured at baseline and 1-year later. The cartilage thickness of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of 2nd to 5th fingers were bilaterally visualized and measured at the middle portion of MCP and PIP joints from a longitudinal dorsal view, with approximately 90 degrees flexion. Cartilage thickness was measured from the base of the cartilage to the interface artefact at the cartilage surface by calculating the pixel counts on DICOM images. [Results] Twenty patients with the median disease duration of 6 years were enrolled. The median DAS28-ESR at baseline was 3.7. The sum of total cartilage thickness from 16 joints per patient ranged from 4.4 to 11.7 mm (median 9.0 mm) at baseline, and it was significantly correlated with disease duration (ρ=-0.559, p=0.012). A significant decrease by the median value of 4.3% was observed in the cartilage thickness after 1-year from the baseline (p=0.002). Furthermore, there were no significant differences in sex, age and treatment between the cartilage thickness decreased groups by 5% or more in one year (progression group: 9 cases) and other groups (non-progression group: 11 cases). The non-progressive group was significantly improved than the progressive group in the rate of change in DAS28 one year after baseline (-25.2% vs -0.6%, respectively, p=0.037). [Conclusions] This pilot study suggested the validity and usefulness of joint cartilage thickness evaluation by ultrasound in patients with RA.

EP1-008

The short term outcome of baricitinib in patients with rheumatoid arthritis; the evidence from NOSRAD (Niigata Orthopedic Surgery RA Database)

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Conflict of interest: None

[Objective] To evaluate the short-term outcome of baricitinib in patients with RA. [Methods] Twenty cases of RA (19 women and a man) were recruited from NOSRAD cohort. The average age was 70 years old (55-84 years old) and the average RA disease duration was 13 years (0.6 to 45 years). Methotrexate was used in 10 cases and the average doses was 7.0 mg/week (2-12 mg/week). Predonisolone was used in 10 cases and the average doses was 5.1 mg/day (2-7.5mg/day). Previously used biological DMARDs were cumulatively 8 cases 11 agents (tocilizumab 4, etanercept 3, and sarilumab, golimumab, certolizumab pegol, and abatacept, 1 each). Baricitinib doses were 2mg/day in 18 cases, and 4 mg/day in 2 cases. Clinical disease activity index (CDAI), DAS28-ESR were evaluated at the administration of baricitinib, and 1, 3, and 6 months after the administration. The continuation rate and the cessation cases were also evaluated. [Results] CDAI was 18.4 at the administration, and decreased to 11.9, 11.5, and 11.4 at 1,3, and 6 months after the administration, respectively. DAS28-ESR was 3.65 at the administration, and decreased to 2.99, 3.26, and 3.11 at 1,3, and 6 months. The continuation rate was 15 cases (75%). The cessation cases were 5 (primary inefficacy in 3, secondary inefficacy in 1, and dysphoria in 1, respectively). [Conclusions] Baricitinib rapidly exerted down regulation of CDAI and DAS28-ESR at 1 month after the administration and maintained the efficacy until 6 months without causing severe adverse events.

EP1-010

Tocilizumab is more effective for rheumatoid arthritis in patients with rapid progression of joint erosion

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Conflict of interest: None

Objective: Treatment of rheumatoid arthritis (RA) is aimed at long-term remission and inhibition of joint destruction by different biologic drugs such as cytokine inhibitors. However, choice of a particular biologic agent based on individual cases of RA remains unestablished. Therefore, this study aimed to investigate predictive factors for the clinical effectiveness of tocilizumab in patients with RA. **Method:** Eighty-five patients with RA participated in this study. Visual analogue scale (VAS), clinical disease activity index (CDAI), and modified health assessment questionnaire (mHAQ) scores at baseline and after 6 months of tocilizumab therapy were measured, and differences in the scores were used to determine the clinical effectiveness of tocilizumab. Delta VAS, CDAI, and mHAQ values were compared to clinical parameters, including disease duration, Steinbrocker class and stage, baseline C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and matrix metalloproteinase-3 (MMP-3), and radiographical parameters, including total Sharp score (TSS), TSS/disease duration year, erosion score, erosion score/disease duration year, joint space narrowing score (JSN), and JSN score/RA duration year. **Results:** Although there were no significant differences between delta HAQ and clinical parameters, significant correlation between baseline CRP and improvement in VAS or CDAI (VAS: rr=0.44, p=0.017; CDAI: rr=0.44, p=0.017) was noted. Improvement in CDAI was significantly associated with the yearly progression of erosion according to the Sharp score (OR 6.1, 95% CI 1.04-1.45). **Conclusion:** We identified predictive factors for the clinical effectiveness of tocilizumab and established that tocilizumab treatment may be more effective in RA with rapidly progressing joint erosion.

EP2-001

Differentiation of rapidly destructive coxopathy in its early stage by MMP-3

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Conflict of interest: None

[Objective] Osteoarthritis is characterized by destruction of joint cartilage and subchondral bone, with degradation of the extracellular matrix. Rapidly destructive coxopathy (RDC) is an unusual subset of osteoarthritis. Potential causes of RDC include subchondral insufficiency fracture resulting from osteoporosis, increasing posterior pelvic tilt as a mechanical factor, and high serum levels of matrix metalloproteinase (MMP)-3 as a biological factor. Although RDC develops chondrolysis >2 mm in 1 year, the process of disease progression in the early stage of RDC is still equivocal. This study aimed to identify pathological factors of rapidly destructive coxopathy (RDC) that differentiate the process of disease progression in its early stage. [Methods] This study included 24 female patients who met the criteria of RDC, chondrolysis >2 mm during 12 months from the onset of hip pain based on a series of radiographs and computed tomography. Cortical thickness index (CTI) correlated with bone mineral density of the hip, pelvic tilt, and serum concentrations of MMP-3 were analyzed. All the data were obtained before the initiation of bone destruction. [Results] RDC were classified into two types based on the absence (type 1, n=11) and presence (type 2, n=13) of subsequent femoral head destruction within 12 months after the onset of hip pain. Femoral head destruction occurred in RDC type 2 over 4 months after the onset of hip pain. MMP-3 significantly increased in RDC type 2 compared with type 1. From logistic regression and receiver operating characteristic curve analyses, MMP-3 differentiated RDC type 2 from type 1 within 4 months after the onset of hip pain before the initiation of femoral head destruction. No difference was found in CTI or pelvic tilt between RDC types. [Conclusions] MMP-3 may be helpful to differentiate RDC type 2 from type 1 at the time before the initiation of bone destruction.

EP2-002

The clinical characteristics and treatment status of psoriatic arthritis

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Conflict of interest: None

[Objective] Psoriatic arthritis (PsA) is a complex musculoskeletal disorder. The clinical features are psoriasis, peripheral arthritis, spinal involvement, enthesitis, and dactylitis. Typically, skin lesions precede osteoarticular lesions in several years. However, sometimes we encounter cases in which osteoarticular lesions precede skin lesions. The object of the study was to validate the onset pattern of PsA and how long the interval between the occurrence of skin lesions and osteoarticular lesions is and the treatment status of PsA. [Methods] 64 PsA patients (49 males and 15 females, the average age was 56 years old) who were fulfilled with CASPAR criteria were recruited and evaluated the onset pattern, distribution pattern, and the treatment status. [Results] Osteoarticular lesions preceded in 17% of patients related to the onset pattern. The mean interval in the cases which skin lesions preceded was 13 years and which osteoarticular lesions preceded was 3 years. About the distribution of arthritis, axial joints were affected in 29% of skin lesion preceded group and 55% of osteoarticular lesions preceded group, but no significant difference was detected. About the treatment status, NSAIDs were used in 38%, csDMARDs were 62%, and bDMARDs were 55%. [Conclusions] The cases which osteoarticular lesions preceded skin lesions are not a few in PsA, so care should be taken about the cases which are rheumatoid factor negative and are lack of skin lesions.

EP2-003

Simplified 7-item criteria for the diagnosis of polyarteritis nodosa

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Conflict of interest: None

[Objective] To investigate sensitivity and specificity of the American College of Rheumatology (ACR) and the Japanese Ministry of Health, Labour and Welfare criteria for the diagnosis of polyarteritis nodosa (PAN) in a single-centre retrospective cohort, and to develop provisional criteria with favourable diagnostic performance. [Methods] All patients with PAN or suspicion of PAN, as indicated on insurance forms, were included. The patient population was classified into PAN and non-PAN groups based on a retrospective chart review. The sensitivity and specificity of the ACR and the Japanese criteria were calculated. Items that contributed to differentiation between the PAN group and the non-PAN group were determined and used as items for our criteria. [Results] Thirteen cases of PAN and 24 cases without PAN were included in this study. Sensitivities of the ACR and the Japanese criteria were 61.5% and 30.8, respectively, whereas specificities were 79.2 and 87.5%, respectively. Our provisional criteria consisted of 7 items, and found that ≧4 items had a sensitivity of 92.3% and specificity of 91.7%. [Conclusions] The simplified 7-item criteria, developed in our real-world cohort of patients suspected of having PAN, had a favourable diagnostic performance and may be useful for the diagnosis purpose of PAN.

EP2-004

The effect for healing of bisphosphonate-associated atypical femoral fractures by "primary iliac cancellous bone graft" method

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Conflict of interest: None

[Objective] We have treated complete atypical femoral fractures (AFF) for proper anatomical reduction of fracture sites and insertion of intramedullary nailing with primary autologous iliac cancellous bone graft (PICBG) method. The aim of this study was to examine the efficacy of PICBG for fracture healing. [Methods] Nineteen patients who underwent open reduction and internal fixation to AFFs from 2011 to 2018 were registered. All fractures were fulfilled with the diagnostic criteria of AFFs. Of 19 fractures, subtrochanteric was 10 and diaphyseal was 9 cases, respectively. The average age was 65.9 years old (44-79 years old). Used bisphosphonates were as follows; alendronate in 11, risedronate in 3, minodronate in 2, ibandronate in 1, denosumab 1, unknown in 1, respectively. The average duration of bisphosphonates was 6.2 years (0.8 to 9.5 years). The treatments were the insertion of intramedullary nailing (IM nail) and just after the insertion of IM nail, beaking site located in the lateral cortical region was curetted and the ipsilateral iliac bone was harvested and grafted into the curetted site to promote fracture healing. After that, teriparatide treatment and low intensity pulsed ultrasound sonography (LIPUS) were treated. The fracture healing was determined with plain femoral X-ray findings. With 2 directional X-ray, more than 3 out of 4 sites radiolucent sign (fracture line) was confirmed unclear, it was defined as "fracture healing" . The time until fracture healing and revision rate were measured. [Results] The average time to heal the fracture was 8.1±7.7 months (minimum - maximum; 1.8 to 30 months). The primary healing rate was 89 % (17 cases). Healing was acquired in 14 cases (74 %) less than 6 months. The revision surgery was required in 2 cases (11%). Both cases were subtrochanteric type. [Conclusions] PICBG with teriparatide and LIPUS treatments is useful method because primary healing rate was high and comparatively shorter average time to heal.

EP2-005

Successful treatment of Takayasu arteritis complicated by ulcerative colitis using JAK inhibitor tofacitinib: suppressive effects of tofacitinib against vasculitis-related cytokines on human CD4+ T cells

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Conflict of interest: None

A 17-year-old female was admitted to our hospital for continuous gastrointestinal (GI) symptoms for ulcerative colitis (UC) and intermittent right neck pain in June 2018. Cervical ultrasound revealed diffuse wall thickness of right carotid artery, showing macaroni sign. Enhanced computed tomography (CT) showed diffuse wall thickness of right carotid artery and stenosis of left subclavian artery. She was diagnosed with Takayasu arteritis (TA) complicated by UC. Because she presented refractory GI symptoms as well as vascular lesions, she received golimumab in combination with oral prednisolone and mesalaszine. However, her symptoms persisted. Next, she received vedolizumab instead of golimumab, which is not effective enough. She still showed wall thickness of carotid artery and progressive stenosis of left subclavian artery with continued GI symptoms of UC, she received JAK inhibitor tofacitinib (TOF) after steroid pulse therapy for both TA and UC treatment. After TOF administration, her GI symptoms rapidly ameliorated and arterial wall of right carotid artery got thinner. JAK inhibitor including TOF inhibits many kinds of cytokine production in immune cells, including $CD4^+$ T cells. Herein, we describe the effect of TOF on human $CD4^+$ T cells. Upon stimulation with anti-CD3 antibody, activated $CD4^+$ T cells from healthy volunteers produced IL-12, IL-17 and interferon (IFN) gamma, in which they are implicated in TA as well as UC pathogenesis. These chemokines successfully inhibited by TOF treatment in accordance with TOF concentration. TOF also inhibited STAT1, 3, 4, 5 and STAT6 phosphorylation under anti-CD3 antibody stimulation, but not in the phosphorylation of ZAP-70, a T cell receptor-associated protein. In conclusion, TOF effectively inhibited cytokine production (IL-12, IL-17 and IFN gamma) on active $CD4^+$ cells in vitro, suggesting TOF can be considered for treatment of refractory TA patients complicated by UC those who were resistant to biologics.

EP2-006

Secondary Operation for Native Compartments after Oxford Partial Knee Arthroplasty

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Conflict of interest: None

[Objective] The knee function after Partial Knee Arthroplasty (PKA) is better than that of TKA because of retained structure of native compartments. Destruction of these compartments cause the reason of secondary operation including revision surgery. The aim of this study is to present frequency of destructive lesion of native compartments. [Methods] We reviewed a series of 243 consecutive primary Oxford medial PKA performed in Kurashiki Medical Center between August 2006 and September 2018. The mean age at implantation was 71.1 years (43-93 years). 188 knees were osteoarthritis (OA), 53 knees were osteonecrosis (ON), and 2 knees were rheumatoid arthritis in remission (RA). Secondary operations for native compartments after Oxford PKA were examined about their destructed compartments, period after primary operation, age at the primary medial UKA, procedures of second operation, and primary disease. [Results] Five knees underwent secondary operations. Three knees had lateral compartment lesions, which are osteonecrosis of the lateral condyle of the femur or tibia, and one of them had lateral progressive arthritis. Primary disease of these three knees was ON of the medial femoral condyle. One of the three knees was revised with primary TKA. Two of the three were treated with staged Bi-UKA which means addition of a lateral UKA. The other two of five secondary operated knees had patellofemoral compartment arthritis and their primary disease was OA. One of the two knees had laxity of MCL, so it was revised with a constrained TKA. The other one was performed addition of patellofemoral PKA. Age of these five patients at the primary medial UKA ranged from 70 to 77 years old. Secondary operation for native compartment after Oxford PKA for OA is 2 of 188, and that for ON is 3 of 53. There is no significant difference between these two incidences. [Conclusions] Secondary operation for native compartments after Oxford PKA is relatively rare.

EP2-007

Effect of vitamin D supplementation on chronic damage in systemic lupus erythematosus: cross-sectional analysis from a lupus registry of nationwide institutions (LUNA)

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Conflict of interest: None

[Objective] Chronic damage accrual is a major concern in patients with systemic lupus erythematosus (SLE). Although vitamin D concentration had been reportedly associated with immunological function and disease activity, benefit of vitamin D supplementation to damage accrual is not elucidated. [Methods] Using data from lupus registry of nationwide institutions (LUNA), a cross-sectional analysis was performed. Patients with past history of bone fracture, use of denosumab, end-stage renal failure, pregnancy, or malignancy were excluded. Primary outcome was disease-related Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI). Disease-related SDI and each item were compared between patients with and without vitamin D supplements. As secondary outcomes, total SDI and current disease activity were also compared. [Results] The median age (interquartile range [IQR]) of enrolled 681 patients was 44 (33-53) years and 604 patients (89%) were female. 341 (50%) patients received vitamin D supplements. Patients with vitamin D supplements were older (45 [37-58] vs. 40 [31-49] years, $p<0.0001$], treated with higher current (7 [5-30] vs. 5 [3-9] mg/day, $p=0.0011$) and maximum (45 [30-60] vs. 40 [30-56] mg/day, $p=0.007$) dose of prednisolone. There were no significant differences in disease-related SDI (0 [0-1] vs. 0 [0-1], $p=0.20$), total SDI (0 [0-1] vs. 0 [0-1], $p=0.18$), and current SLE disease activity score (4 [2-8] vs. 4 [2-8], $p=0.82$) between patients with and without vitamin D supplements. Of the items consisting SDI, 'claudication' was less frequent in patients with vitamin D supplements than those without (2 of 341 [1%] vs. 10 of 340 [3%], $p=0.02$). 'Peripheral vascular damage' was tended to be less frequent in patients with vitamin D than those without but not significant (9 of 341 [3%] vs. 18 of 340 [5%], $p=0.08$). [Conclusion] Vitamin D supplements could not reduce disease-related damage but might reduce vascular damage.

EP2-008

The timing of appearnace of the effects of rituximab (RIX) for treatment of granulomatosis with polyangiitis (GPA)

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Conflict of interest: None

[Back ground] Although the role of rituximab (RIX) for GPA has been established, it is difficult to identify delays between its injection and appearance of its effect, because the drug is usually administered with other immunosuppressive drugs. [Case] A 68-year-old man was admitted to our hospital because of cough. Three weeks before admission, he began coughing with occasional hemosputum. Ten days before, as he experienced nasal hemorrhage, he visited a local hospital where abnormal shadows on chest X-ray were noted. He was transferred to our hospital, after ineffective antibiotic treatment. On admission, crackles of bilateral lower lung field were audible. Laboratory data included leukocyte 7720/μl, Hb 13.1 g/dl, platelet 304000/μl, CRP 1.88 mg/dl, and Cr 0.76 mg/dl. Urinalysis was normal. PR3-ANCA was elevated to 45 IU/ml, while MPO-ANCA was negative. Chest CT revealed nodular shadows of lungs and persistent infiltrative shadows. Head CT showed diffuse thickening of nasal mucosa. These findings met the ACR 1990 classification criteria for GPA. Steroid pulse therapy followed by 60mg of PSL combined with IVCY was done with some favorable effect. However, as PSL was tapered to 15mg, the pulmonary shadows were relapsed. Subsequent addition of azathioprine (AZP) did not improve the medical condition. While taking 15mg of PSL and 50 mg of AZP, as the abnormal nodular shadows with cavities grew, RIX (375mg/m2 x 4) was introduced. Then the shadows gradually improved after a month and almost disappeared in two months with normalization of laboratory findings. As the dose of PSL and AZP remained unchanged, the effect of RIX was likely to appear in these timings. He is still well after two years with 5mg of PSL without immunosuppressants (IS), his B cell count keeping lower than 6/μl. [Conclusions] This case shows an excellent role of RIX for a patient with GPA refractory to conventional treatment with PSL and IS. Its effect appeared after one month and maximized in two months.

EP2-009

Predictive factors for recurrence or insufficient response to initial treatment in patients with lupus enteritis

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Conflict of interest: None

[Objective] Although Lupus enteritis (LE) is a rare but well-known complication of systemic lupus erythematosus (SLE), little knowledge about risk factors for recurrence or insufficient response to initial treatment have been reported. Thus, this study was conducted to identify poor-prognostic factors in patients with LE. [Methods] Patients diagnosed as having LE at our hospital were consecutively registered from January 2009 to November 2019. The diagnosis of LE was made according to the criteria of BILAG 2004 which is defined as either vasculitis or inflammation of small or large bowel with supportive imaging and/or biopsy findings. Poor prognosis was defined as relapse or insufficient response to initial therapy. We retrospectively compared clinical characteristics collected from medical records of patients with good vs. poor prognosis. [Results] A total of 12 patients (16 episodes) were diagnosed with LE and reviewed in this study. The mean age was 43.6 years and 11 were females. Six patients had a history of SLE (mean disease duration; 7.1 years), of which 4 had a history of LE prior to the study period. And in the remaining 6 patients, LE was the first symptom. The comorbidities were 4 lupus cystitis, 1 biopsy-proven lupus nephritis, 1 pseudo-obstruction and 1 protein-losing enteropathy. CT exams of all 16 episodes showed small bowel wall thickening. Dilatation of intestine was observed in 81.3%, ascites in 81.3%, comb sign in 80.0% and target sign in 62.5%. When comparing clinical characteristics between the groups revealed that CT findings were similar in both groups, however serum CH50 levels (15.4±7.5U/mL vs 36.0±13.8U/mL, $p=0.011$) were significantly lower in poor prognosis group. And the rate of lower dose of steroid (≦PSL0.6mg/kg/day) at induction therapy was significantly higher in poor prognosis group. [Conclusions] Lower level of CH50 and low-middle dose of steroid at initial treatment were significantly associated with poor prognosis in LE.

EP3-001

Inhibition of IL-18 Receptor Signaling Pathway Ameliorates Disease in a Murine Model of Rheumatoid Arthritis

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Conflict of interest: Yes

Objectives: IL-18 plays a prominent role in the onset and maintenance of an inflammatory response during rheumatoid arthritis. It has been reported that IL-18 expression in synovial tissue correlates with the severity of joint inflammation and levels of the pro-inflammatory cytokines. However, the role of IL-18/IL-18Rα signaling pathway in autoimmune arthritis is not known. The goal of this study was to evaluate IL-18Rα deficiency in the collagen-induced arthritis (CIA) model and understand the mechanisms for the new therapeutic target. **Methods:** Wild-type (WT) and IL-18Rα knockout (KO) mice were immunized with bovine type II collagen before the onset of arthritis induced by lipopolysaccharide injection. Disease activity was evaluated by semiquantitative scoring and histologic assessment. Serum inflammatory cytokines and anticollagen antibody levels were quantified by enzyme-linked immunosorbent assay (ELISA). In vitro inflammatory cytokine response was measured by ELISA. Expression of joint cytokines and matrix metalloproteinases-3 was determined by quantitative polymerase chain reaction. As systemic immunoresponse, splenic suppressors of cytokine signaling (SOCS) were determined by Western blot analysis. **Results:** IL-18Rα KO mice showed a lower arthritis score and a suppressed increase of histological score in bone erosion and synovitis, increased levels of proinflammatory cytokines such as IL-6, -18, TNF, and IFN-γ, the infiltration of CD4+ T cells and F4/80+ cells as pan macrophages. Conversely, mRNA expression and protein levels of the SOCS3 was also significantly increased in the IL-18Rα KO mice. **Conclusions:** We observed up-regulation of SOCS3 in IL-18Rα KO mice compared with WT mice. By up-regulation of SOCS, pro-inflammtory cytokines were decreased through IL-18/IL-18Rα signaling pathway. These results suggested that the blocking IL-18/IL-18Rα signaling pathway could be the new therapeutic agents for rheumatoid arthritis.

EP3-002

Histomorphometry of femoral head cancellous bone in patients who underwent total hip arthroplasties due to destructive rheumatoid arthritis

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Conflict of interest: Yes

[Objective] Bone histomorphometry of subchondral bone in hip joints due to rheumatoid arthritis (RA) remains unknown. The aim was to evaluate bone histomorphometry of cancellous bones of destructive femoral heads in patients with RA. [Methods] Femoral heads extracted from 26 RA patients (28 hips) were classified into two groups depending on Larsen grade on X-ray: the destructive hip (Des-) group, Larsen grade IV, 18 hips, and the neck fracture hip (Fx-) group, Larsen grade 0 or I, 10 hips. Bone histomorphometric data were analyzed in both experiments. [Results] Femoral heads showed higher trabecular thickness in the Des-group than in the Fx-group (179 vs 151 μm, p=0.02). Osteoid volume/tissue volume (OV/TV) and osteoid volume/bone volume (OV/BV) were both higher in the Des-group than in the Fx-group (OV/TV; 0.72±0.70 vs 0.27±0.32 %, p=0.028, and OV/BV; 2.96±2.85 vs 1.24±1.31 %, p=0.039). Osteoblast surface in the Des group was higher than in the Fx group (9.80±10.9 vs 0.15±0.15, p=0.0005). Osteoclast surface in the Des-group was higher than in the Fx-group (0.34±0.48 vs 0.06±0.06, p=0.0285). [Conclusions] Osteoid parameters and resorption parameters were significantly increased in the Des-group, suggesting that a high bone turnover state reflects hyper bone remodeling in response to destructive changes in the hip.

EP3-003

The reduction of S1pr1 by miR223-3p and their roles in the pathogenesis of SLE

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Conflict of interest: None

[Objective] To identify new candidate genes regulated by micro RNAs and involved in the pathogenesis of systemic lupus erythematosus (SLE), we integrated micro and messenger RNA expression profiling data in CD4+ splenic T cells derived from MRL/lpr lupus-prone mice (MRL) and C57BL6/J mice. The reduction of sphingosine-1-phosphate receptor 1 (*S1pr1*) and upregulation of miR-223-3p in the splenic T cells in MRL was identified and we investigated the role of *S1pr1* as a predicated target of *Mir223* in SLE. [Methods] *S1pr1* -3'UTR region and luciferase reporter containing retrovirus was introduced into a human umbilical vein endothelial cell (HUVEC) and evaluated by luciferase assay. miR-223-3p mimic or control mimic was transfected into EL4 mouse T cell lines by lipofection. The transfection efficacy of miR-223-3p was confirmed by quantitative PCR. We constructed and analyzed *Mir223* knockout lupus-prone B6. MRL-Faslpr mice (*Mir223*-/-Faslpr/lpr). Serum anti-dsDNA antibody levels and histopathological indexes of glomerulosclerosis were assessed at 44 weeks of age. The rate of apoptosis cells and *S1pr1* expressions in B and T cell subsets in the lymph nodes and spleen were analyzed by flow cytometry. [Results] Transfection of miR-223-3p into HUVEC significantly suppressed a luciferase-reporter containing the *S1pr1*-3'UTR. The mRNA levels of *S1pr1* was significantly decreased upon overexpression of miR-223-3p. *Mir223* deficiency tended to exacerbate emaciation, proteinuria and glomerulonephritis. The proportion of early apoptosis cells in CD4+T cells was significantly increased in *Mir223*-/-Faslpr/lpr, and the numbers of CD19+CD138-cells and CD3+CD4+S1PR1+ cells in spleen were also significantly increased. [Conclusions] *Mir223*-/-Faslpr/lpr tended to exacerbate the lupus phenotypes despite increasing *S1pr1* expression in CD4+Tcells. miR-223-3p may suppress the disease activity of SLE through reduction of early apoptosis cells.

EP3-004

Nitric Oxide causes Mitochondrial Dysfunction in Osteoarthritis

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Conflict of interest: Yes

[Introductions] We reported that Osteoarthritis (OA) caused mitochondrial dysfunction and stimulated glycolysis. In addition, a glycolysis inhibitor; 2-Deoxyglucose (2DG) rescued mitochondria from dysfunction. Our objective is to reveal OA metabolic mechanism by focusing on mitochondria. [Methods] Primary bovine and human chondrocytes were used for our eperiments. OA model was made by adding IL1β in culture medium. MMP3, MMP13 and i-NOS mRNA were measured by Real-Time PCR. i-NOS and MMP13 protein were measured by Western Blotting. Seahorse XF analyzer (Agilent) was used to measure Glycolysis and mitochondrial respiration. Nitric Oxide (NO) and Reactive Oxygen Species (ROS) was measured by each Assay Kit. Mitochondrial membranes were stained by Tetramethylrhodamine (R) and Mito Tracker Green (G). Those intensity was compared as R / G Ratio. An i-NOS inhibitor (1400W) was used to confirm relation between i-NOS and OA. [Results] IL1β increased Non-mitochondrial Oxygen Consumption (NMOC), i-NOS mRNA, and NO in culture medium. Other cytokines; TNFα, LPS showed same trend as IL1β. Furthermore, R / G Ratio was significantly decreased by IL1β. All above data were inhibited by 2DG. Although 1400W rescued from OA metabolic change, MMPs were not affected. [Discussions] We hypothesized that IL1β-elevated NMOC implies the production of Reactive Oxygen Species (ROS). Therefore, we take notice in NO which is concerned with ROS and mitochondrial dysfunction. As expected, IL1β-increased i-NOS mRNA, NO, and ROS. Interestingly,1400W reversed IL1β-induced metabolic change. However, we need to prove that NO and ROS caused cartilage degradation. For these results, NO and ROS might be a trigger for metabolic changes on Osteoarthritis. We are expecting that measurement of NO and ROS in joint fluid will be a new examine marker on OA and Rheumatoid Arthritis.

EP3-006

Comprehensive analysis of anti-centromere autoantibodies with the centromere protein library in Sjögren's syndrome, systemic sclerosis, and primary biliary cholangitis

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Conflict of interest: None

Background: Anti-centromere antibodies are detected in the serum of patients with various autoimmune diseases such as Sjögren's syndrome (SjS), systemic sclerosis (SSc), and primary biliary cholangitis (PBC), suggesting the correlation with clinical phenotypes. However, their corresponding antigens are not sufficiently clarified. **Objective**: The aim of this study is to conduct a comprehensive elucidation of centromere autoantigens across multiple autoimmune diseases. **Methods**: We created an antigen library by cloning 41 proteins belonging to human centromere region. The centromere proteins immobilized on beads were used to detect autoantibodies contained in the serum of patients with SjS, SSc, PBC, patients with two or more diseases above, or healthy volunteers. **Results**: We have revealed that most of the centromere proteins are potential autoantigens including novel targets of anti-centromere antibody. The reactivity to each centromere protein was mutually correlated that suggested common ways of epitope-spreading across disease phenotypes. Although the antigen specificity for each disease phenotype was not significant, patients with two or more diseases showed higher prevalence of antibodies against each of centromere proteins. **Conclusions**: Our study showed that SjS, SSc, PBC patients have a wide variety of autoantibodies against centromere proteins including novel autoantigens. The epitope-spreading to centromere proteins may contribute to the spread of disease phenotypes.

EP3-007

Soluble guanylate cyclase reduced the gastrointestinal fibrosis in bleomycin-induced mouse model of systemic sclerosis

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Conflict of interest: None

[Objective] Systemic scleroderma (SSc) is characterized by fibrotic changes of various organs including gastrointestinal tract. The aim of this study is to investigate whether bleomycin (BLM)-treated mice show gastrointestinal fibrosis, and find a therapeutic strategy to the lesion. [Methods] Female C57BL/6J mice were treated with BLM or normal saline by subcutaneous implantation of osmotic minipump. These mice were sacrificed on day 28 or day 42. Gastrointestinal pathologies were examined by Masson Trichrome staining. The expression of fibrosis-related genes in gastrointestinal tract were analyzed by real-time PCR, and the levels of collagen in the tissue was measured by Sircol collagen assay. To evaluate peristaltic movement, the small intestinal transport (ITR%) was calculated as [Dyeing distance×(Duodenum- Appendix)] -1 ×100 (%). We treated BLM-treated mice with soluble guanylate cyclase (sGC) orally and analyzed them on day 42. [Results] Histological examination revealed that fibrosis from lamina propria to muscularis mucosa in the esophagus was significantly increased in BLM-treated mice, suggesting that BLM induces esophageal fibrosis in C57BL/6J mice. In addition, the levels of Col3a1 and CTGF were significantly increased in BLM-treated mice. More severe fibrosis was observed in the mice sacrificed on day 42 than the mice sacrificed on day 28. The ITR% was found to be significantly lower in BLM-treated mice, suggesting that gastrointestinal peristaltic movement was reduced in BLM-treated mice. Furthermore, we demonstrated that sGC treatment significantly reduced fibrosis of esophagus and intestine in BLM-treated mice, by histological examination and Sircol collagen assay. [Conclusion] These findings suggest that BLM induces gastrointestinal fibrosis in C57BL/6J mice, and treatment with sGC improves the BLM-induced gastrointestinal lesion.

EP3-008

Distinguishing autoimmune diseases using transcriptome and splicing data

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Conflict of interest: Yes

[Background] There are many criteria for defining autoimmune diseases. However, little has been reported on the characterization of autoimmune diseases using transcriptome and splicing isoforms in various immune cell subsets. [Methods] Previously, we sorted and sequenced RNA from 30 immune cell subsets of peripheral blood mononuclear cells (PBMCs) from 418 patients: 67 with systemic sclerosis (SSc), 62 with systemic lupus erythematosus (SLE), 59 with myositis (Myo), 79 healthy volunteers (HC), and seven with other autoimmune diseases. We used STAR to align reads, HTSeq-count to calculate gene counts, and Leafcutter to estimate the intron usage ratio of splicing isoforms. We randomly separated the samples into training and test sets, trained random forest classifiers (RF) using subset-gene and subset-isoform pairs as features, and made predictions using the test set. [Results] RF differentiated SLE from HC and those with other diseases with high accuracy and precision (F1scores 0.95 and 0.89, respectively), Myo from HC and others (F1score 0.91 and 0.74), and SSc from HC and others (0.86 and 0.65). We evaluated the importance of genes and the isoform ratio to reveal disease-specific features. [Conclusions] Transcriptome and splicing data for PBMC immune cell subsets contain considerable information for distinguishing autoimmune diseases.

EP3-009

TGF beta1 suppresses RANKL-induced osteoclastogenesis via down-regulation of NFATc1 by blocking nuclear translocation of NF-kappa B in humans

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Conflict of interest: None

[Objective] Although transforming growth factor beta1 (TGFβ1) is known to be a multifunctional cytokine essential for bone remodeling in skeletal metabolism, the role of TGFβ1 on osteoclastogenesis remains controversial. Here, we investigated the effect of TGFβ1 on receptor activator of nuclear factor (NF) κ-B ligand (RANKL) induced osteoclast generation in humans. [Methods] Peripheral blood monocytes obtained from rheumatoid arthritis (RA) patients and healthy controls were cultured with macrophage colony-stimulating factor (M-CSF) and/or RANKL with or without TGFβ1. Osteoclastogenesis was identified by tartrate-resistant acid phosphatase staining and the ability of bone resorption using Osteo Plate. The expression levels of NF of activated T cells, cytoplasmic 1 (NFATc1), the master regulator of osteoclast differentiation, were examined using real-time RT-PCR and western blotting. Transcription activities of NF-κB subunit p65 and/or TGFβ1 in human NFATc1 promoter region were evaluated by luciferase assay using HEK293T cells. The p65 nuclear translocation in the early stage of osteoclastogenesis was analyzed by immunofluorescence assay. [Results] TGFβ1 suppressed RANKL-mediated osteoclast generation in a dose-dependent manner. Moreover, TGFβ1 effectively functioned during the early stage of osteoclastogenesis. Peripheral blood monocytes from RA patients had less affect for TGFβ1 than healthy controls. TGFβ1 reduced the gene and protein expressions of NFATc1. Luciferase assay indicated that human NFATc1 expression was enhanced by p65 and TGFβ1 directly suppressed p65-induced transcriptional activity. Immunofluorescence analysis demonstrated that TGFβ1 abrogated nuclear translocation of p65 induced by RANKL stimulation.

[Conclusions] TGFβ1 inhibits human RANKL-induced osteoclastogenesis via downregulation of NFATc1 by blocking nuclear translocation of p65. These findings suggest that TGFβ1 may be a potential therapeutic target for osteoclastogenesis in RA.

EP3-011

Exploration of pathomechanisms and biomarkers using principal components analysis of serum cytokines in polymyositis/dermatomyositis complicated with interstitial lung disease

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Conflict of interest: None

[Objective] To address the pathomechanism of interstitial lung disease (ILD) complicated with polymyositis (PM)/dermatomyositis (DM) using serum cytokine profile. [Methods] Consecutive forty patients with PM/DM-ILD were enrolled. Serum levels of sixteen cytokines were quantitatively measured by a cytometric bead array method. Principal components analysis (PCA) and cluster analysis, based on cytokine profiles, were performed to classify patients into subgroups. Also, we compared cytokine profiles between the survivors and dead patients. Furthermore, we examined the association of various cytokines with prognosis of ILD. [Results] Median age was 66.5 years, and twenty-eight patients were female. Three patients had PM, and others had DM. Fifteen patients had anti-MDA5 antibody positive and thirteen patients had anti-ARS antibody patients. Ten patients died due to exacerbation of ILD. The PCA data allowed classification of the cytokine profile into three groups: group 1, neutrophilic and M1-macrophage-driven cytokines; group 2, type 1 Th cell-driven and M2-macrophage-induced cytokines; and group 3, M2-macrophage-driven cytokines. Also, cluster analysis showed the presence of PM/DM-ILD patient groups with high or low levels of total cytokines. Ninety percent of patients who died of ILD were included in clusters with high cytokine levels. Serum cytokine levels of patients in group 1, especially IL-6 and CXCL10, were significantly higher in the death group than in the survival group, initially and at 2 and 4 weeks after treatment initiation. [Conclusions] These findings suggested that the activation of monocytes, macrophages and type 1 Th cells, and neutrophils play roles in the pathomechanism of PM/DM-ILD. Group 1 cytokines could be useful biomarkers for predicting prognosis of PM/DM-ILD.

EP3-012

Combined inhibition of autophagy and glutamine metabolism suppresses cell growth of RA synoviocytes and ameliorates arthritis in SKG mice

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Conflict of interest: None

[Objective] Recently immunometabolism was revealed to play an important role in the pathogenesis of rheumatoid arthritis (RA). We have previously shown that the expression of glutaminase 1 (GLS1), a key enzyme in glutaminolysis, is upregulated in fibroblast-like synoviocytes from RA patients (RA-FLS) and that GLS1 inhibition suppresses RA-FLS proliferation. Recent studies showed inhibiting glutaminolysis promoted autophagy. Here, we examined the effects of inhibiting both glutaminolysis and autophagy on RA-FLS and autoimmune arthritis in SKG mice. [Methods] GLS1 inhibitor, compound 968 (C968), was used to suppress glutaminolysis, and Chloroquine (CQ) was used to inhibit autophagy. To detect autophagy, the expression of ATG5 and LC3B was measured by real-time PCR and the production of LC3-II was analyzed by Western blotting. The formation of autophagic vacuoles was identified by immunfluorescense. Cell growth was evaluated by BrdU assay. Apoptosis was analyzed by flow cytometry staining with Annexin V-FITC and PI. C968 and CQ were administered subcutaneously to Zymosan A-injected SKG mice. [Results] C968 upregulated the expression of ATG5 and LC3B, and increased the protein level of LC3-II in RA-FLS. C968 also facilitated autophagosome formation. These results suggested that inhibition of glutaminolysis promoted autophagy in RA-FLS. The combined treatment with C968 and CQ significantly suppressed cell proliferation of RA-FLS more strongly than did C968 or CQ alone. In addition, C968 combined with CQ increased the apoptosis rate, whereas either C968 or CQ alone did not. Furthermore, combination of C968 and CQ significantly attenuated the degree of arthritis in SKG mice, while C968 or CQ monotherapy did not. [Conclusions] The GLS1 inhibitor C968 promoted autophagy in RA-FLS. C968 in combination with CQ reduced proliferation and enhanced apoptosis in RA-FLS, and ameliorated the arthritis in SKG mice. Suppressing C968-induced autophagy may be a promising therapy for arthritis.

EP3-013

Baricitinib inhibits the IL-23/STAT3 activation signal in Th17 cells from patients with systemic lupus erythematosus

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Conflict of interest: None

[Objective] Although IL-23 is a crucial for the expansion and maintenance of T helper 17 (Th17) cells, the role and cellular mechanism of action of IL-23 in the pathogenesis of systemic lupus erythematosus (SLE) remains unclear. To elucidate the molecular mechanisms underlying pathogenic Th17 cells, we investigated the modulation of epigenetic modifications and its association with SLE. [Methods] Naive $CD4^+$ T cells were cultured in Th17-polarizing conditions for 5 days and then treated with various cytokines, including IL-23. Expression of Th17 cell-related markers and phosphorylation of STATs (p-STATs) were analyzed using flow cytometry and quantitative PCR. Histone modifications were assessed using chromatin immunoprecipitation-PCR. T cell phenotypes and p-STATs were analyzed in blood samples of patients with SLE. Finally, the effects of baricitinib on memory Th17 cells were investigated in SLE patients. [Results] Stimulation with IL-23 promoted Th17 cell maturation activating p-STAT3 but not p-STAT4. IL-23-induced STAT3 directly bound the RORγT gene locus. This was accompanied by induction of the H3H4me3 permissive mark and reduction of the H3K27me3 repressive mark, leading to enhanced RORγT gene expression. IL-23-induced expansion of Th17 cells and p-STAT3 was significantly suppressed by the addition of baricitinib in a concentration-dependent manner. In memory Th17 cells from SLE patients, p-STAT3 was hypersensitized by IL-23 stimulation and inhibited by baricitinib. [Conclusions] Together, in humans, IL-23/STAT3 signaling plays a fundamental role in maturation of Th17 cells in patients with SLE through transcriptional and epigenetic modification. This could be responsible for pathogenic Th17 cell expansion, and understanding this mechanism might lead to the identification of novel therapeutic targets for SLE.

EP3-014

Apremilast attenuates the progression of bleomycin-induced skin fibrosis in mice

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Conflict of interest: None

[Objective] Apremirast, a phosphodiesterase (PDE) 4 inhibitor, has been approved for the treatment of psoriasis and other inflammatory diseases. In addition to anti-inflammatory effects of apremilast, recently its anti-fibrotic effects have been reported using such as a mouse model of pulmonary fibrosis. The aim of our present study is to investigate whether apremilast could attenuate the progression of skin fibrosis using human skin fibroblasts and a preclinical systemic sclerosis (SSc) mouse model. [Methods] Skin fibroblasts obtained from healthy individuals and patients

with diffuse cutaneous SSc were used. A mouse model of bleomycin-induced skin fibrosis was established by administering a subcutaneous injection of 100 μg bleomycin five times a week for four weeks on the back of BALB/c mice. Mice were administered either PBS or apremilast (1 mg/kg or 5 mg/kg) peritoneally five times a week for four weeks. Skin thickness, collagen content, and the number of αSMA-positive myofibroblasts and immune cells in mice skin were evaluated. [Results] Apremilast significantly suppressed the expression of *COL1A1*, *COL1A2*, *CTGF* and *ACTA2* mRNA in TGF-β1-stimulated healthy skin fibroblasts and SSc skin fibroblasts. Similarly, apremilast decreased the protein levels of type I collagen and cellular communication network factor (CCN) 2 in SSc skin fibroblasts. In normal healthy skin fibroblasts, apremilast diminished the TGF-β1-induced phosphorylation of AKT and ERK1/2, but not Smad3, suggesting that its anti-fibrotic effects was via a non-Smad signaling pathway. Apremilast significantly attenuated skin thickness and decreased the number of αSMA-positive myofibroblasts and CD3-positive cells in the skin specimen of bleomycin-treated mice. [Conclusions] The results of the present study indicate that apremilast attenuates the progression of skin fibrosis in *in vitro* and *in vivo*, suggesting that apremilast may be a candidate of drug-repositioning for the treatment of tissue fibrosis in SSc.

EP3-015

Autophagy-related molecules and structures in the synovium of rheumatoid arthritis and osteoarthritis

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Conflict of interest: None

[Objective] Synovial membrane tissues surgically obtained from rheumatoid arthritis (RA) (n=10) and osteoarthritis (OA) (n=10) joints. [Methods] i) Immunohistochemical analysis: The expression of autophagy was determined by immunofluorescence in paraffin-embedded specimens. Then the conventional immunofluorescence staining method was performed. ii) Electron microscopic observation: The ultrathin sections were stained with lead citrate and uranyl acetate then observed by transmission electron microscopy. [Results] i) Immunohistochemical analysis: Anti-WIPI-2 positive signals were shown in autophagy-cells in RA and OA synovial lining layers of anti-CD68 positive macrophages, anti-TEM-1 positive fibroblasts respectively. However, many dual positive cells were found with anti-WIPI-2 and anti-CD68 staining, when compared with those with dual anti-WIPI-2 and anti-TEM-1 staining. The mean percentage of CD68 positive signal area in the total synovium in RA was 23%±2.8%, while in OA this was 10.9%±1.2%, p=0.001 (non-paired t-test). ii) Electron microscopic observation: In the process of autophagy, the autophagy structures that formed after other cellular components had been digested in the phagosome were abundantly seen in macrophages in RA, confirming the result of immunofluorescence staining. [Conclusions] WIPI-2 signals were mainly autophagy-related. The results of immunofluorescence staining in RA and OA indicated that the phenomenon of autophagy occurred abundantly in macrophages, less in fibroblasts, because anti-CD68 positive signals were principally coinciding with Anti-WIPI-2 positive signals, while TEM-1 positive signals infrequently overlay WIPI-2 positive signals. Besides, the expression of an autophagy-related protein, WIPI-2 in RA synovial lining layers was significantly higher than in OA, probably due to prolonged and intensive inflammation. Autophagy structure observed by an electron microscope could support the immunohistochemical findings and significance.

EP3-016

LncRNA NRON upregulation associates with clinical manifestations of Sjögren's syndrome by keeping NFATc1 and PIM-1 in the cytoplasm in labial salivary glands

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Conflict of interest: None

[Objective] Sjögren's syndrome (SS) is a chronic autoimmune disease with an unclear pathogenesis. Long non-coding RNA (LncRNA) has recently drawn the attention of investigators because of its pathophysiological functions, but the expression of lncRNA in salivary glands (SGs) (a main target organ in SS) has not been histologically investigated. We hypothesized that one or more NFAT-regulation mechanisms that involve the expressions of the lncRNA non-coding repressor of NFAT (NRON) and PIM-1 exist in the SGs of SS. The aim of this study is to analyse the expressions of NRON, NFATc1, and related substances and to assess the histological findings and clinical manifestations in SS. [Methods] The expressions of NRON, NFATc1, CD4 and PIM-1, a serine/threonine kinase that participates in the localisation and phosphorylation of NFATc1, were examined by *in situ* hybridisation, immunohistochemical analysis and immunofluorescence in labial SGs (LSGs) obtained from 11 patients with SS and five control subjects. The micro-cell count method has been applied to calculate the NFATc1-positive area/infiltrating cell area in LSGs, and we compared those results to the infiltrating cell area, focus score, serum IgG, and EULAR SS Disease Activity Index (ESSDAI). [Results] The NRON expression in cell infiltration lesions of the SS patients were prominent. The NFATc1 expression was strong in infiltrating mononuclear cells (MNCs) and weak in ducts of both SS and controls. In SS, the NFATc1-positive area/infiltrating cell area was positively correlated with the infiltrating cell area, but inversely correlated with serum IgG and ESSDAI. CD4 was expressed in infiltrating MNCs, and PIM-1 colocalised with NFATc1 in the cytoplasm. [Conclusions] This is the first study revealing the intracellular localisation in LSGs of the lncRNA NRON, which is involved in the pathophysiology of SS. NFATc1 activation regulated by NRON and PIM-1 in LSGs appears to participate in SS pathophysiology and disease activity.

EP3-018

Analysis of TIGIT expression on T cells in patients with rheumatoid arthritis

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Conflict of interest: None

[Background] Rheumatoid arthritis (RA) is a systemic, inflammatory autoimmune disorder. T cells are considered to be involved in its pathogenesis. It has already reported some peripheral T cell subsets in RA patients are activated than those of healthy control. 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 in patients of RA. On the other hand, the expression on T cell subsets has not been fully elucidated. [Objective] To analyze the expression levels of TIGIT in peripheral blood T cell subsets of rheumatoid arthritis patients. [Methods] We enrolled active RA patients and healthy controls (HC). We separated CD4+T cells into 9 subsets (Th1, Th2, Th 17, naïve, central memory (CM), effector memory (EM), T follicular helper (Tfh), regulatory T (Treg), T follicular regulatory (Tfr)), and CD8+T cells into 4 subsets (naïve, CM, EM, effector memory re-expresses CD45RA (TEMRA)). We analyzed the levels of TIGIT expression of those subsets. Patient clinical information was collected from medical records. [Results] In the peripheral blood of active RA patients, the expression levels of TIGIT in effector, Tfh, Treg, and Tfr was significantly higher in CD4+ T cells compared with that of HC. There were no significant differences in the other subsets. [Conclusions] We identified cells TIGIT expression on various T cells in peripheral blood in patients with active RA.

EP3-019

Tankyrase controls bone dynamics through regulation of multiple osteoclastogenic pathways

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Conflict of interest: None

[Objective] 3BP2 is an adapter protein that is required for the activation of SRC family kinase. The previous study has reported that mutations in the 3BP2 gene cause cherubism, which is an autosomal-dominant syndrome characterized by inflammatory destructive bony lesions resulting in symmetrical deformities of the facial bones. The Wnt/β-catenin pathway, which is inhibited by AXIN, suppresses osteoclast differentiation. “Tankyrase”, a member of the poly (ADP-ribose) polymerase (PARP) family, regulates the protein levels of 3BP2 and AXIN through ADP-ribosylation. In the present study, we investigate the role of Tankyrase for osteoclastogenesis through its substrates. [Methods and Results] We show that inhibition of tankyrase enhances osteoclast differentiation in mouse primary macrophages. Additionally, the enhancing effects on osteoclastogenesis are abolished by the treatment with lithium chloride which stabilizes β-catenin, demonstrating that this effect is through suppression of the Wnt/β-catenin pathway. Tankyrase inhibition promoted SRC activation and osteoclast differentiation through an increase of the 3BP2 protein level, whereas this effect is rescued in 3BP2 knockout macrophages. [Conclusions] Our study reveals that tankyrase controls osteoclast differentiation through regulation of the Wnt/β-catenin pathway and the 3BP2 pathway.

EP3-020

A new mechanism of action exerted by anti-TNF agents: Antibody-dependent cellular phagocytosis (ADCP) against transmembrane TNF-expressing cells

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Conflict of interest: None

[Objective] Antibody-dependent cellular phagocytosis (ADCP) is an important mechanism of cell-mediated immune defense. Target cells are phagocytosed and destroyed through ADCP by macrophages that recognized antibodies by their Fc receptors. ADCP has been drawn attention to understand the action mechanism of anti-cancer monoclonal antibodies, however, no biologics for rheumatoid arthritis (RA) have been studied for ADCP. [Methods] We used ADCP reported bioassay (Promega) to detect the cellular immune response of anti-TNF agents (IFX, ADA, GLM, ETN, CZP). Transmembrane TNF (tmTNF)-expressing cells were cultured in the presence of FcgRIIa-H-expressing effector cells and anti-TNF agents. Target tmTNF-expressing cells bound by anti-TNF agents were recognized by FcgRIIa-H-expressing effector cells whose activation resulted in NFAT-induced activation of luciferase activity. [Results] All the anti-TNF agents except CZP showed ADCP dose-dependently. This result is understandable because CZP does not carry Fc portion of IgG. For the other anti-TNF agents, ADA and IFX had nearly equal abilities to induce the activation of ADCP which were stronger than GLM and ETN. [Conclusions] This is the first report demonstrating the ADCP activity of anti-TNF agents against tmTNF-expressing cells. These results will contribute to understand and explain the differential effects of anti-TNF agents in rheumatic diseases.

AUTHORS' INDEX

PL .... **Presidential Lecture**

RS .... **Representative Session**

SS .... **Special Symposium**

S .... **Symposium**

EL .... **Educational Lecture**

MTE .... **Meet the Expert**

LS .... **Luncheon Seminar**

ES .... **Evening Seminar**

W .... **Workshop**

ICW .... **International Concurrent Workshop**

P .... **Poster Session**

EP .... **English Poster Session**

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Modern Rheumatology Abstract Supplement

The 64th Annual Scientific Meeting of the

Japan College of Rheumatology

Publishing date: August 18, 2020

Publishers: Japan College of Rheumatology (JCR)
Modern Rheumatology Editorial Board

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